Reference number
1959-A

SPECIALTY GUIDELINE MANAGEMENT

ACTEMRA (tocilizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDS).
2. Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis.
3. Patients 2 years of age and older with active systemic juvenile idiopathic arthritis.
4. Adult patients with giant cell arteritis.
5. Adults and pediatric patients 2 years of age and older with chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome.

B. Compendial Uses
1. Unicentric Castleman's disease
2. Multicentric Castleman's disease
3. Oligoarticular juvenile idiopathic arthritis
4. Refractory/severe immunotherapy-related inflammatory arthritis not responding to corticosteroids and anti-inflammatory agents

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
   b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Active articular juvenile idiopathic arthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active articular juvenile idiopathic arthritis.

2. Authorization of 12 months may be granted for the treatment of active articular juvenile idiopathic arthritis when any of the following criteria are met:
   a. The member had an inadequate response to methotrexate or another non-biologic DMARD administered at an adequate dose and duration.
   b. The member has risk factors (See Appendix B) and the member also meets one of the following:

i. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
ii. High disease activity.
iii. Are judged to be at high risk for disabling joint disease.

C. Active Systemic Juvenile Idiopathic Arthritis (sJIA)

Authorization of 12 months may be granted for members who have previously received a biologic indicated for active systemic juvenile idiopathic arthritis.

Authorization of 12 months may be granted for the treatment of active sJIA when any of the following criteria is met:
1. Member has an inadequate response to at least a 1-month trial of NSAIDs.
2. Member has an inadequate response to at least a 2-week trial of corticosteroids.
3. Member has an inadequate response to at least a 3-month trial of methotrexate or leflunomide.

D. Giant Cell Arteritis

Authorization of 12 months may be granted for the treatment of giant cell arteritis when the patient's diagnosis was confirmed by the following:
1. Temporal artery biopsy or cross-sectional imaging; or
2. Acute-phase reactant elevation (i.e., high erythrocyte sedimentation rate [ESR] and/or high serum C-reactive protein [CRP])

E. Chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome

Authorization of 1 month may be granted for the treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome.

F. Unicentric Castleman's Disease

Authorization of 12 months may be granted for treatment of unicentric Castleman's disease when all of the following are met:
1. The member is HIV-negative.
2. The member is human herpesvirus-8-negative.
3. The requested drug will be used as monotherapy.
4. The requested drug is being used as second-line therapy for relapsed/refractory disease.

G. Multicentric Castleman's Disease

Authorization of 12 months may be granted for treatment of multicentric Castleman's disease when both of the following are met:
1. The requested drug will be used as monotherapy.
2. The requested drug is being used as second-line therapy for relapsed/refractory or progressive disease.

H. Immunotherapy-related Inflammatory Arthritis

Authorization of 12 months may be granted for treatment of severe/refractory immunotherapy-related inflammatory arthritis that is not responding to corticosteroids and anti-inflammatory agents.

III. CONTINUATION OF THERAPY

Chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome and immunotherapy-related inflammatory arthritis

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

All other diagnoses

Authorization of 12 months may be granted for all members (including new members) who are using Actemra for an indication outlined in section II and who achieve or maintain a positive clinical response as

evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Rinvoq, Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer tocilizumab to members with active TB infection. If there is latent disease,
TB treatment must be started before initiation of tocilizumab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Member cannot use Actemra concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDIX A: Examples of contraindications to methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

APPENDIX B: Risk factors for articular juvenile idiopathic arthritis

1. Positive rheumatoid factor
2. Positive anti-cyclic citrullinated peptide antibodies
3. Pre-existing joint damage

VI. REFERENCES

1. Actemra [package insert]. South San Francisco, CA: Genentech, Inc.; June 2019.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. https://www.nccn.org. Accessed June 14, 2019.
3. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
4. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017;*0*:1-18.

5. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res*. 2011;63(4):465-482.
6. Ringold S, Weiss PF, Beukelman T, et al. 2013 Update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis: Recommendations for the Medical Therapy of Children With Systemic Juvenile Idiopathic Arthritis and Tuberculosis Screening Among Children Receiving Biologic Medications. *Arthritis & Rheumatism.* 2013;65:2499-2512.
7. Ringold S, Angeles-Han S, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. *American College of Rheumatology.* 2019;1-18.
8. Stone, J. H., Tuckwell, K., Dimonaco, S., et al. Effiacy and safety of tocilizumab in patients with giant cell arteritis: Primary and secondary outcomes from a phase 3, randomized, double-blind, placebo-controlled trial. 2016 ACR/ARHP Annual meeting. Abstract number 911.
9. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on 21 June 2019 from: https://www.cdc.gov/tb/topic/basics/risk.htm.

Reference number(s)
1848-A

INDICATION- SPECIFIC SPECIALTY GUIDELINE MANAGEMENT

H.P. ACTHAR GEL (repository corticotropin injection)

POLICY

I. INDICATIONS

The indication-specific Specialty Guideline Management (SGM) program provides coverage for specific, but not all FDA labeled or compendial supported drug use based on plan design and the scope of the pharmacy benefit. This program provides coverage for H.P. Acthar Gel for the treatment of infantile spasms and exacerbations of multiple sclerosis if all of the approval criteria are met.

A. Infantile spasms: as monotherapy for the treatment of infantile spasms in infants and children under 2 years of age
B. Multiple Sclerosis: treatment of acute exacerbations of multiple sclerosis in adults

The use of H.P. Acthar for the treatment of all other indications listed in the FDA product labeling has not been proven to be superior to conventional therapies (e.g., corticosteroids, immunosuppressive agents) and has a significantly higher cost than the standard of care agents. Use of H. P. Acthar for these conditions is considered not medically necessary and is not a covered benefit.

A. **Rheumatic Disorders:** as adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in: psoriatic arthritis; rheumatoid arthritis, including juvenile rheumatoid arthritis, ankylosing spondylitis
B. **Collagen Diseases:** during an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus, systemic dermatomyositis (polymyositis)
C. **Dermatologic Diseases:** severe erythema multiforme, Stevens-Johnsonsyndrome
D. **Allergic States:** serum sickness
E. **Ophthalmic Diseases:** severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: keratitis, iritis, iridocyclitis, diffuse posterior uveitis and choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation
F. **Respiratory Diseases:** symptomatic sarcoidosis
G. **Edematous State:** to induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for requests for treatment of multiple sclerosis exacerbations: chart notes detailing the outcomes of the most recent trial with IV methylprednisolone, including dosage and duration of treatment.

III. CRITERIA FOR INITIAL APPROVAL

A. Infantile Spasms
Authorization of 4 weeks may be granted for treatment of infantile spasms in members who are less than 2 years of age.

B. Multiple Sclerosis
Authorization of 3 weeks may be granted for treatment of acute exacerbations of multiple sclerosis when the member has had an inadequate response to a trial of IV methylprednisolone (for the current exacerbation).

IV. CONTINUATION OF THERAPY

A. Infantile Spasms
Authorization of 4 weeks may be granted to members requesting H.P. Acthar Gel for continuation of therapy when the member has shown substantial clinical benefit from therapy.

B. Multiple sclerosis
Authorization of 3 weeks may be granted for members requesting re-authorization for H.P. Acthar therapy when all initial authorization criteria are met.

V. REFERENCES

1. H.P. Acthar Gel [package insert]. Hazelwood, MO: Mallinckrodt Pharmaceuticals, Inc.; April 2018.
2. Pellock JM, Hrachovy R, Shinnar S, et al. Infantile spasms: A U.S. consensus report. *Epilepsia*. 2010:51:2175-2189.
3. Go CY, Mackay MT, Weiss SK, et al. Evidence-based guideline update: Medical treatment of infantile spasms: Report of the Guideline Development Subcommittee of the American Academy of Neurologyand the Practice Committee of the Child Neurology Society. *Neurology.* 2012;78:1974-1980.
4. Hancock EC, Osborne JP, Edwards SW. Treatment of infantile spasms. *Cochrane Database SystRev*. 2013;6:CD001770.
5. Riikonen R. Recent advances in pharmacotherapy of infantile spasms. *CNS Drugs* 2014; 28:279-290.
6. Pavone P, et al. Infantile spasms syndrome, West Syndrome and related phenotypes: what we knowin 2013. *Brain & Development* 2014; 739-751.
7. Citterio A, La Mantia L, Ciucci G, et al. Corticosteroids or ACTH for acute exacerbations in multiple sclerosis. *Cochrane Database Syst Rev 4*:CD001331.
8. Thompson AJ, Kennard C, Swash M, et al. Relative efficacy of intravenous methylprednisolone and ACTH in the treatment of acute relapse in MS. *Neurology* 1989; 39:969-971.
9. Berkovich R, Agius MA. Mechanisms of action of ACTH in the management of relapsing forms of multiple sclerosis. *Ther Adv Neurol Disord* 2014; 7(2):83-96.
10. Frohman EM, Shah A, Eggenberger E, et al. Corticosteroids for multiple sclerosis: I. Application for treatment exacerbations. *Neurotherapeutics* 2007; 4(4): 618-626.
11. Sellebjerg F, Barnes D, Filippini G, at al. EFNS guidelines on treatment of multiple sclerosis relapses: report of an EFNS task force on treatment of multiple sclerosis. *European Journal of Neurology* 2005; 12:939-946.

Reference number(s)
2375-A

SPECIALTY GUIDELINE MANAGEMENT

ACTIMMUNE (Interferon gamma-1b)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Reducing the frequency and severity of serious infections associated with chronic granulomatous disease
2. Delaying time to disease progression in patients with severe, malignant osteopetrosis

B. Compendial Uses
1. Mycosis Fungoides/Sezary Syndrome
2. Atopic dermatitis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Granulomatous Disease
Authorization of 24 months may be granted for the treatment of chronic granulomatous disease.

B. Severe, Malignant Osteopetrosis
Authorization of 24 months may be granted for treatment of severe, malignant osteopetrosis.

C. Mycosis Fungoides/Sezary Syndrome
Authorization of 12 months may be granted for the treatment of mycosis fungoides or Sezary syndrome.

D. Atopic Dermatitis
Authorization of 12 months may be granted for the treatment of atopic dermatitis.
.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Actimmune [package insert]. Roswell, GA: Vidara Therapeutics Inc.; May 2017.
2. The NCCN Drugs & Biologics Compendium™ © 2015 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed October 18, 2017.

3. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed October 18, 2017.
4. CVS Caremark Clinical Programs Review: Focus on Dermatology; November 2010.

Reference number(s)
1641-A

SPECIALTY GUIDELINE MANAGEMENT

Adempas (riociguat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Pulmonary Arterial Hypertension (PAH)

Adempas is indicated for the treatment of adults with pulmonary arterial hypertension (PAH), (World Health Organization [WHO] Group 1), to improve exercise capacity, WHO functional class and to delay clinical worsening.

2. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

Adempas is indicated for the treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH), (WHO Group 4) after surgical treatment, or inoperable CTEPH, to improve exercise capacity and WHO functional class.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Pulmonary Arterial Hypertension (PAH)

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (Refer to Appendix)
2. PAH was confirmed by right heart catheterization with all of the following pretreatment results:
    1. mPAP ≥ 25 mmHg
    2. PCWP ≤ 15 mmHg
    3. PVR > 3 Wood units

B. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

Authorization of 12 months may be granted for treatment of CTEPH when ALL of the following criteria are met:

1. Member has CTEPH defined as WHO Group 4 class of pulmonary hypertension (Refer to Appendix)
2. Member meets either criterion (i) or criterion (ii) below:
    i. Recurrent or persistent CTEPH after pulmonary endarterectomy (PEA)
    ii. Inoperable CTEPH with diagnosis confirmed by BOTH of the following (a. and b.):
        a. Computed tomography (CT)/magnetic resonance imaging (MRI) angiography or pulmonary angiography
        b. Pretreatment right heart catheterization with all of the following results:
            - mPAP ≥ 25 mmHg
            - PCWP ≤ 15 mmHg
            - PVR > 3 Wood units

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing

benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
- 4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.2.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma
  - Germ cell tumours of the testis
  - Other tumours
- 4.2.3 Non-malignant tumours
  - Uterine leiomyoma
- 4.2.4 Arteritis without connective tissue disease
- 4.2.5 Congenital pulmonary artery stenosis
- 4.2.6 Parasites
  - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

V. REFERENCES

1. Adempas [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals, Inc.; January 2018.
2. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
3. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
4. Badesch DB, Champion HC, Gomez-Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S55-S66.
5. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol.* 2013;62:D34-S41.
6. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S78-S84.
7. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
8. Jaff MR, McMurty MS, Archer SL, et al. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the American Heart Association. *Circulation*. 2011;123(16):1788-1830.
9. Fedullo P, Kerr KM, Kim NH, Auger WR. Chronic thromboembolic pulmonary hypertension. *Am J Respir Crit Care Med*. 2011;183(12):1605-1613.
10. Jenkins D, Mayer E, Screaton N, Madani M. State-of-the-art chronic thromboembolic pulmonary hypertension diagnosis and management. *Eur Respir Rev.* 2012;21(123):32-39.
11. Klinger, JR., Elliott, CG, Levine, DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019:155(3): 565-586.
12. Galie, N., McLaughlin, VV, Rubin, LJ, Simonneau, G. An overview of the 6th World Symposium on Pulmonary Hypertension. Eur Respir J 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.

Reference number(s)
1877-A

SPECIALTY GUIDELINE MANAGEMENT
Alpha$_1$-Proteinase Inhibitors

ARALAST NP (alpha$_1$-proteinase inhibitor [human])
GLASSIA (alpha$_1$-proteinase inhibitor [human])
PROLASTIN-C (alpha$_1$-proteinase inhibitor[human])
ZEMAIRA (alpha$_1$-proteinase inhibitor [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Aralast NP
   Chronic augmentation therapy in adults with clinically evident emphysema due to severe congenital deficiency of alpha$_1$-proteinase inhibitor (alpha$_1$-antitrypsin deficiency)

2. Glassia
   Chronic augmentation and maintenance therapy in adults with clinically evident emphysema due to severe hereditary deficiency of alpha$_1$-proteinase inhibitor (alpha$_1$-antitrypsin deficiency)

3. Prolastin-C
   Chronic augmentation and maintenance therapy in adults with clinical evidence of emphysema due to severe hereditary deficiency of alpha$_1$-proteinase inhibitor (alpha$_1$-antitrypsin deficiency)

4. Zemaira
   Chronic augmentation and maintenance therapy in adults with alpha$_1$-proteinase inhibitor deficiency and clinical evidence of emphysema

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Indefinite authorization may be granted for treatment of alpha$_1$-antitrypsin (AAT) deficiency when all of the following criteria are met:

1. The member has clinically evident emphysema.
2. The member's pretreatment serum AAT level is less than 11 micromol/L (80 mg/dl byradial immunodiffusion or 50 mg/dl by nephelometry).
3. The member's pretreatment post-bronchodilation forced expiratory volume in 1 second (FEV_1) is greater than or equal to 25% and less than or equal to 80% of the predicted value.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Aralast NP [package insert]. Westlake Village, CA: Baxalta US Inc.; September 2015.
2. Glassia [package insert]. Westlake Village, CA: Baxalta US Inc.; June 2017.
3. Prolastin-C [package insert]. Research Triangle Park, NC: Grifols Therapeutics Inc.; August 2016.
4. Zemaira [package insert]. Kankakee, IL: CSL Behring LLC; September 2015.
5. American Thoracic Society/European Respiratory Society statement: standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency. Am J Respir Crit Care Med. 2003;168:818-900.
6. Marciniuk DD, Hernandez P, Balter M, et al. Alpha-1 antitrypsin deficiency targeted testing and augmentation therapy: a Canadian Thoracic Society clinical practice guideline. Can Respir J. 2012;19:109-116.

Reference number(s)
1836-A

SPECIALTY GUIDELINE MANAGEMENT

AMPYRA (dalfampridine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication: Ampyra is indicated as a treatment to improve walking in patients with multiple sclerosis. This was demonstrated by an increase in walking speed.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 30 days may be granted to members with a diagnosis of multiple sclerosis if the member has sustained walking impairment (prior to initiating therapy with Ampyra).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted to members with multiple sclerosis if the member has experienced an improvement in walking speed or other objective measure of walking ability since starting Ampyra.

IV. REFERENCES

1. Ampyra [package insert]. Ardsley, NY: Acorda Therapeutics, Inc.; September 2017.

Reference number
1616-A

SPECIALTY GUIDELINE MANAGEMENT

ARANESP (darbepoetin alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and patients not on dialysis.
2. Treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.

B. Compendial Uses

1. Symptomatic anemia in patients with myelodysplastic syndromes(MDS)
2. Anemia in patients whose religious beliefs forbid bloodtransfusions
3. Symptomatic anemia in patients with primary myelofibrosis, post-polycythemia vera myelofibrosis, and post-essential thrombocythemia myelofibrosis
4. Cancer patients who are undergoing palliative treatment

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Note: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion. All members must be assessed for iron deficiency anemia and have adequate iron stores or are receiving iron therapy before starting Aranesp. Members may not use Aranesp concomitantly with other erythropoiesis stimulating agents.

A. Anemia Due to CKD

Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

B. Anemia Due to Myelosuppressive Chemotherapy

Authorization of 12 weeks may be granted for members with nonmyeloid malignancy with pretreatment hemoglobin < 10 g/dL.

C. Anemia in MDS

Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL whose pretreatment serum EPO level is < 500 MU/ml.

D. Anemia in Members Whose Religious Beliefs Forbid Blood Transfusions

Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

E. Anemia in Primary Myelofibrosis (MF), Post-polycythemia Vera MF, and Post-Essential Thrombocythemia MF
Authorization of 12 weeks may be granted for members who meet ALL of the following criteria:
1. Pretreatment hemoglobin < 10 g/dL
2. Pretreatment serum erythropoietin level < 500 mU/mL

F. Anemia Due to Cancer
Authorization of 12 weeks may be granted for members who have cancer and are undergoing palliative treatment

III. CONTINUATION OF THERAPY

Note: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion. Members may not use Aranesp concomitantly with other erythropoiesis stimulating agents.

For all indications below: all members (including new members) requesting authorization for continuation of therapy after at least 12 weeks of ESA treatment must show a response with a rise in hemoglobin of ≥ 1 g/dL. Members who completed less than 12 weeks of ESA treatment and have not yet responded with a rise in hemoglobin of ≥ 1 g/dL may be granted authorization of up to 12 weeks to allow for sufficient time to demonstrate a response.

A. Anemia due to CKD
Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

B. Anemia Due to Myelosuppressive Chemotherapy
Authorization of 12 weeks may be granted for continuation of treatment in members with nonmyeloid malignancy when the current hemoglobin is < 12 g/dL.

C. Anemia in MDS
Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

D. Anemia in members whose religious beliefs forbid blood transfusions
Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

E. Anemia in Primary Myelofibrosis, Post-polycythemia Vera Myelofibrosis, and Post-Essential Thrombocythemia Myelofibrosis
Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

F. Anemia Due to Cancer
Authorization of 12 weeks may be granted for members who have cancer and are undergoing palliative treatment

IV. REFERENCES

1. Aranesp [package insert]. Thousand Oaks, CA: Amgen Inc.; January 2018.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed September 18, 2018.
3. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed September 18, 2018.
4. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney Int. 2012; Suppl 2:279-335.
5. National Kidney Foundation. KDOQI Clinical Practice Guideline and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease: 2007 Update of Hemoglobin Target. http://www2.kidney.org/professionals/KDOQI/guidelines_anemiaUP/. Accessed September 18, 2018.
6. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Cancer- and Chemotherapy-Induced Anemia. Version 3.2018. http://www.nccn.org/professionals/physician_gls/pdf/anemia.pdf. Accessed September 18, 2018.
7. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes. Version 1.2019. http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed September 18, 2018.
8. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 1.2019. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed September 18,2018.
9. Gabrilove J, Paquette R, Lyons R, Mushtaq C, Sekeres M, et al. Phase 2, single-arm trial to evaluate the effectiveness of darbepoetin alfa for correcting anaemia in patients with myelodysplastic syndromes. Br J Haematol. 2008 Aug; 142(3): 379–393.

Reference number
1800-A

SPECIALTY GUIDELINE MANAGEMENT

ARCALYST (rilonacept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Treatment of Cryopyrin Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 years of age and older.

B. Compendial Uses
Prevention of gout flares in patients initiating or continuing urate-lowering therapy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Cryopyrin-Associated Periodic Syndrome (CAPS)
Authorization of 24 months may be granted for treatment of CAPS, including FCAS and MWS.

B. Prevention of Gout Flares in Members Initiating or Continuing Urate-Lowering Therapy
Authorization of 4 months may be granted when ALL of the following criteria are met:
1. Member had two or more gout flares within the previous 12 months
2. Member had an inadequate response, intolerance or contraindication to maximum tolerated doses of non-steroidal anti-inflammatory drugs and colchicine
3. Member will receive Arcalyst concurrently with urate-lowering therapy (i.e., allopurinol orfebuxostat)

III. CONTINUATION OF THERAPY

A. Cryopyrin-Associated Periodic Syndrome (CAPS)
All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

B. Prevention of Gout Flares in Members Initiating or Continuing Urate-LoweringTherapy
Authorization of 4 months may be granted to members who meet ALL of the following criteria:
1. Member has achieved or maintained a clinical benefit (i.e., a fewer number of gout attacks or fewer flare days) compared to baseline
2. Member will receive Arcalyst concurrently with urate-lowering therapy (i.e., allopurinol orfebuxostat)

IV. REFERENCES

1. Arcalyst [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; September 2016.
2. DRUGDEX® System (electronic version). Micromedex Truven Health Analytics. Available with subscription. URL: www.micromedexsolutions.com. Accessed January 01, 2018.
3. Mitha E, Schumacher HR, Fouche L, et al. Rilonacept for gout flare prevention during initiation of uric acid-lowering therapy: results from the PRESURGE-2 international, phase 3, randomized, placebo-controlled trial. *Rheumatology (Oxford)*. 2013; 52(7):1285-1292. URL: http://rheumatology.oxfordjournals.org/content/52/7/1285.long.
4. Schumacher HR Jr, Evans RR, Saag KG, et al: Rilonacept (interleukin-1 trap) for prevention of gout flares during initiation of uric acid-lowering therapy: results from a phase III randomized, double-blind, placebo-controlled, confirmatory efficacy study. *Arthritis Care Res (Hoboken).* 2012; 64(10):1462-1470.
5. Clinical Consult. CVS/caremark Clinical Programs Review. Focus on Rheumatology Clinical Programs. July 2015.

Reference number(s)
1837-A

SPECIALTY GUIDELINE MANAGEMENT

AVONEX (interferon beta-1a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication: Avonex is indicated for the treatment of patients with relapsing forms of multiple sclerosis to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations. Patients with multiple sclerosis in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis.

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 24 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis.

B. First clinical episode of multiple sclerosis
Authorization of 24 months may be granted to members for the treatment of a first clinical episode of multiple sclerosis.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Avonex [package insert]. Cambridge, MA: Biogen Inc.; March 2016.

Reference number
2280-A

SPECIALTY GUIDELINE MANAGEMENT

VIDAZA (azacitidine)
azacitidine (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Myelodysplastic syndromes (MDS): Vidaza is indicated for treatment of patients with the following French-American-British (FAB) myelodysplastic syndrome subtypes: refractory anemia (RA) or refractory anemia with ringed sideroblasts (if accompanied by neutropenia or thrombocytopenia or requiring transfusions), refractory anemia with excess blasts (RAEB), refractory anemia with excess blasts in transformation (RAEB-T), and chronic myelomonocytic leukemia (CMMoL).

B. Compendial Uses
1. Acute myeloid leukemia (AML)
2. Accelerated phase or blast phase myelofibrosis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Myelodysplastic Syndromes (MDS)
Authorization of 12 months may be granted for the treatment of MDS.

B. Acute Myeloid Leukemia (AML)
Authorization of 12 months may be granted for the treatment of AML.

C. Accelerated Phase or Blast Phase Myelofibrosis
Authorization of 12 months may be granted for the treatment of accelerated phase or blast phase myelofibrosis.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Vidaza [package insert]. Summit, NJ: Celgene Corporation; July 2018.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed August 07, 2018.

Reference number(s)
1602-A

SPECIALTY GUIDELINE MANAGEMENT

BERINERT (C1 esterase inhibitor [human])

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Treatment of acute abdominal, facial, or laryngeal attacks of hereditary angioedema (HAE) in adult and pediatric patients

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. C4 levels and C1 inhibitor functional and antigenic protein levels
B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
C. Chart notes confirming family history of angioedema, if applicable

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of hereditary angioedema attacks when the medication will not be used with Firazyr, Kalbitor, or Ruconest and either of the following criteria is met:

A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
   1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
   2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)

B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

A. Member meets the criteria for initial approval.
B. Member has experienced reduction in severity and/or duration of attacks when they use Berinert to treat an acute attack.

V. REFERENCES

1. Berinert [package insert]. Kankakee, IL: CSL Behring LLC; September 2017.

2. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
3. Cicardi M, Bork K, Caballero T, et al. Hereditary Angioedema International Working Group. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy.* 2012;67:147-157.
4. Kreuz W, Martinez-Saguer I, Aygoren-Pursun E. C1-inhibitor concentrate for individual replacement therapy in patients with severe hereditary angioedema refractory to danazol prophylaxis. *Transfusion.* 2009;49:1987-1995.
5. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol: In Practice*. 2013; 1(5): 458-467.
6. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. *Allergy Asthma Proc*. 2012; 33(6):S145-S156.
7. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Allergy*. 2018;00:1-22.
8. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109:395-202.
9. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014;69: 602-616.
10. Bowen T. Hereditary angioedema: beyond international consensus – circa December 2010 – The Canadian Society of Allergy and Clinical Immunology Dr. David McCourtie Lecture. *Allergy Asthma Clin Immunol*. 2011;7(1):1.
11. Bernstein J. Update on angioedema: Evaluation, diagnosis, and treatment. *Allergy and Asthma Proceedings.* 2011;32(6):408-412.
12. Longhurst H, Cicardi M. Hereditary angio-edema. *Lancet.* 2012;379:474-481.
13. Farkas H, Martinez-Saguer I, Bork K, et al. International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency. *Allergy.* 2017;72(2):300-313.
14. Henao MP, Kraschnewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management.* 2016; 12: 701-711.

Reference number(s)
1602-A

SPECIALTY GUIDELINE MANAGEMENT

Targretin (bexarotene) capsules
bexarotene capsules (generic)
Targretin (bexarotene) gel 1%

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Targretin/bexarotene capsules are indicated for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma (CTCL) in patients who are refractoryto at least one prior systemic therapy.
2. Targretin gel is indicated for the topical treatment of cutaneous lesions in patients with CTCL (Stage IA and IB) who have refractory or persistent disease after other therapies or who have not tolerated other therapies.

B. Compendial Uses

1. Targretin/bexarotene capsules
   i. Mycosis fungoides (MF)
   ii. Sezary syndrome (SS)
   iii. Primary cutaneous CD30+ T-cell lymphoproliferative disorders:
      a. Primary cutaneous anaplastic large cell lymphoma (ALCL)
      b. Lymphomatoid papulosis (LyP)
2. Targretin gel
   i. Mycosis fungoides (MF)
   ii. Chronic or smoldering adult T-cell leukemia/lymphoma (ATLL)
   iii. Primary cutaneous B-cell lymphoma:
      a. Primary cutaneous marginal zone lymphoma
      b. Primary cutaneous follicle center lymphoma

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Targretin/bexarotene Capsules

1. Mycosis Fungoides (MF)/Sézary Syndrome (SS)

Authorization of 12 months may be granted for the treatment of MF or SS.

2. Primary Cutaneous Anaplastic Large Cell Lymphoma (ALCL)/Lymphomatoid Papulosis (LyP)

Authorization of 12 months may be granted for the treatment of primary cutaneous ALCL or LyP.

B. Targretin Gel

1. **Cutaneous T-cell Lymphoma (CTCL): Mycosis Fungoides (MF)** (excluding Sézarysyndrome)

Authorization of 12 months may be granted for the treatment of MF.

2. **Adult T-cell Leukemia/Lymphoma (ATLL)**
   Authorization of 12 months may be granted for the treatment of chronic or smoldering ATLL.

3. **Primary Cutaneous B-cell Lymphoma**
   Authorization of 12 months may be granted for the treatment of primary cutaneous marginal zone lymphoma or primary cutaneous follicle center lymphoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES

1. Targretin capsules [package insert]. St. Petersburg, FL: Catalent Pharma Solutions LLC; July 2015.
2. Targretin gel [package insert]. San Antonio, TX: DPT Laboratories, Ltd.; October 2016.
3. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed January 08, 2018.

Reference number
1783-A

SPECIALTY GUIDELINE MANAGEMENT

CAPRELSA (vandetanib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Treatment of symptomatic or progressive medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease

Use Caprelsa in patients with indolent, asymptomatic or slowly progressing disease only after careful consideration of the treatment related risks of Caprelsa.

B. Compendial Uses
1. Follicular, Hurthle cell, and papillary thyroid carcinoma
2. Non-small cell lung cancer with RET gene rearrangements

All other indications are considered experimental/investigational and are not a covered benefit.

I. DOCUMENTATION

Submission of RET gene rearrangement documentation is necessary to initiate the prior authorization review for the indication of non-small cell lung cancer.

II. CRITERIA FOR INITIAL APPROVAL

A. Thyroid carcinoma (follicular, Hürthle cell, papillary)
Authorization of 12 months may be granted for the treatment of radioiodine refractory follicular, Hürthle cell, or papillary thyroid carcinoma.

B. Medullary thyroid carcinoma
Authorization of 12 months may be granted for the treatment of medullary thyroid carcinoma.

C. Non-small cell lung cancer (NSCLC)
Authorization of 12 months may be granted for the treatment of NSCLC with RET gene rearrangements.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

IV. REFERENCES

Reference number
1783-A

1. Caprelsa [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals; October 2018.
2. The NCCN Drugs & Biologics Compendium™ © 2018 National Comprehensive Cancer Network, Inc. https://www.nccn.org Accessed October 24, 2018.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology® Thyroid Carcinoma (Version 1.2018). https://www.nccn.org Accessed October 24, 2018.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology® Non-Small Cell Lung Cancer (Version 1.2019). https://www.nccn.org. Accessed October 24, 2018.

Reference number(s)
1880-A

SPECIALTY GUIDELINE MANAGEMENT

CAYSTON (aztreonam for inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Cayston is indicated to improve respiratory symptoms in cystic fibrosis patients with *Pseudomonas aeruginosa.*

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis
Authorization of 24 months may be granted for members with cystic fibrosis when Pseudomonas aeruginosa is present in airway cultures OR the member has a history of Pseudomonas aeruginosa infection or colonization in the airways.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Cayston [package insert]. Foster City, CA: Gilead Sciences, Inc.; May 2014.
2. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med.* 2013; 187:680-689.

Reference number(s)
2005-A

SPECIALTY GUIDELINE MANAGEMENT

CIMZIA (certolizumab pegol)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Moderately to severely active rheumatoid arthritis (RA)
2. Active psoriatic arthritis (PsA)
3. Active ankylosing spondylitis (AS)
4. Moderately to severely active Crohn's disease (CD)
5. Moderate to severe plaque psoriasis (PsO)

B. Compendial Uses
Axial spondyloarthritis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
1. Authorization of 24 months may be granted for members who have previously received Cimzia or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
   b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Active psoriatic arthritis (PsA)
Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

C. Active ankylosing spondylitis (AS) and axial spondyloarthritis
1. Authorization of 24 months may be granted for members who have previously received Cimzia or any other biologic DMARD indicated for active ankylosing spondylitis.

2. Authorization of 24 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).

b. Member has an intolerance or contraindication to two or more NSAIDs.

D. Moderately to severely active Crohn's disease (CD)

1. Authorization of 24 months may be granted for members who have previously received Cimzia or any other biologic indicated for the treatment of Crohn's disease.

2. Authorization of 24 months may be granted for treatment of moderately to severely active CD when the member has an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix B).

E. Moderate to severe plaque psoriasis (PsO)

1. Authorization of 24 months may be granted for members who have previously received Cimzia, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe chronic plaque psoriasis.

2. Authorization of 24 months may be granted for treatment of moderate to severe chronic plaque psoriasis when all of the following criteria are met:
   a. At least 5% of body surface area (BSA) is affected OR crucial bodyareas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   b. Member meets any of the following criteria:
      i. Member has had an inadequate response or intolerance to either phototherapy (e.g.,UVB, PUVA) or a pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      ii. Member has a clinical reason to avoid pharmacologic treatment withmethotrexate, cyclosporine or acitretin (see Appendix C).
      iii. Member has severe psoriasis that warrants a biologic DMARD as first-linetherapy.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Cimzia as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Cimzia or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity

7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
   a. Oral budesonide, oral mesalamine
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternatives: oral budesonide, methotrexate intramuscularly (IM)
3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenously (IV)
   b. Alternatives: methotrexate IM
4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM
5. Perianal and fistulizing disease – induction of remission:
   a. Metronidazole ± ciprofloxacin
6. Perianal and fistulizing disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM

Appendix C: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy (male or female)
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Cimzia [package insert]. Smyrna, GA: UCB, Inc.; May 2018.
2. van der Heijde D, Ramiro S, Landewe R, et al. 2016 Update of the international ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis.* 2017;0:1-14.
3. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017*;0*:1-18.
4. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guidelinefor the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
5. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59(6):762-784.

6. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis andpsoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol.* 2011;65(1):137-174.
7. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies; 2015 update. *Ann Rheum Dis*. 2016;75(3):499-510.
8. Gladman DD, Antoni C, P Mease, et al. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis.* 2005;64(Suppl II):ii14–ii17.
9. Peluso R, Lervolino S, Vitiello M, et al. Extra-articular manifestations in psoriatic arthritis patients. [Published online ahead of print May 8, 2014]. *Clin Rheumatol*. 2014.
10. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULARrecommendations for the management of ankylosing spondylitis. *Ann Rheum Dis.* 2011;70:896–904.
11. Landewe R, Braun J, Deodhar A, et al. Efficacy of certolizumab pegol on signs and symptoms of axial spondyloarthritis including ankylosing spondylitis: 24-week results of a double-blind randomised placebo-controlled Phase 3 study. *Ann Rheum Dis.* 2014;73(1):39-47.
12. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Associationof America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis*. Arthritis Rheumatol.* 2015: 10.1002/art.39298. [Epub ahead of print].
13. Talley NJ, Abreu MT, Achkar J, et al. An evidence-based systematic review on medical therapies for inflammatory bowel disease. *Am J Gastroenterol*. 2011;106(Suppl 1):S2-S25.

Reference number(s)
1604-A

SPECIALTY GUIDELINE MANAGEMENT

CINRYZE (C1 esterase inhibitor [human])

POLICY

VI. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Routine prophylaxis against angioedema attacks in adults, adolescents and pediatric patients (6 years of age or older) with hereditary angioedema (HAE)

All other indications are considered experimental/investigational and are not a covered benefit.

VII. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. C4 levels and C1 inhibitor functional and antigenic protein levels
B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
C. Chart notes confirming family history of angioedema, if applicable

VIII. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for prevention of hereditary angioedema attacks when Cinryze will not be used in combination with Haegarda or Takhzyro and either of the following criteria is met:

A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing.
   1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test; *or*
   2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)

B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

IX. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

A. Member meets the criteria for initial approval.
B. Member has experienced reduction in frequency, severity, and/or duration of attacks since starting treatment.

X. REFERENCES

1. Cinryze [package insert]. Lexington, MA: ViroPharma Biologics; June 2018.
2. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Allergy*. 2018;00:1-22.

3. Cicardi M, Bork K, Caballero T, et al. Hereditary Angioedema International Working Group. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy.* 2012;67:147-157.
4. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
5. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol: In Practice*. 2013; 1(5): 458-467.
6. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. *Allergy Asthma Proc*. 2012; 33(6):S145-S156.
7. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109:395-202.
8. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014;69: 602-616.
9. Bowen T. Hereditary angioedema: beyond international consensus – circa December 2010 – The Canadian Society of Allergy and Clinical Immunology Dr. David McCourtie Lecture. *Allergy Asthma Clin Immunol*. 2011;7(1):1.
10. Bernstein J. Update on angioedema: Evaluation, diagnosis, and treatment. *Allergy and Asthma Proceedings.* 2011;32(6):408-412.
11. Longhurst H, Cicardi M. Hereditary angio-edema. *Lancet.* 2012;379:474-481.
12. Farkas H, Martinez-Saguer I, Bork K, et al. International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency. *Allergy.* 2017;72(2):300-313.
13. Henao MP, Kraschnewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management.* 2016; 12: 701-711.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS **COMPOUNDED DRUG PRODUCTS**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

COVERAGE CRITERIA

Compounded drug products will be covered with prior authorization when the following criteria are met:

- The request is for any of the following: intraveneous (IV) injection or infusion, anti-infective for injectable use (examples of anti-infectives may include antibacterials, antivirals, antifungals), total parenteral nutrition (TPN), leuprolide acetate for infertility in a patient unable to utilize the FDA-approved commercially available product (1mg per 0.2mL kit), pyrimethamine, hydroxyprogesterone

OR

- Each of the active ingredients in the compound are FDA-approved drugs
- Each of the active ingredients in the compound are FDA-approved for the indication for which the compound is being prescribed
- The compound route of administration (ROA) is the same as the FDA-approved route of administration for each active ingredient
- The dosage or concentration of each active ingredient in the compound is equal to or below the FDA-approved dosage or concentration
- The request is not for a topical compound or a topical compound kit for use on skin (e.g., cream, gel, lotion, ointment)
- The compound is not intended for anti-aging or cosmetic use, or is not a compound kit, or does not contain any of the following ingredients: bulk powder (examples may include cidofovir, estriol, fentanyl, fluticasone, heparin, hydromorphone, idebenone, ketamine, mometasone, oxycodone, phentolamine), or dietary supplements (examples may include coenzyme Q10, pyridoxal, resveratrol, tetrahydrobiopterin)
- The request is not for a hormone therapy compound for menopause or for androgen decline due to aging, (e.g., testosterone, estrogen, progestin, bioidentical hormone)
- Coverage is provided for additional fills of the compounded drug if patient needs more than 1 fill per month (necessity may include continuation of antibiotic therapy, stability is less than a month, dose adjustment)
  AND
- There is a current supply shortage of the commercially manufactured product
  OR
- The patient has a medical need for a dosage form or dosage strength that is not available commercially or manufactured
  OR
- The patient had an intolerance or contraindication to the commercially manufactured product (examples may include allergen or adverse effects due to inactive ingredients)
  OR
- The commercial product has been discontinued by the pharmaceutical manufacturer for reasons other than lack of safety or effectiveness

REFERENCES

1. 21 USC 353a: Pharmacy compounding From Title 21-FOOD AND DRUGS CHAPTER 9-FEDERAL FOOD, DRUG, AND COSMETIC ACT SUBCHAPTER V-DRUGS AND DEVICES Part A-Drugs and Devices. Available at: http://uscode.house.gov/view.xhtml?req=%28compound+drugs%29&f=treesort&fq=true&num=15&hl=true&edition=prelim&granuleId=USC-prelim-title21-section353a. Accessed February 2018.
2. Title 21 – Food and Drugs. 353a. Pharmacy compounding. Available at: https://www.gpo.gov/fdsys/pkg/USCODE-2014-title21/pdf/USCODE-2014-title21-chap9-subchapV-partA-sec353a.pdf. Accessed February 2018.
3. Compounding Quality Act. U.S. Food and Drug Administration. Pharmacy Compounding. Available at: http://www.gpo.gov/fdsys/pkg/BILLS-113hr3204enr/pdf/BILLS-113hr3204enr.pdf. Accessed February 2018.
4. Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM469119.pdf. Accessed February 2018.
5. Human Drug Compounding Available at: https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm. Accessed February 2018.
6. Compounding and the FDA: Questions and Answers. Available at: http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm339764.htm. Accessed February 2018.
7. USP Compounding Standards & Resources. Available at: http://www.usp.org/usp-healthcare-professionals/compounding. Accessed February 2018.
8. USP-NF Chapters on Pharmacy Compounding, 795. Available at: http://www.usp.org/usp-nf/official-text/revision-bulletins/pharmaceutical-compounding-nonsterile-preparations. Accessed February 2018.
9. Is it Really FDA Approved? Available at: https://www.fda.gov/forconsumers/consumerupdates/ucm047470.htm. Accessed February 2018.
10. The Special Risks of Pharmacy Compounding. Available at: https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm107836.htm. Accessed February2018.
11. Bio-Identicals: Sorting Myths from Facts. Available at: http://www.fda.gov/forconsumers/consumerupdates/ucm049311.htm. Accessed February 2018.
12. FDA Drug Safety Communication: FDA cautions about using testosterone products for low testosterone due to aging; requires labeling change to inform of possible increased risk of heart attack and stroke with use. Available at: http://www.fda.gov/downloads/Drugs/DrugSafety/UCM436270.pdf. Accessed February 2018.
13. Menopause. Medicines to Help You. Available at: https://www.fda.gov/downloads/ForConsumers/ByAudience/ForWomen/UCM383348.pdf. Accessed February2018.
14. Drug Information (Drugs@FDA). Available at: http://www.fda.gov/Drugs/default.htm. Accessed February 2018.
15. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. February 2018.
16. Micromedex Solutions [database online]. Greenwood Village, CO: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. February 2018.
17. Drug Nomenclature Monographs. Route of Administration. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/DataStandardsManualmonographs/ucm071650.htm. Accessed February 2018.

Reference number
2017-A

SPECIALTY GUIDELINE MANAGEMENT

COSENTYX (secukinumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Moderate to severe plaque psoriasis (PsO)
2. Active psoriatic arthritis (PsA)
3. Active ankylosing spondylitis (AS)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderate to severe plaque psoriasis (PsO)

1. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Cosentyx, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.

2. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis in members who are 18 years of age or older when all of the following criteria are met:
   a. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet,face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   b. Member meets any of the following criteria:
      i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      ii. Member has a clinical reason to avoid pharmacologic treatment withmethotrexate, cyclosporine or acitretin (see Appendix A).
      iii. Member has severe psoriasis that warrants a biologic DMARD as first-linetherapy.

B. Active psoriatic arthritis (PsA)

Authorization of 24 months may be granted for treatment of active psoriatic arthritis in members who are 18 years of age or older.

C. Active ankylosing spondylitis (AS)

1. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Cosentyx or any other biologic DMARD indicated for active ankylosing spondylitis.

2. Authorization of 24 months may be granted for treatment of active ankylosing spondylitis in members 18 years of age or older when any of the following criteria is met:

a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
b. Member has an intolerance or contraindication to two or more NSAIDs.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Cosentyx as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Cosentyx or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy (male or female)
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Cosentyx [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2018.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
3. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis*. 2016;75(3):499-510.
4. McInnes IB, Mease PJ, Kirkham B, et al. Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2015;386(9999):1137-46.
5. Braun J, van den Berg R, Baraliakos, X et al. 2010 update of the ASAS/EULARrecommendations for the management of ankylosing spondylitis. *Ann Rheum Dis.* 2011;70:896–904.
6. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Associationof America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol.* 2015: 10.1002/art.39298. [Epub ahead of print].

7. Baeten D, Sieper J, Braun J, et al. Secukinumab, an Interleukin-17A Inhibitor, in Ankylosing Spondylitis. *N Engl J Med*. 2015;373(26):2534-48.

Reference number(s)
2136-A, 2675-A

SPECIALTY GUIDELINE MANAGEMENT

DAKLINZA (daclatasvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Daklinza is indicated for use with sofosbuvir, with or without ribavirin, for the treatment of patients with chronic hepatitis C virus (HCV) genotype 1 or genotype 3 infection.

Limitations of Use:
Sustained virologic response (SVR12) rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving Daklinza in combination with sofosbuvir for 12 weeks.

B. Compendial Uses
Chronic hepatitis C genotype 2, 4, 5 or 6 infection

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with Sovaldi

1. Genotype 1 infection

a. Authorization of up to 12 weeks total may be granted for treatment-naive members without cirrhosis or with compensated cirrhosis.
b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV).

2. Genotype 2 infection

a. Authorization of up to 12 weeks total may be granted for treatment-naive members without cirrhosis.
b. Authorization of up to 24 weeks total may be granted for treatment-naïve members with compensated cirrhosis.
c. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV.
d. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV.

3. Genotype 3 infection

a. Authorization of up to 12 weeks total may be granted for treatment-naive members without cirrhosis.
b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV.
c. Authorization of up to 24 weeks total may be granted for treatment-naive members with compensated cirrhosis.

4. **Decompensated cirrhosis (Child Turcotte Pugh [CTP] class B or C)**
   Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 2, 3 or 4 infection and documented anemia (baseline hemoglobin [Hgb] below 10 g/dL) or RBV ineligibility (see Section III).

B. Chronic hepatitis C virus, in combination with Sovaldi and Ribavirin

1. **Genotype 3 infection**
   a. Authorization of up to 24 weeks total may be granted for treatment-naive members with compensated cirrhosis.
   b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV and have the Y93H substitution associated with daclatasvir resistance.

2. **Decompensated cirrhosis (CTP class B or C)**
   Authorization of up to 12 weeks total may be granted for members with HCV genotype 1, 2, 3 or 4 infection.

3. **Recurrent HCV infection post liver transplantation**
   a. Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 2, or 3 infection post liver transplantation.
   b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have recurrent HCV genotype 4, 5 or 6 infection post liver transplantation.

4. **Kidney transplant recipients**
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 2, 3, 5, or 6 infection.

C. HCV and HIV coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

III. APPENDIX: RIBAVIRIN INELIGIBILITY

RBV ineligibility is defined as one or more of the below:

- Intolerance to RBV
- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

IV. REFERENCES

1. Daklinza [package insert]. Princeton, NJ: Bristol Myers Squibb Company; February 2017.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Last changes made September 21, 2017. Accessed September 22, 2017.

Reference number(s)
2136-A, 2675-A

SPECIALTY GUIDELINE MANAGEMENT

DAKLINZA (daclatasvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Daklinza is indicated for use with sofosbuvir, with or without ribavirin, for the treatment of patients with chronic hepatitis C virus (HCV) genotype 1 or genotype 3 infection.

Limitations of Use:
Sustained virologic response (SVR12) rates are reduced in HCV genotype 3-infected patients with cirrhosis receiving Daklinza in combination with sofosbuvir for 12 weeks.

B. Compendial Uses
Chronic hepatitis C genotype 2, 4, 5 or 6 infection

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with Sovaldi

1. Genotype 1 infection
a. Authorization of up to 12 weeks total may be granted for treatment-naive members without cirrhosis or with compensated cirrhosis.
b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV).

2. Genotype 2 infection
a. Authorization of up to 12 weeks total may be granted for treatment-naive members without cirrhosis.
b. Authorization of up to 24 weeks total may be granted for treatment-naïve members with compensated cirrhosis.
c. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV.
d. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV.

3. Genotype 3 infection
a. Authorization of up to 12 weeks total may be granted for treatment-naive members without cirrhosis.
b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV.
c. Authorization of up to 24 weeks total may be granted for treatment-naive members with compensated cirrhosis.

4. Decompensated cirrhosis (Child Turcotte Pugh [CTP] class B or C)
Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 2, 3 or 4 infection and documented anemia (baseline hemoglobin [Hgb] below 10 g/dL) or RBV ineligibility (see Section III).

B. Chronic hepatitis C virus, in combination with Sovaldi and Ribavirin

1. Genotype 3 infection
a. Authorization of up to 24 weeks total may be granted for treatment-naive members with compensated cirrhosis.
b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with PEG-IFN and RBV and have the Y93H substitution associated with daclatasvir resistance.

2. Decompensated cirrhosis (CTP class B or C)
Authorization of up to 12 weeks total may be granted for members with HCV genotype 1, 2, 3 or 4 infection.

3. Recurrent HCV infection post liver transplantation
a. Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 2, or 3 infection post liver transplantation.
b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have recurrent HCV genotype 4, 5 or 6 infection post liver transplantation.

4. Kidney transplant recipients
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 2, 3, 5, or 6 infection.

C. HCV and HIV coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX: RIBAVIRIN INELIGIBILITY

RBV ineligibility is defined as one or more of the below:
- Intolerance to RBV
- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

V. REFERENCES

1. Daklinza [package insert]. Princeton, NJ: Bristol Myers Squibb Company; November 2017.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Last changes made May 24, 2018. Accessed July 16, 2018.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

DALIRESP
(roflumilast)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Daliresp is indicated as a treatment to reduce the risk of COPD exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations.

Limitations of Use

Daliresp is not a bronchodilator and is not indicated for the relief of acute bronchospasm.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed to reduce the risk of chronic obstructive pulmonary disease (COPD) exacerbations in a patient with severe COPD associated with chronic bronchitis and a history of exacerbations

REFERENCES

1. Daliresp [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; August 2017.
2. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed November 2017.
3. Micromedex Solutions [database online]. Greenwood Village, CO: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed November 2017.

Reference number
2288-A

SPECIALTY GUIDELINE MANAGEMENT

DACOGEN (decitabine)
decitabine (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Myelodysplastic syndromes (MDS): Dacogen (decitabine) is indicated for treatment of patients with myelodysplastic syndromes (MDS) including previously treated and untreated, *de novo* and secondary MDS of all French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups.

B. Compendial Uses

1. Chronic myeloid leukemia (CML)
2. Acute myeloid leukemia (AML)
3. Accelerated phase or blast phase myelofibrosis
4. Lower risk myelodysplastic syndromes (MDS) associated with thrombocytopenia, neutropenia, symptomatic anemia, or increased marrow blasts

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Myelodysplastic Syndromes (MDS)

Authorization of 12 months may be granted for the treatment of MDS.

B. Chronic myeloid leukemia (CML)

Authorization of 12 months may be granted for the treatment of CML.

C. Acute Myeloid Leukemia (AML)

Authorization of 12 months may be granted for the treatment of AML.

D. Accelerated Phase or Blast Phase Myelofibrosis

Authorization of 12 months may be granted for the treatment of accelerated phase or blast phase myelofibrosis.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an

indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Dacogen [package insert]. Rockville, MD: Otsuka America Pharmaceutical, Inc.; December 2018.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed July 10, 2019.

Reference number(s)
1873-A

SPECIALTY GUIDELINE MANAGEMENT

TIKOSYN (dofetilide)
dofetilide (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Maintenance of normal sinus rhythm (delay in time to recurrence of atrial flutter/atrial fibrillation [AF/AFI]) in patients with AF/AFl of greater than one week duration who have beenconverted to normal sinus rhythm
   2. Conversion of AF/AFI to normal sinus rhythm

B. Compendial Uses
   1. Supraventricular tachycardia
   2. Ventricular tachyarrhythmia

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

1. Atrial flutter/Atrial fibrillation
Authorization of 24 months may be granted for the maintenance of, or conversion to, normal sinus rhythm after atrial flutter or atrial fibrillation.

2. Supraventricular tachycardia
Authorization of 24 months may be granted for the treatment and prevention of supraventricular tachycardia.

3. Ventricular tachyarrhythmia
Authorization of 24 months may be granted for the treatment and prevention of ventricular tachyarrhythmia.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES

1. Tikosyn [package insert]. New York, NY: Pfizer Inc.; July 2016.
2. Dofetilide [package insert]. Greenville, NC: Mayne Pharma; March 2016.

3. Micromedex Solutions [database online]. Cambridge, MA: IBM Watson Health. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed March 28, 2018.
4. Page RL, Joglar JA, Caldwell MA, et al. 2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia. A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2016;67(13).

Reference number(s)
1966-A, 2084-A

SPECIALTY GUIDELINE MANAGEMENT

ELIGARD (leuprolide acetate)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Palliative treatment of advanced prostate cancer

B. Compendial Uses
1. Prostate cancer
2. Gender Dysphoria (also known as gender non-conforming or transgender persons)
   NOTE: Some plans may opt-out of coverage for gender dysphoria.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Prostate cancer
Authorization of 12 months may be granted for treatment of prostate cancer.

B. Gender dysphoria
1. Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment in an adolescent member when ALL of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria
   b. The member has reached Tanner stage 2 of puberty

2. Authorization of 12 months may be granted for gender reassignment in an adultmember when ALL of the following criteria are met:
   a. The member has a diagnosis of gender dysphoria
   b. The member will receive Eligard concomitantly with cross sex hormones

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Eligard [package insert]. For Collins, CO: Tolmar Pharmaceuticals; November 2017.

2. The NCCN Drugs & Biologics Compendium® © 2017 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed November 29, 2017.
3. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: prostate cancer. Version 2.2017. http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed November 29, 2017.
4. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2017:102(11):3869–3903.
5. Gender Identity Research and Education Society. Guidance for GPs and other clinicians on the treatment of gender variant people. UK Department of Health. Published March 10, 2008.
6. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, 7th version. ©2012 World Professional Association for Transgender Health. Available at http://www.wpath.org.

Reference number(s)
2003-A

SPECIALTY GUIDELINE MANAGEMENT

ENBREL (etanercept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Moderately to severely active rheumatoid arthritis (RA)
2. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)
3. Active psoriatic arthritis (PsA)
4. Active ankylosing spondylitis (AS)
5. Moderate to severe chronic plaque psoriasis (PsO)

B. Compendial Uses
1. Axial spondyloarthritis
2. Reactive arthritis
3. Hidradenitis suppurativa, severe, refractory

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
1. Authorization of 24 months may be granted for members who have previously received Enbrel or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

2. Authorization of 24 months may be granted for treatment of moderately to severely active RAwhen any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
   b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)
1. Authorization of 24 months may be granted for members who have previously received Enbrel or any other biologic DMARD indicated for moderately to severely active polyarticular juvenile idiopathic arthritis.

2. Authorization of 24 months may be granted for treatment of active pJIA when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial ofmethotrexate.
   b. Member has intolerance or contraindication to methotrexate (see Appendix A).

C. Active psoriatic arthritis (PsA)
Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis
1. Authorization of 24 months may be granted for members who have previously received Enbrel or any other biologic DMARD indicated for active ankylosing spondylitis.

2. Authorizations of 24 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
   b. Member has an intolerance or contraindication to two or more NSAIDs.

E. Moderate to severe chronic plaque psoriasis
1. Authorization of 24 months may be granted for members who have previously received Enbrel, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe chronic plaque psoriasis.

2. Authorization of 24 months may be granted for treatment of moderate to severe chronic plaque psoriasis when all of the following criteria are met:
   a. At least 5% of body surface area (BSA) is affected OR crucial bodyareas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   b. Member meets any of the following criteria:
      i. Member has had an inadequate response or intolerance to either phototherapy (e.g.,UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      ii. Member has a clinical reason to avoid pharmacologic treatment withmethotrexate, cyclosporine or acitretin (see Appendix B).
      iii. Member has severe psoriasis that warrants a biologic DMARD as first-linetherapy.

F. Reactive arthritis
Authorization of 24 months may be granted for treatment of reactive arthritis.

G. Hidradenitis suppurativa
Authorization of 24 months may be granted for treatment of severe, refractory hidradenitis suppurativa.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Enbrel as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Enbrel or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from all requirements related to TB screening in this Policy.

V. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease, or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Enbrel [package insert]. Thousand Oaks, CA: Immunex Corporation; November 2017.
2. van der Heijde D, Ramiro S, Landewe R, et al. 2016 Update of the international ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis.* 2017;0:1-14.
3. Flagg SD, Meador R, Hsia E, et al. Decreased pain and synovial inflammation after etanercept therapy in patients with reactive and undifferentiated arthritis: an open-label trial. Arthritis Rheum. 2005;53(4):613-617.
4. DRUGDEX® System [Internet database]. Ann Arbor, MI: Truven Health Analytics. Updated periodically. Accessed August 17, 2018.
5. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017*;0*:1-18.
6. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guidelinefor the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
7. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum*. 2008;59(6):762-784.
8. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res*. 2011;63(4):465-482.
9. Menter A, Gottlieb A, Feldman SR, et al. Guidelines for the management of psoriasis and psoriatic arthritis. Section 1: Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. *J Am Acad Dermatol.* 2008;58(5):826-850.

10. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
11. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies; 2015 update. *Ann Rheum Dis*. 2016;75(3):499-510.
12. Gladman DD, Antoni C, P Mease, et al. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis.* 2005;64(Suppl II):ii14–ii17.
13. Peluso R, Lervolino S, Vitiello M, et al. Extra-articular manifestations in psoriatic arthritis patients. [Published online ahead of print May 8, 2014]. *Clin Rheumatol.* 2014.Accessed August 22, 2014.
14. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis* 2011;70:896–904.
15. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Associationof America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis*. Arthritis Rheumatol.* 2015: 10.1002/art.39298. [Epub ahead of print].

Reference number(s)
2004-A

SPECIALTY GUIDELINE MANAGEMENT

ENTYVIO (vedolizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Moderately to severely active ulcerative colitis(UC)
2. Moderately to severely active Crohn's disease(CD)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active ulcerative colitis(UC)

1. Authorization of 4 months may be granted for members who are 18 years of age or older who have previously received Entyvio or any other biologic or targeted synthetic drug (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.

2. Authorization of 4 months may be granted for treatment of moderately to severely active UC in members who are 18 years of age or older who had an inadequate response, intolerance or contraindication to EITHER of the following:
   a. At least ONE conventional therapy option (See Appendix A)
   b. At least ONE TNF-alpha inhibitor indicated forUC:
      i. Humira (adalimumab)
      ii. Remicade (infliximab)
      iii. Simponi (golimumab)

B. Moderately to severely active Crohn's disease(CD)

1. Authorization of 4 months maybe granted for members who are 18 years of age or older who have previously received Entyvio or any other biologic indicated for the treatment of Crohn'sdisease.

2. Authorization of 4 months may be granted for treatment of moderately to severely active CD in members who are 18 years of age or older who had an inadequate response, intolerance or contraindication to EITHER of the following:
   a. At least ONE conventional therapy option (See Appendix B)
   b. At least ONE TNF-alpha inhibitor indicated forCD:
      i. Cimzia (certolizumab)
      ii. Humira (adalimumab)
      iii. Remicade (infliximab)

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Entyvio as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. APPENDICES

Appendix A: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
   a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
   b. Rectal mesalamine (e.g., Canasa, Rowasa)
   c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
   d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
   a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
   b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
   a. Prednisone, hydrocortisone IV, methylprednisolone IV
   b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: sulfasalazine
5. Pouchitis: Metronidazole, ciprofloxacin
   a. Alternative: rectal mesalamine

Appendix B: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
   a. Oral budesonide
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine
3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenously (IV)
   b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC
5. Perianal and fistulizing disease – induction of remission
   a. Metronidazole ± ciprofloxacin, tacrolimus
6. Perianal and fistulizing disease – maintenance of remission
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

V. REFERENCES

1. Entyvio [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; February2018.

2. Kornbluth A, Sachar DB, and the Practice Parameters Committee of the American College of Gastroenterology. Ulcerative Colitis Practice Guidelines in Adults. *Am J Gastroenterol.* 2010; 105:501–523. Available at http://s3.gi.org/physicians/guidelines/UlcerativeColitis.pdf. Accessed September 6, 2016.
3. Lichtenstein GR, Hanauer SB, Sandborn WJ, and the Practice Parameters Committee of the American College of Gastroenterology. Management of Crohn's disease in adults. *Am J Gastroenterol.* 2009. Available at http://s3.gi.org/physicians/guidelines/CrohnsDiseaseinAdults2009.pdf. AccessedSeptember 6,, 2016.
4. Talley NJ, Abreu MT, Achkar J, et al. An evidence-based systematic review on medical therapies for inflammatory bowel disease. *Am J Gastroenterol*. 2011;106(Suppl 1):S2-S25.
5. Lichtenstein GR, Loftus Jr EV, Isaacs KI, et al. ACG Clinical Guideline: Management of Crohn's Diseasein Adults. Am J Gastroenterol. 2018;113:481-517.

Reference number(s)
2137-A, 2676-A

SPECIALTY GUIDELINE MANAGEMENT

EPCLUSA (sofosbuvir and velpatasvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Epclusa is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5 or 6 infection:
A. without cirrhosis or with compensated cirrhosis
B. with decompensated cirrhosis for use in combination with ribavirin

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, without ribavirin

1. Genotype 1 infection

a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV) with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have genotype 1b infection and who failed prior treatment with non-NS5A inhibitor, sofosbuvir-containing regimen.

2. Genotype 2 infection

a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV.

b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) andribavirin.

3. Genotype 3 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV.

4. Genotype 4, 5 or 6 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

5. Decompensated cirrhosis (Child Turcotte Pugh [CTP] class B or C)
Authorization of up to 24 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection who have decompensated cirrhosis and documented anemia (baseline hemoglobin [Hgb] below 10 g/dL) or RBV ineligibility (see Section IV).

B. Chronic hepatitis C virus infection, in combination with ribavirin

1. Genotype 3 infection

a. Authorization of up to 12 weeks total may be granted for members with the Y93H substitution associated with velpatasvir resistance who are either of the following:
   i. Treatment-naïve with compensated cirrhosis
   ii. Failed prior treatment with PEG-IFN and RBV without cirrhosis
b. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV.

2. Decompensated cirrhosis (CTP class B or C)

a. Authorization of up to 12 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection and decompensated cirrhosis.
b. Authorization of up to 24 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection and decompensated cirrhosis who failed prior treatment with a sofosbuvir- or NS5A inhibitor-based regimen.

3. Recurrent HCV infection post liver transplantation
Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis or decompensated cirrhosis and recurrent HCV genotype 2 or 3 infection post liver transplantation.

C. HCV and HIV coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX: RIBAVIRIN INELIGIBILITY

RBV ineligibility is defined as one or more of the below:
A. Intolerance to RBV
B. Pregnant female or male whose female partner is pregnant
C. Hemoglobinopathy
D. Coadministration with didanosine
E. History of significant or unstable cardiac disease

V. REFERENCES

1. Epclusa [package insert]. Foster City, CA: Gilead Sciences, Inc.; August 2017.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Last changes made September 21, 2017. Accessed September22, 2017.

Reference number(s)
2137-A, 2676-A

SPECIALTY GUIDELINE MANAGEMENT

EPCLUSA (sofosbuvir and velpatasvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Epclusa is indicated for the treatment of adult patients with chronic hepatitis C virus (HCV) genotype 1, 2, 3, 4, 5 or 6 infection:
A. without cirrhosis or with compensated cirrhosis
B. with decompensated cirrhosis for use in combination with ribavirin

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, without ribavirin

1. Genotype 1 infection

a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV) with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).
b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have genotype 1b infection and who failed prior treatment with non-NS5A inhibitor, sofosbuvir-containing regimen.

2. Genotype 2 infection

a. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV.
b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) andribavirin.

3. Genotype 3 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV.

4. Genotype 4, 5 or 6 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor (boceprevir, simeprevir or telaprevir).

5. Decompensated cirrhosis (Child Turcotte Pugh [CTP] class B or C)
Authorization of up to 24 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection who have decompensated cirrhosis and documented anemia (baseline hemoglobin [Hgb] below 10 g/dL) or RBV ineligibility (see Section IV).

B. Chronic hepatitis C virus infection, in combination with ribavirin

1. Genotype 3 infection

a. Authorization of up to 12 weeks total may be granted for members with the Y93H substitution associated with velpatasvir resistance who are either of the following:
   i. Treatment-naïve with compensated cirrhosis
   ii. Failed prior treatment with PEG-IFN and RBV without cirrhosis
b. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV.

2. Decompensated cirrhosis (CTP class B or C)

a. Authorization of up to 12 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection and decompensated cirrhosis.
b. Authorization of up to 24 weeks total may be granted for members with genotype 1, 2, 3, 4, 5 or 6 infection and decompensated cirrhosis who failed prior treatment with a sofosbuvir- or NS5A inhibitor-based regimen.

3. Recurrent HCV infection post liver transplantation
Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis or decompensated cirrhosis and recurrent HCV genotype 2 or 3 infection post liver transplantation.

C. HCV and HIV coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX: RIBAVIRIN INELIGIBILITY

RBV ineligibility is defined as one or more of the below:
- Intolerance to RBV
- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

V. REFERENCES

1. Epclusa [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2017.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Last changes made May 24, 2017. Accessed August 02,2018.

Reference number(s)
1619-A

SPECIALTY GUIDELINE MANAGEMENT

EPOGEN, PROCRIT, RETACRIT (epoetin alfa)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Epoetin alfa is indicated for the treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and not on dialysis to decrease the need for red blood cell (RBC)transfusion.
2. Epoetin alfa is indicated for the treatment of anemia due to zidovudine administered at ≤ 4200 mg/week in HIV-infected patients with endogenous serum erythropoietin levels of ≤ 500mUnits/mL.
3. Epoetin alfa is indicated for the treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.
4. Epoetin alfa is indicated to reduce the need for allogeneic RBC transfusions among patients with perioperative hemoglobin > 10 to ≤ 13 g/dL who are at high risk for perioperative blood loss from elective, noncardiac, nonvascular surgery. Epoetin alfa is not indicated for patients who are willing to donate autologous blood preoperatively.

Limitations of Use:

1. Epoetin alfa has not been shown to improve quality of life, fatigue, or patient well-being.
2. Epoetin alfa is not indicated for use:
   - In patients with cancer receiving hormonal agents, biologic products, or radiotherapy, unless also receiving concomitant myelosuppressive chemotherapy.
   - In patients with cancer receiving myelosuppressive chemotherapy whenthe anticipated outcome is cure.
   - In patients with cancer receiving myelosuppressive chemotherapy in whom anemia canbe managed by transfusion.
   - In patients scheduled for surgery who are willing to donate autologous blood.
   - In patients undergoing cardiac or vascular surgery.
   - As a substitute for RBC transfusions in patients who require immediate correction of anemia.

B. Compendial Uses

1. Symptomatic anemia in patients with myelodysplastic syndromes (MDS)
2. Anemia in congestive heart failure
3. Anemia in rheumatoid arthritis
4. Anemia due to hepatitis C treatment with ribavirin in combination with either interferon alfa or peginterferon alfa
5. Anemia in patients whose religious beliefs forbid blood transfusions
6. Symptomatic anemia in patients with primary myelofibrosis, post-polycythemia vera myelofibrosis, and post-essential thrombocythemia myelofibrosis

7. Cancer patients who are undergoing palliative treatment

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Note: Requirements regarding pretreatment hemoglobin level exclude values due to a recent transfusion.

A. Anemia Due to CKD
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

B. Anemia Due to Myelosuppressive Chemotherapy
Authorization of 12 weeks may be granted for members with nonmyeloid malignancy who meet ALL of the following criteria:
1. The intent of chemotherapy is non-curative
2. Pretreatment hemoglobin < 10 g/dL

C. Anemia in MDS
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

D. Reduction of Allogeneic Red Blood Cell Transfusion in Patients Undergoing Elective, Noncardiac, Nonvascular Surgery
Authorization of 12 weeks may be granted for members scheduled to have an elective, noncardiac, nonvascular surgery when the pretreatment hemoglobin is > 10 to ≤ 13 g/dL.

E. Anemia in Congestive Heart Failure (CHF)
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 9 g/dL.

F. Anemia in Rheumatoid Arthritis (RA)
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

G. Anemia Due to Hepatitis C Treatment
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL who are receiving ribavirin in combination with either interferon alfa or peginterferon alfa.

H. Anemia Due to Zidovudine in HIV-infected Patients
Authorization of 12 weeks may be granted for members currently receiving zidovudine with pretreatment hemoglobin < 10 g/dL.

I. Anemia in Members Whose Religious Beliefs Forbid Blood Transfusions
Authorization of 12 weeks may be granted for members with pretreatment hemoglobin < 10 g/dL.

J. Anemia in Primary Myelofibrosis (MF), Post-polycythemia Vera MF, and Post-Essential Thrombocythemia MF
Authorization of 12 weeks may be granted for members who meet ALL of the following criteria:
1. Member has symptomatic anemia
2. Pretreatment hemoglobin < 10 g/dL
3. Pretreatment serum erythropoietin level < 500 mU/mL

K. Anemia Due to Cancer

Authorization of 12 weeks may be granted for members who have cancer and are undergoing palliative treatment

III. CONTINUATION OF THERAPY

Note: Requirements regarding current hemoglobin level exclude values due to a recent transfusion.

For all indications below: all members (including new members) requesting authorization for continuation of therapy after at least 12 weeks of ESA treatment must show a response with a rise in hemoglobin of ≥ 1 g/dL. Members who completed less than 12 weeks of ESA treatment and have not yet responded with a rise in hemoglobin of ≥ 1 g/dL may be granted authorization of up to 12 weeks to allow for sufficient time to demonstrate a response.

A. Anemia Due to CKD
Authorization of 12 weeks may be granted for continuation of therapy when the current hemoglobin is ≤ 12 g/dL.

B. Anemia Due to Myelosuppressive Chemotherapy
Authorization of 12 weeks may be granted for the continuation of therapy in members with nonmyeloid malignancy who meet ALL of the following criteria:
1. The intent of chemotherapy is non-curative
2. Current hemoglobin is < 11 g/dL

C. Anemia in MDS
Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

D. Anemia in CHF, RA
Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

E. Anemia Due to Hepatitis C Treatment
Authorization of 12 weeks may be granted for continuation of treatment when the member meets ALL of the following criteria:
1. The member is receiving ribavirin in combination with either interferon alfa or peginterferonalfa
2. The current hemoglobin is ≤ 12 g/dL.

F. Anemia Due to Zidovudine in HIV-infected Patients
Authorization of 12 weeks may be granted for continuation of therapy in members receiving zidovudine when the current hemoglobin is ≤ 12 g/dL.

G. Anemia in Members Whose Religious Beliefs Forbid Blood Transfusions
Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

H. Anemia in Primary Myelofibrosis, Post-polycythemia Vera Myelofibrosis, and Post-Essential Thrombocythemia Myelofibrosis
Authorization of 12 weeks may be granted for continuation of treatment when the current hemoglobin is ≤ 12 g/dL.

I. Anemia Due to Cancer

Authorization of 12 weeks may be granted for members who have cancer and are undergoing palliative treatment

IV. REFERENCES

1. Epogen [package insert]. Thousand Oaks, CA: Amgen Inc.; July 2018.
2. Procrit [package insert]. Horsham, PA: Janssen Products.; July 2018.
3. Retacrit [package insert]. Lake Forest, IL: Hospira Inc.; May 2018
4. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed September 19, 2018.
5. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed September 19, 2018.
6. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed September 19, 2018.
7. Kidney Disease: Improving Global Outcomes (KDIGO) AnemiaWork Group. KDIGO Clinical Practice Guideline for Anemia in Chronic Kidney Disease. Kidney Int. 2012;Suppl 2:279-335.
8. National Kidney Foundation. KDOQI Clinical Practice Guideline and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease: 2007 Update of Hemoglobin Target. http://www2.kidney.org/professionals/KDOQI/guidelines_anemiaUP/. Accessed September 19, 2018.
9. Rizzo JD, Brouwers M, Hurley P, et al. American Society of Clinical Oncology/American Society of Hematology clinical practice guideline update on the use of epoetin and darbepoetin in adult patients with cancer. *J Clin Oncol.* 2010;28(33):4996-5010.
10. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Cancer- and Chemotherapy-Induced Anemia. Version 3.2018. http://www.nccn.org/professionals/physician_gls/pdf/anemia.pdf. Accessed September 19, 2017.
11. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes. Version 1.2019. http://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed Accessed September 19, 2017.
12. Qaseem A, Humphrey LL, Fitterman N, Starkey M, Shekelle P, for the Clinical Guidelines Committee of the American College of Physicians. Treatment of Anemia in Patients with Heart Disease: A Clinical Practice Guideline from the American College of Physicians. *Ann Intern Med*. 2013;159:770-779.
13. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 1.2019. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed September 19, 2017.
14. Cervantes F, Alvarez-Larran A, Hernandez-Boluda JC, et al. Erythropoietin treatment of the anemia of myelofibrosis with myeloid metaplasia: results in 20 patients and review of the literature. Br J Haematol. 2004;127(4):399-403.

Reference number(s)
1642-A

SPECIALTY GUIDELINE MANAGEMENT

Flolan (epoprostenol for injection)
Veletri (epoprostenol for injection)
epoprostenol for injection (generic)

POLICY

XI. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Epoprostenol/Flolan/Veletri is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group I) to improve exercise capacity. Studies establishing effectiveness included predominantly patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

All other indications are considered experimental/investigational and are not a covered benefit.

XII. CRITERIA FOR INITIAL APPROVAL

Indefinite authorization may be granted for treatment of PAH when ALL of the following criteria are met:

A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
   4. Pretreatment right heart catheterization with all of the following results:
      i. mPAP ≥ 25 mmHg
      ii. PCWP ≤ 15 mmHg
      iii. PVR > 3 Wood units
   5. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      i. Post cardiac surgery
      ii. Chronic heart disease
      iii. Chronic lung disease associated with prematurity
      iv. Congenital diaphragmatic hernia

XIII. CONTINUATION OF THERAPY

Indefinite authorization may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

XIV. APPENDIX

WHO Classification of Pulmonary Hypertension
1 PAH

1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.3 Chronic thromboembolic PH
4.4 Other pulmonary artery obstructions
- 4.4.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.4.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma
  - Germ cell tumours of the testis
  - Other tumours
- 4.4.3 Non-malignant tumours
  - Uterine leiomyoma
- 4.4.4 Arteritis without connective tissue disease
- 4.4.5 Congenital pulmonary artery stenosis
- 4.4.6 Parasites
  - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.5 Complex congenital heart disease

XV. REFERENCES

1. Flolan [package insert]. Research Triangle Park, NC: GlaxoSmithKline; December 2018.
2. Veletri [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; December 2018.
3. Epoprostenol Sodium for Injection. North Wales, PA: Teva Pharmaceuticals USA; March 2019.
4. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.

5. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
6. Badesch DB, Champion HC, Gomez-Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S55-S66.
7. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol.* 2013;62:D34-S41.
8. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
9. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S78-S84.
10. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
11. Abman, SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.
12. Klinger, JR., Elliott, CG, Levine, DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019:155(3): 565-586.
13. Galie, N., McLaughlin, VV, Rubin, LJ, Simonneau, G. An overview of the 6th World Symposium on Pulmonary Hypertension. Eur Respir J 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.

Reference number(s)
1881-A

SPECIALTY GUIDELINE MANAGEMENT

ESBRIET (pirfenidone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Esbriet is indicated for the treatment of idiopathic pulmonary fibrosis.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Idiopathic Pulmonary Fibrosis (IPF)
Authorization of 24 months may be granted for treatment of idiopathic pulmonary fibrosis when the member has undergone a diagnostic work-up which includes the following:

1. Other known causes of interstitial lung disease (e.g., domestic and occupational environmental exposures, connective tissue disease, drug toxicity) have been excluded AND
2. The member has completed a high-resolution computed tomography (HRCT) study of the chest or a lung biopsy which reveals a result consistent with the usual interstitial pneumonia (UIP) pattern, OR has completed an HRCT study of the chest which reveals a result other than the UIP pattern (e.g., probable UIP, indeterminate for UIP) and the diagnosis is supported by a lung biopsy. If a lung biopsy has not been previously conducted, the diagnosis is supported by a multidisciplinary discussion between a radiologist and pulmonologist who are experienced in IPF.

III. CONTINUATION OF THERAPY

Idiopathic Pulmonary Fibrosis (IPF)
All members (including new members) requesting authorization for continuation of therapy may be granted an authorization of 24 months when the member is currently receiving treatment with Esbriet, excluding when Esbriet is obtained as samples or via manufacturer's patient assistance programs.

IV. REFERENCES

1. Esbriet [package insert]. South San Francisco, CA: Genentech USA, Inc.; October 2017.
2. Raghu G, Remy-Jardin M, Myers JL, et al. Diagnosis of Idiopathic Pulmonary Fibrosis. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. *Am J Respir Crit Care Med*. 2018 Sep1;198(5):e44-e68.
3. Vancheri C, Kreuter M, Richeldi L, et al. Nintedanib with add-on pirfenidone in idiopathic pulmonary fibrosis: results of the Injourney trial. *Am J Respir Crit Care Med.* 2017 Sept 10. doi: 10.1164/rccm.201706-1301OC. [Epub ahead of print].

Reference number(s)
1881-A

SPECIALTY GUIDELINE MANAGEMENT

ESBRIET (pirfenidone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Esbriet is indicated for the treatment of idiopathic pulmonary fibrosis.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Idiopathic Pulmonary Fibrosis (IPF)
Authorization of 24 months may be granted for treatment of idiopathic pulmonary fibrosis when the member has undergone a diagnostic work-up which includes the following:

1. The member does not have a known etiology for interstitial lung disease such as sarcoidosis, scleroderma, polymyositis/dermatomyositis, systemic lupus erythematosus, bronchiolitis obliterans organizing pneumonia, or drug toxicity AND
2. The member has completed a high-resolution computed tomography (HRCT) study of the chest or surgical lung biopsy which reveals a result consistent with the usual interstitial pneumonia (UIP) pattern, OR has completed an HRCT study of the chest which reveals a result consistent with the possible UIP pattern and the diagnosis is supported by surgical lung biopsy (SLB). If SLB has not been previously conducted, the diagnosis is supported by a multidisciplinary discussion between a radiologist and pulmonologist who are experienced in IPF.

III. CONTINUATION OF THERAPY

Idiopathic Pulmonary Fibrosis (IPF)
All members (including new members) requesting authorization for continuation of therapy may be granted an authorization of 24 months when the member is currently receiving treatment with Esbriet, excluding when Esbriet is obtained as samples or via manufacturer's patient assistance programs.

IV. REFERENCES

1. Esbriet [package insert]. South San Francisco, CA: Genentech USA, Inc.; October 2017.
2. Raghu G, Collard HR, Egan JJ, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med.* 2011;183:788-824.
3. Raghu G, Rochwerg B, Zhang Y, et al. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline: Treatment of Idiopathic Pulmonary Fibrosis. An Update of the 2011 Clinical Practice Guideline. *Am J Respir Crit Care Med.* 2015;192:e3-e19.

4. Vancheri C, Kreuter M, Richeldi L, et al. Nintedanib with add-on pirfenidone in idiopathic pulmonary fibrosis: results of the Injourney trial. *Am J Respir Crit Care Med.* 2017 Sept 10. doi: 10.1164/rccm.201706-1301OC. [Epub ahead of print].

Reference number(s)
1621-A

SPECIALTY GUIDELINE MANAGEMENT

FERRIPROX (deferiprone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Initial requests: pretreatment serum ferritin level
B. Continuation requests: current serum ferritin level

III. CRITERIA FOR INITIAL APPROVAL

Transfusional Iron Overload

Authorization of 6 months may be granted for treatment of transfusional iron overload due to thalassemia syndromes when both of the following criteria are met:

A. Pretreatment serum ferritin level is consistently greater than 1000 mcg/L.
B. Dose of Ferriprox will not exceed 99 mg/kg per day.

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III when both of the following criteria are met:

A. Member is experiencing benefit from therapy as evidenced by a decrease in serum ferritin levels as compared to pretreatment baseline.
B. Serum ferritin level is not consistently below 500 mcg/L.

V. REFERENCES

1. Ferriprox [package insert]. Rockville, MD: ApoPharma USA, Inc.; May 2017.
2. Micromedex Solutions [database online]. Truven Health Analytics, Inc. Ann Arbor, MI. Available at: www.micromedexsolutions.com. Accessed October 15, 2018.
3. AHFS DI (Adult and Pediatric) [database online]. Lexi-Comp, Inc. Hudson, OH. Available at: http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed October 15, 2018.
4. Clinical Pharmacology [Internet]. Elsevier. Tampa (FL). Available from: http://www.clinicalpharmacology.com. Accessed October 15, 2018.
5. Cappellini MD, Cohen A, Porter J, et al. Guidelines for the management of transfusion dependent thalassaemia (TDT) 3rd Edition [Internet]. *Thalassaemia International Federation* 2014;20:1-253.

Reference number(s)
1621-A

Ferriprox 1621-A SGM P2018

Reference number(s)
1606-A

SPECIALTY GUIDELINE MANAGEMENT

FIRAZYR (icatibant)

POLICY

XVI. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Treatment of acute attacks of hereditary angioedema in adults 18 years of age and older

All other indications are considered experimental/investigational and are not a covered benefit.

XVII. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. C4 levels and C1 inhibitor functional and antigenic protein levels
B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
C. Chart notes confirming family history of angioedema, if applicable

XVIII. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of acute hereditary angioedema attacks when the requested medication will not be used in combination with Berinert, Kalbitor, or Ruconest and either of the following criteria is met:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
1. C1 inhibitor (C1-INH) antigenic level is below the lower limit of normal as defined by the laboratory performing the test, or
2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test).

B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

XIX. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced reduction in severity and/or duration of attacks when they use the requested medication to treat an acute attack.

XX. REFERENCES

1. Firazyr [package insert]. Lexington, MA: Shire Orphan Therapies, Inc.; December 2015.
2. icatibant [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; March 2019.

3. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
4. Cicardi M, Bork K, Caballero T, et al. Hereditary Angioedema International Working Group. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy*. 2012;67:147-157.
5. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol: In Practice*. 2013; 1(5): 458-467.
6. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. Allergy Asthma Proc. 2012; 33(6):S145-S156.
7. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Allergy*. 2018;00:1-22.
8. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109:395-202.
9. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014;69: 602-616.
10. Bowen T. Hereditary angioedema: beyond international consensus – circa December 2010 – The Canadian Society of Allergy and Clinical Immunology Dr. David McCourtie Lecture. *Allergy Asthma Clin Immunol*. 2011;7(1):1.
11. Bernstein J. Update on angioedema: Evaluation, diagnosis, and treatment. *Allergy and Asthma Proceedings*. 2011;32(6):408-412.
12. Longhurst H, Cicardi M. Hereditary angio-edema. *Lancet*. 2012;379:474-481.
13. Farkas H, Martinez-Saguer I, Bork K, et al. International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency. *Allergy*. 2017;72(2):300-313.
14. Henao MP, Kraschnewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management.* 2016; 12: 701-711.

Reference number
2075-A

SPECIALTY GUIDELINE MANAGEMENT

GAZYVA (obinutuzumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Chronic Lymphocytic Leukemia (CLL)
   Gazyva, in combination with chlorambucil, is indicated for the treatment of patients with previously untreated CLL.

2. Follicular Lymphoma
   - Gazyva, in combination with bendamustine followed by Gazyva monotherapy, is indicated for the treatment of patients with follicular lymphoma who relapsed after, or are refractory to, a rituximab-containing regimen.
   - Gazyva, in combination with chemotherapy followed by Gazyva monotherapy in patients achieving at least a partial remission, is indicated for the treatment of adult patients with previously untreated stage II bulky, III or IV follicular lymphoma.

B. Compendial Uses

1. Chronic lymphocytic leukemia
2. Small lymphocytic lymphoma (SLL) (managed in the same manner as CLL)
3. Follicular lymphoma
4. Gastric MALT lymphoma, second-line or subsequent therapy in combination with bendamustine for recurrent or progressive disease, maintenance therapy, or substitute for rituximab in patients experiencing rare complications from rituximab
5. Non-gastric MALT lymphoma, second-line or subsequent therapy in combination with bendamustine for refractory or progressive disease, maintenance therapy, or substitute for rituximab in patients experiencing rare complications from rituximab
6. Nodal marginal zone lymphoma, second-line or subsequent therapy in combination with bendamustine for refractory or progressive disease, maintenance therapy, or substitute for rituximab in patients experiencing rare complications from rituximab
7. Splenic marginal zone lymphoma, second-line (if prior treatment with rituximab) or subsequent therapy in combination with bendamustine for recurrent disease, maintenance therapy, or substitute for rituximab in patients experiencing rare complications from rituximab
8. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma substitute for rituximab in patients experiencing rare complications from rituximab
9. Mantle cell lymphoma, substitute for rituximab in patients experiencing rare complications from rituximab
10. Diffuse large B-cell lymphoma, substitute for rituximab in patients experiencing rare complications from rituximab
11. High-grade B-cell lymphomas, substitute for rituximab in patients experiencing rare complications from rituximab
12. Burkitt lymphoma, substitute for rituximab in patients experiencing rare complications from rituximab
13. AIDS-related B-cell lymphomas, substitute for rituximab in patients experiencing rare complications from rituximab
14. Post-transplant lymphoproliferative disorders, substitute for rituximab in patients experiencing rare complications from rituximab
15. Castleman's disease, substitute for rituximab in patients experiencing rare complications from rituximab

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITAL APPROVAL

A. Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)

Authorization of 6 months may be granted for the treatment of CLL/SLL.

B. Follicular Lymphoma (FL)

Authorization of 6 months, up to 30 months total, may be granted for the treatment of follicular lymphoma when any of the following criteria are met:

1. The requested medication will be used in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen, CVP (cyclophosphamide, vincristine and prednisone) regimen, or bendamustine.
2. The requested medication will be used as maintenance therapy
3. The requested medication will be used as a substitute for rituximab in members experiencing rare complications from rituximab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

C. Gastric MALT Lymphoma, Non-gastric MALT Lymphoma, Nodal and Splenic Marginal Zone Lymphoma

Authorization of 6 months may be granted for the treatment of gastric MALT lymphoma, non-gastric MALT lymphoma, nodal marginal zone lymphoma, or splenic marginal zone lymphoma when any of the following criteria are met:

1. The requested medication will be used as second-line or subsequent therapy in combination with bendamustine.
2. The requested medication be used as maintenance therapy when the member has been previously treated with the requested medication and bendamustine.
3. The requested medication is used as a substitute for rituximab in members experiencing rare complications from rituximab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

D. Histologic Transformation of Marginal Zone Lymphoma to Diffuse Large B-Cell Lymphoma, Mantle Cell Lymphoma, Diffuse Large B-Cell Lymphoma, High-Grade B-Cell Lymphomas, Burkitt Lymphoma, AIDS-Related B-Cell Lymphomas, Post-Transplant Lymphoproliferative Disorders, and Castleman's Disease

Authorization of 6 months may be granted for the treatment of histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, high-grade B-cell lymphomas, Burkitt lymphoma, AIDS-related B-cell lymphomas, post-transplant lymphoproliferative disorders, or Castleman's disease when the requested medication is used as a substitute for rituximab in members experiencing rare complications from rituximab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

III. CONTINUATION OF THERAPY

A. Follicular Lymphoma (FL)

Authorization of 12 months, up to 30 months total, may be granted for continued treatment in members requesting reauthorization for follicular lymphoma who have not experienced disease progression or an unacceptable toxicity while on the current regimen.

B. All other indications

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity while on the current regimen.

IV. REFERENCES

1. Gazyva [package insert]. South San Francisco, CA: Genentech, Inc.; November 2017.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed July 09, 2019.

3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 5.2019. https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed July 09, 2019.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: B-Cell Lymphomas. Version 4.2019. https://www.nccn.org/professionals/physician_gls/pdf/b-cell_blocks.pdf. Accessed July 09, 2019.

Reference number(s)
1741-A, 1742-A

SPECIALTY GUIDELINE MANAGEMENT

GENOTROPIN (somatropin)
HUMATROPE (somatropin)
NORDITROPIN (somatropin)
NUTROPIN AQ (somatropin)
OMNITROPE (somatropin)
SAIZEN (somatropin)
ZOMACTON (somatropin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no contraindications or exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Pediatric patients with growth failure due to any of the following:
   a. Growth hormone (GH) deficiency
   b. Turner syndrome
   c. Noonan syndrome
   d. Small for gestational age (SGA)
   e. Prader-Willi syndrome
   f. Chronic kidney disease (CKD)
   g. Short stature homeobox-containing gene (SHOX) deficiency
   h. Idiopathic short stature (ISS)*
2. Adults with childhood-onset or adult-onset GH deficiency

** ISS may not be covered by some plans*

B. Compendial Uses
1. Human immunodeficiency virus (HIV)-associated wasting/cachexia
2. Short bowel syndrome (SBS)
3. Growth failure associated with any of the following:
   a. Cerebral palsy
   b. Congenital adrenal hyperplasia
   c. Cystic fibrosis
   d. Russell-Silver syndrome

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review (where applicable):
A. Medical records supporting the diagnosis of neonatal GH deficiency

B. Pretreatment growth hormone provocative test result(s) (laboratory report or medical record documentation)
C. Pretreatment and/or current IGF-1 level (laboratory report or medical record documentation)*
D. The following laboratory test reports must be provided:
1. Diagnostic karyotype results in Turner syndrome
2. Diagnostic genetic test results in Prader-Willi syndrome
3. Diagnostic molecular or genetic test results in SHOX deficiency

* IGF-1 levels vary based on the laboratory performing the analysis. Laboratory-specific values must be provided to determine whether the value is within the normal range.

III. PRESCRIBER SPECIALTIES

For all diagnoses excluding HIV-associated wasting/cachexia, therapy must be prescribed by or in consultation with any of the following specialists:
A. Endocrinologist
B. Pediatric endocrinologist
C. Geneticist
D. Pediatric nephrologist (CKD only)
E. Gastroenterologist/Nutritional support specialist (SBS only)

IV. INITIAL CRITERIA FOR APPROVAL

A. Pediatric GH Deficiency

Authorization of 12 months may be granted to members with pediatric GH deficiency when EITHER criteria 1. or 2. below is met:
1. Member is a neonate or was diagnosed with GH deficiency as a neonate. Medical records must be available to support the diagnosis of neonatal GH deficiency (e.g., hypoglycemia with random GH level, evidence of multiple pituitary hormone deficiency, chart notes, or magnetic resonance imaging [MRI] results).
2. Member meets ALL of the following:
   a. Member has EITHER:
      i. Two pretreatment pharmacologic provocative GH tests with both results demonstrating a peak GH level < 10 ng/mL, OR
      ii. A documented pituitary or CNS disorder (refer to Appendix A) and a pretreatment IGF-1 level > 2 standard deviations (SD) below the mean.
   b. For members < 2.5 years of age at initiation of treatment:
      i. Pretreatment height is > 2 SD below the mean and growth velocity is slow.
   c. For members ≥ 2.5 years of age at initiation of treatment:
      i. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
      ii. Pretreatment 1-year height velocity is > 2 SD below the mean.
   d. Epiphyses are open.

B. Idiopathic Short Stature *(may not be covered by some plans)*

Authorization of 12 months may be granted to members with ISS when ALL of the following criteria are met:
1. Pretreatment height is > 2.25 SD below the mean.
2. Predicted adult height is < 5'3" for boys and < 4'11" for girls.
3. Pediatric GH deficiency has been ruled out with a provocative GH test (peak GH level > 10 ng/mL).

4. Epiphyses are open.

C. Small for Gestational Age

Authorization of 12 months may be granted to members born SGA when ALL of the following criteria are met:

1. Member meets at least one of the following:
   a. Birth weight < 2500 g at gestational age > 37 weeks
   b. Birth weight or length less than 3rd percentile for gestational age
   c. Birth weight or length ≥ 2 SD below the mean for gestational age
2. Pretreatment age is ≥ 2 years.
3. Member failed to manifest catch-up growth by age 2 (i.e., pretreatment height > 2 SD below the mean).
4. Epiphyses are open.

D. Turner Syndrome

Authorization of 12 months may be granted to members with Turner syndrome when ALL of the following criteria are met:

1. Diagnosis was confirmed by karyotyping.
2. Patient's pretreatment height is less than the 5th percentile for age.
3. Epiphyses are open.

E. Growth Failure Associated with Chronic Kidney Disease, Cerebral Palsy, Congenital Adrenal Hyperplasia, Cystic Fibrosis, and Russell-Silver Syndrome

Authorization of 12 months may be granted to members with CKD, cerebral palsy, congenital adrenal hyperplasia, cystic fibrosis, or Russell-Silver syndrome when ALL of the following criteria are met:

1. For members < 2.5 years of age at initiation of treatment:
   a. Pretreatment height is > 2 SD below the mean and growth velocity is slow.
2. For members ≥ 2.5 years of age at initiation of treatment:
   a. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean, OR
   b. Pretreatment 1-year height velocity is > 2 SD below the mean.
3. Epiphyses are open.

F. Prader-Willi Syndrome

Authorization of 12 months may be granted to members with Prader-Willi syndrome when the following criteria are met:

1. The diagnosis of Prader-Willi syndrome was confirmed by genetic testing demonstrating any of the following:
   a. Deletion in the chromosomal 15q11.2-q13 region
   b. Maternal uniparental disomy in chromosome 15
   c. Imprinting defects or translocations involving chromosome 15

G. Noonan Syndrome

Authorization of 12 months may be granted to members with Noonan syndrome when ALL of the following criteria are met:

1. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean OR pretreatment 1-year height velocity is > 2 SD below the mean.
2. Epiphyses are open.

H. Short Stature Homeobox-Containing Gene Deficiency

Authorization of 12 months may be granted to members with SHOX deficiency when ALL of the following criteria are met:

1. The diagnosis of SHOX deficiency was confirmed by molecular or genetic analyses.
2. Pretreatment height is > 2 SD below the mean and 1-year height velocity is > 1 SD below the mean OR pretreatment 1-year height velocity is > 2 SD below the mean.
3. Epiphyses are open.

I. Adult GH Deficiency

Authorization of 12 months may be granted to members with adult GH deficiency when ANY of the following criteria is met:

1. Member has had 2 pretreatment pharmacologic provocative GH tests and both results demonstrated GH levels < 5 ng/mL, unless the agent is Macrilen in which case a GH level of less than 2.8 ng/ml confirms the presence of adult GHD.
2. Member has had 1 pretreatment pharmacologic provocative GH test that demonstrated a GH level < 5 ng/mL AND has a pretreatment IGF-1 level that is low for age and gender, unless the agent is Macrilen in which case a GH level of less than 2.8 ng/ml confirms the presence of adult GHD.
3. Member has a structural abnormality of the hypothalamus or pituitary (refer to Appendix A) and ≥3 documented pituitary hormone deficiencies (refer to Appendix B).
4. Member has childhood-onset GH deficiency and a congenital abnormality of the hypothalamus or pituitary (refer to Appendix A).

J. HIV-Associated Wasting/Cachexia

Authorization of 12 weeks may be granted to members with HIV-associated wasting or cachexia when ALL of the following criteria are met:

1. Member has tried and had a suboptimal response to alternative therapies (e.g., cyproheptadine, dronabinol, megestrol acetate or testosterone if hypogonadal) unless the member has a contraindication or intolerance to alternative therapies.
2. Member is currently on antiretroviral therapy.
3. Pretreatment BMI is < 18.5 kg/m^2 (see Appendix C).

K. Short Bowel Syndrome

Authorization of a lifetime total of 8 weeks may be granted to members with short bowel syndrome when GH will be used in conjunction with optimal management of SBS.

V. CONTINUATION OF THERAPY

A. Pediatric GH Deficiency, Turner Syndrome, Noonan Syndrome, CKD, SGA, ISS, SHOX deficiency, Congenital Adrenal Hyperplasia, Cerebral Palsy, Cystic Fibrosis, and Russell-Silver Syndrome

Authorization of 12 months may be granted for continuation of therapy when ALL of the following criteria are met:

1. Epiphyses are open (confirmed by X-ray or X-ray is not available).
2. Member's growth rate is > 2 cm/year unless there is a documented clinical reason for lack of efficacy (e.g., on treatment less than 1 year, nearing final adult height/late stages of puberty).

B. Prader-Willi Syndrome

Authorization of 12 months may be granted for continuation of therapy when the member's body composition and psychomotor function have improved or stabilized in response to GH therapy.

C. Adult GH Deficiency

Authorization of 12 months may be granted for continuation of therapy when all criteria for initial authorization are met (refer to Section IV. I. above).

D. HIV-Associated Wasting/Cachexia

Authorization of 12 weeks may be granted for continuation of therapy when ALL of the following criteria are met:

1. Member is currently on antiretroviral therapy.
2. Current BMI is < 27 kg/m^2 (see Appendix C).

VI. APPENDICES

A. Appendix A: Examples of Hypothalamic/Pituitary/CNS Disorders

1. Congenital genetic abnormalities
   a. Known mutations in growth-hormone-releasing hormone (GHRH) receptor, GH gene, GH receptor, or pituitary transcription factors
2. Congenital structural abnormalities
   a. Optic nerve hypoplasia/septo-optic dysplasia
   b. Agenesis of corpus callosum
   c. Empty sella syndrome
   d. Ectopic posterior pituitary
   e. Pituitary aplasia/hypoplasia
   f. Pituitary stalk defect
   g. Anencephaly or prosencephaly
   h. Other mid-line defects
   i. Vascular malformations
3. Acquired structural abnormalities (or causes of hypothalamic/pituitary damage)
   a. CNS tumors/neoplasms (e.g., craniopharyngioma, glioma, pituitary adenoma)
   b. Cysts (Rathke cleft cyst or arachnoid cleft cyst)
   c. Surgery
   d. Radiation
   e. Chemotherapy
   f. CNS infections
   g. CNS infarction (e.g., Sheehan's syndrome)
   h. Inflammatory lesions (e.g., autoimmune hypophysitis)
   i. Infiltrative lesions (e.g., sarcoidosis, histiocytosis)
   j. Head trauma/traumatic brain injury
   k. Aneurysmal subarachnoid hemorrhage

B. Appendix B: Pituitary Hormones (Other than Growth Hormone)

1. Adrenocorticotropic hormone (ACTH)
2. Antidiuretic hormone (ADH)
3. Follicle stimulating hormone (FSH)
4. Luteinizing hormone (LH)
5. Thyroid stimulating hormone (TSH)
6. Prolactin

C. Appendix C: Calculation of BMI

$$\text{BMI} = \frac{\text{Weight (pounds)} \times 703}{[\text{Height (inches)}]^2} \quad \text{OR} \quad \frac{\text{Weight (kg)}}{[\text{Height (m)}]^2}$$

BMI classification:		
	Underweight	< 18.5 kg/m^2
	Normal weight	18.5 – 24.9 kg/m^2

Overweight	25 – 29.9 kg/m^2
Obesity (class 1)	30 – 34.9 kg/m^2
Obesity (class 2)	35 – 39.9 kg/m^2
Extreme obesity	≥ 40 kg/m^2

VII. REFERENCES

1. Genotropin [package insert]. New York, NY: Pfizer Inc.; December 2016.
2. Humatrope [package insert]. Indianapolis, IN: Eli Lilly and Company; December 2016.
3. Norditropin [package insert]. Plainsboro, NJ: Novo Nordisk Inc.; February 2018.
4. Nutropin AQ [package insert]. South San Francisco, CA: Genentech, Inc.; December 2016.
5. Saizen [package insert]. Rockland, MA: EMD Serono Inc.; December 2016.
6. Zomacton [package insert]. Parsippany, NJ: Ferring Pharmaceuticals Inc.; January 2018.
7. Omnitrope [package insert]. Princeton, NJ: Sandoz Inc.; December 2016.
8. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed February 16, 2017.
9. Nemechek PM, Polsky B, Gottlieb MS. Treatment Guidelines for HIV-Associated Wasting. *Mayo Clin Proc.* 2000;75:386-394.
10. Grinspoon S, Mulligan K for the Department of Health and Human Services Working Group on the Prevention and Treatment of Wasting andWeight Loss. Weight loss and wasting in patients infected with human immunodeficiency virus. *Clin Infect Dis.* 2003;36(Suppl 2):S69-78.
11. Polsky B, Kotler D, Steinhart C. HIV-associated wasting in the HAART era: guidelines for assessment, diagnosis, and treatment. *AIDS Patient Care STDS*. 2001;15(8):411-23.
12. Parekh NR, Steiger E. Criteria for the use of recombinant human growth hormone in short bowel syndrome. *Nutrition Clin Prac.* 2005;20:503-508.
13. Caremark Clinical Programs Review: Focus on growth hormones, growth hormone releasing hormone, Increlex, Somavert. December 18, 2006.
14. Congilio SJ, Stevenson RD, Rogol AD. Apparent growth hormone deficiencyin children with cerebral palsy. *Dev Med Child Neurol.* 1996;38(9):797-804.
15. Shim ML, Moshang T, Oppenheim WL, et al. Is treatment with growth hormone effective in children with cerebral palsy? *Dev Med Child Neurol*. 2004;46(8):569-71.
16. Gallagher MP, Levine LS, Oberfield SE. A review of the effects of therapy on growth and bone mineralization in children with congenital adrenal hyperplasia. *Growth Horm IGF Res*. 2005;15Suppl A:S26-30.
17. Lin-Su K, Vogiatzi MG, Marshall I, et al. Treatment with growth hormone and luteinizing hormone releasing hormone analog improves final adult height in children with congenital adrenal hyperplasia. *J Clin Endocrinol Metab*. 2005;90:3318-3325.
18. Quintos JB, Vogiatzi MG, Harbison MD, et al. Growth hormone therapy alone or in combination with gonadotropin-releasing hormone analog therapy to improve the height deficit in children with congenital adrenal hyperplasia. *J Clin Endocrinol Metab*. 2001;86(4):1511-1517.
19. Hardin DS, Adams-Huet B, Brown D, et al. Growth hormone treatment improves growth and clinical status in prepubertal children with cystic fibrosis: results of a multicenter randomized controlled trial. *J Clin Endocrinol Metab*. 2006; 91(12):4925-9.
20. Hardin DS, Ellis KJ, Dyson M, et al. Growth hormone improves clinical status in prepubertal children with cystic fibrosis: Results of a randomized controlled clinical trial. *J Pediatr*. 2001;139:636-42.
21. Hardin DS, Rice J, Ahn C, et al. Growth hormone treatment enhances nutrition and growth in children with cystic fibrosis receiving enteral nutrition. *J Pediatr*. 2005;146:324-8.
22. Ranke MB, Lindberg A. Growth hormone treatment of short children born small for gestational age or with Silver-Russell syndrome: Results from KIGS (Kabi International Growth Study), including the first report on final height. *Acta Paediatr Suppl*. 1996;417:18-26.

23. American Association of Clinical Endocrinologists Growth Hormone Task Force. Medical guidelines for clinical practice for growth hormone use in adults and children 2003 Update. *Endocr Pract*. 2003;9(1):64-76.
24. Caremark Clinical Programs Review: Focus on pediatric endocrinology. April 23, 2014.
25. Caremark Clinical Programs Review: Focus on pediatric endocrinology. April 16, 2012.
26. National Institute for Clinical Excellence: Guidance on the use of human growth hormone (somatropin) for the treatment of growth failure in children. May 2010. http://www.nice.org.uk/nicemedia/live/12992/48715/48715.pdf. Accessed February 10, 2017.
27. Wilson TA, Rose SR, Cohen P, et al. Update of Guidelines for the Use of Growth Hormone in Children: The Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. *J Pediatr*. 2003;143:415-421.
28. Franklin SL, Geffner ME. Growth hormone: the expansion of available products and indications. *Pediatr Clin North Am.* 2011;58:1141-1165.
29. Grimberg A, DiVall SA, Polychronakos C, et al. Guidelines for growth hormone and insulin-like growth factor-I treatment in children and adolescents: growth hormone deficiency, idiopathic short stature, and primary insulin-like growth factor-I deficiency. *Horm Res Paediatr.* 2016;86:361-397.
30. Growth Hormone Usage in Short Children: American Association of Clinical Endocrinologists Position Statement. https://www.aace.com/files/position-statements/shortchildren.pdf. Accessed February 14, 2017.
31. Caremark Clinical Programs Review: Focus on pediatric endocrinology. December 8, 2009.
32. Deal CL, Tony M, Hoybye C, et al. Growth Hormone Research Society workshop summary: consensus guidelines for recombinant human growth hormone therapy in Prader-Willi syndrome. *J Clin Endocrinol Metab.* 2013;98:E1072-E1087.
33. Blum WF, Crowe BJ, Quigley CA, et al. Growth hormone is effective in treatment of short stature associated with short stature homeobox-containing gene deficiency: two-year results of a randomized, controlled, multicenter trial. *J Clin Endocrinol Metab.* 2007;92:219-228.
34. Blum WF, Ross JL, Zimmermann AG, et al. GH treatment to final height produces similar height gains in patients with SHOX deficiency and Turner syndrome: results of a multicenter trial. J *Clin Endocrinol Metab*. 2013;98(8):E1383-92.
35. American Association of Clinical Endocrinologists. Medical guidelines for clinical practice for growth hormone use in growth hormone-deficient adults and transition patients 2009 update. *Endocr Pract*. 2009;15(2):1-28.
36. Caremark Clinical Programs Review: Focus on pediatric endocrinology. March 30, 2011.
37. Molitch ME, Clemmons DR, Malozowski S, et al. Evaluation and treatment of adult growth hormone deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2011;96:1587-1609.
38. National Institute for Clinical Excellence: Human growth hormone (somatropin) in adults with growth hormone deficiency. August 2003.
39. Caremark Clinical Programs Review: Focus on pediatric endocrinology. May 15, 2013.
40. Caremark Clinical Programs Review: Focus on pediatric endocrinology. September 10, 2007.
41. Deal C, Hasselmann C, Pfaffle RW, et al. Associations between pituitary imaging abnormalities and clinical and biochemical phenotypes in children with congenital growth hormone deficiency: data from an international observational study. *Horm Res Paediatr.* 2013;79:283-292.
42. National Heart, Lung, and Blood Institute. Obesity Education Initiative: The practical guide: identification, evaluation, and treatment of overweight and obesity in adults. Bethesda, MD: US Dept of Health and Human Services, National Heart, Lung, and Blood Institute; 2000. NIH Publication No. 00-4084.
43. Macrilen [package insert]. Goettingen, Germany: Allphamed Pharbil Arzneimittel GmbH; December 2017.

Reference number(s)
2100-A

SPECIALTY GUIDELINE MANAGEMENT

HAEGARDA (C1 Esterase Inhibitor Subcutaneous [Human])

POLICY

XXI. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Routine prophylaxis to prevent Hereditary Angioedema (HAE) attacks in adolescent and adult patients

All other indications are considered experimental/investigational and are not a covered benefit.

XXII. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

D. C4 levels and C1 inhibitor functional and antigenic protein levels
E. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
F. Chart notes confirming family history of angioedema, if applicable

XXIII. CRITERIA FOR APPROVAL

Authorization of 12 months may be granted for prevention of hereditary angioedema attacks when Haegarda will not be used in combination with Cinryze or Takhzyro and either of the following criteria is met:

C. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing.
1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)

D. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

XXIV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:
C. Member meets the criteria for initial approval.
D. Member has experienced reduction in frequency, severity, and/or duration of attacks since starting treatment.

XXV. REFERENCES

1. Haegarda [package insert]. Kankakee, IL: CSL Behring LLC; October 2017.

2. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Allergy*. 2018;00:1-22.
3. Cicardi M, Bork K, Caballero T, et al. Hereditary Angioedema International Working Group. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy.* 2012;67:147-157.
4. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
5. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol: In Practice*. 2013; 1(5): 458-467.
6. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. *Allergy Asthma Proc*. 2012; 33(6):S145-S156.
7. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109:395-202.
8. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014;69: 602-616.
9. Bowen T. Hereditary angioedema: beyond international consensus – circa December 2010 – The Canadian Society of Allergy and Clinical Immunology Dr. David McCourtie Lecture. *Allergy Asthma Clin Immunol*. 2011;7(1):1.
10. Bernstein J. Update on angioedema: Evaluation, diagnosis, and treatment. *Allergy and Asthma Proceedings.* 2011;32(6):408-412.
11. Longhurst H, Cicardi M. Hereditary angio-edema. *Lancet.* 2012;379:474-481.
12. Farkas H, Martinez-Saguer I, Bork K, et al. International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency. *Allergy.* 2017;72(2):300-313.
13. Henao MP, Kraschnewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management.* 2016; 12: 701-711.

Reference number(s)
2134-A, 2677-A

SPECIALTY GUIDELINE MANAGEMENT

HARVONI (ledipasvir and sofosbuvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Harvoni is indicated for the treatment of:

1. Adult patients with chronic hepatitis C virus (HCV):
   a. genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis
   b. genotype 1 infection with decompensated cirrhosis, for use in combination with ribavirin
   c. genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, for use in combination with ribavirin

2. Pediatric patients 12 years of age and older or weighing at least 35 kg with HCV genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, without ribavirin

1. Genotype 1 infection

a. Authorization of up to 12 weeks total may be granted for treatment-naïve members with compensated cirrhosis.
b. Authorization of up to 12 weeks total may be granted for treatment-naïve members without cirrhosis who have HIV co-infection, are African American, are less than 18 years of age, or have pre-treatment HCV RNA greater than or equal to 6 million IU/mL.
c. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis who have pre-treatment HCV RNA below 6 million IU/mL and are HIV-uninfected and non-African American.
d. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV) with or without an HCV protease inhibitor (telaprevir, boceprevir, or simeprevir).
e. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

2. Genotype 4 infection

a. Authorization of up to 12 weeks total may be granted for treatment-naïve members without cirrhosis or with compensated cirrhosis.
b. Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

3. Genotype 5 infection

Authorization of up to 12 weeks total may be granted for members who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

4. **Genotype 6 infection**
   Authorization of up to 12 weeks total may be granted for members who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

5. **Decompensated cirrhosis (CTP class B or C)**
   Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection and documented anemia (baseline Hgb below 10 g/dL) or RBV ineligibility (see Section IV).

6. **Kidney transplant recipients**
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 1 or 4 infection.

B. Chronic hepatitis C virus infection, in combination with ribavirin

1. **Genotype 1 infection**
   a. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.
   b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) plus RBV with or without PEG-IFN.

2. **Genotype 4 infection**
   Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

3. **Decompensated cirrhosis (CTP class B or C)**
   a. Authorization of up to 12 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection.
   b. Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection who failed prior treatment with a sofosbuvir-based regimen (eg, sofosbuvir and RBV, sofosbuvir plus PEG-IFN and RBV, sofosbuvir plus simeprevir with or without RBV).
   c. Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 4, 5 or 6 infection post liver transplantation and decompensated cirrhosis (see section B.4 below).

4. **Recurrent HCV infection post liver transplantation**
   Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 4, 5 or 6 infection post liver transplantation.

C. HCV and HIV coinfection

Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX: RIBAVIRIN INELIGIBILITY

RBV ineligibility is defined as one or more of the below:

- Intolerance to RBV
- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

V. REFERENCES

1. Harvoni [package insert]. Foster City, CA: Gilead Sciences; April 2017.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Last changes made September 21, 2017. Accessed September 22. 2017.

Reference number(s)
2134-A, 2677-A

SPECIALTY GUIDELINE MANAGEMENT

HARVONI (ledipasvir and sofosbuvir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Harvoni is indicated for the treatment of:

1. Adult patients with chronic hepatitis C virus (HCV):
   a. genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis
   b. genotype 1 infection with decompensated cirrhosis, for use in combination with ribavirin
   c. genotype 1 or 4 infection who are liver transplant recipients without cirrhosis or with compensated cirrhosis, in combination with ribavirin

2. Pediatric patients 12 years of age and older or weighing at least 35 kg with HCV genotype 1, 4, 5, or 6 infection without cirrhosis or with compensated cirrhosis.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, without ribavirin

1. Genotype 1 infection

a. Authorization of up to 12 weeks total may be granted for treatment-naïve members with compensated cirrhosis.
b. Authorization of up to 12 weeks total may be granted for treatment-naïve members without cirrhosis who have HIV co-infection, are African American, are less than 18 years of age, or have pre-treatment HCV RNA greater than or equal to 6 million IU/mL.
c. Authorization of up to 8 weeks total may be granted for treatment-naive members without cirrhosis who have pre-treatment HCV RNA below 6 million IU/mL and are HIV-uninfected and non-African American.
d. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with peginterferon alfa (PEG-IFN) and ribavirin (RBV) with or without an HCV protease inhibitor (telaprevir, boceprevir, or simeprevir).
e. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV proteaseinhibitor.

2. Genotype 4 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

3. Genotype 5 infection

Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

4. **Genotype 6 infection**
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who are treatment-naïve or who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

5. **Decompensated cirrhosis (CTP class B or C)**
   Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection and documented anemia (baseline Hgb below 10 g/dL) or RBV ineligibility (see Section IV).

6. **Kidney transplant recipients**
   Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have HCV genotype 1 or 4 infection.

B. Chronic hepatitis C virus infection, in combination with ribavirin

1. **Genotype 1 infection**
   a. Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.
   b. Authorization of up to 12 weeks total may be granted for members without cirrhosis who failed prior treatment with sofosbuvir (Sovaldi) plus RBV with or without PEG-IFN.

2. **Genotype 4 infection**
   Authorization of up to 12 weeks total may be granted for members with compensated cirrhosis who failed prior treatment with PEG-IFN and RBV with or without an HCV protease inhibitor.

3. **Decompensated cirrhosis (CTP class B or C)**
   a. Authorization of up to 12 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection.
   b. Authorization of up to 24 weeks total may be granted for members with HCV genotype 1, 4, 5 or 6 infection who failed prior treatment with a sofosbuvir-based regimen (eg, sofosbuvir and RBV, sofosbuvir plus PEG-IFN and RBV, sofosbuvir plus simeprevir with or without RBV).
   c. Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 4, 5 or 6 infection post liver transplantation and decompensated cirrhosis (see section B.4 below).

4. **Recurrent HCV infection post liver transplantation**
   Authorization of up to 12 weeks total may be granted for members with recurrent HCV genotype 1, 4, 5 or 6 infection post liver transplantation.

C. HCV and HIV coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A or B above are met.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. APPENDIX: RIBAVIRIN INELIGIBILITY

RBV ineligibility is defined as one or more of the below:

- Intolerance to RBV
- Pregnant female or male whose female partner is pregnant
- Hemoglobinopathy
- Coadministration with didanosine
- History of significant or unstable cardiac disease

V. REFERENCES

1. Harvoni [package insert]. Foster City, CA: Gilead Sciences; November 2017.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Last changes made May 24, 2018. Accessed August 02.2018.

Reference number(s)
1905-A

SPECIALTY GUIDELINE MANAGEMENT

HERCEPTIN (trastuzumab)
KANJINTI (trastuzumab-anns)
OGIVRI (trastuzumab-dkst)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Adjuvant breast cancer
   Treatment of human epidermal growth factor receptor 2 (HER2)-overexpressing node positive or node negative (estrogen receptor (ER)/progesterone receptor (PR) negative or with one high risk feature) breast cancer:
   a. As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
   b. As part of a treatment regimen with docetaxel and carboplatin
   c. As a single agent following multi-modality anthracycline based therapy
2. Metastatic breast cancer
   a. In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer
   b. As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease
3. Metastatic gastric cancer
   In combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma, who have not received prior treatment for metastatic disease

B. Compendial Uses

A. HER2-positive breast cancer
   a. Neoadjuvant therapy
   b. Treatment of recurrent or stage IV (M1) disease
B. Intra-cerebrospinal fluid (CSF) treatment for leptomeningeal metastases from breast cancer
C. HER2-positive esophageal and esophagogastric junction cancer
D. HER2- positive advanced and recurrent uterine serous carcinoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast Cancer

1. Authorization of 6 months may be granted for neoadjuvant treatment of HER2-positive breast cancer.
2. Authorization of up to 12 months total may be granted for adjuvant treatment of HER2-positive breast cancer.
3. Authorization of 12 months may be granted for treatment of HER2-positive recurrent or metastatic breast cancer.
4. Authorization of 12 months may be granted for intra-CSF treatment for leptomeningeal metastases from breast cancer.

B. Esophageal, Gastric, or Gastroesophageal Junction Cancer

Authorization of 12 months may be granted for treatment of HER2-positive esophageal, gastric, or gastroesophageal junction cancer.

C. Uterine Serous Carcinoma

Authorization of 12 months may be granted for treatment of HER2-positive advanced and recurrent uterine serous carcinoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Herceptin [package insert]. South San Francisco, CA: Genentech, Inc.; November 2018.
2. Kanjinti [package insert]. Thousand Oaks, CA: Amgen, Inc.; June 2019.
3. Ogivri [package insert]. Zurich, Switzerland: Mylan GmbH; December 2017.
4. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed January 26, 2019.
5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 3.2018. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed January 26, 2019.
6. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Esophageal and Esophagogastric Junction Cancers. Version 2.2018. https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf. Accessed January 26, 2019.

Reference number(s)
2043-A

SPECIALTY GUIDELINE MANAGEMENT

Subcutaneous Immune Globulin (SCIG): Hizentra®, HyQvia®, Cutaquig®, Cuvitru™ and Xembify®

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Cutaquig (Immune Globulin Subcutaneous [Human] - hipp, 16.5% Solution)
   Cutaquig is indicated as replacement therapy for primary humoral immunodeficiency (PI) in adults.
2. Cuvitru (Immune Globulin Subcutaneous [Human], 20% Solution)
   Cuvitru is indicated as replacement therapy for primary humoral immunodeficiency in adult and pediatric patients two years of age and older.
3. Hizentra (Immune Globulin Subcutaneous [Human], 20% Liquid)
   a. Hizentra is indicated as replacement therapy for primary humoral immunodeficiency in adults and pediatric patients 2 years of age and older.
   b. Hizentra is indicated for the treatment of adult patients with chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment.
   Limitations of Use:
   Hizentra maintenance therapy in CIDP has been systematically studied for 6 months and for a further 12 months in a follow-up study. Maintenance therapy beyond these periods should be individualized based upon the patient's response and need for continued therapy.
4. HyQvia (Immune Globulin Infusion 10% [Human] with Recombinant Human Hyaluronidase)
   HyQvia is indicated for the treatment of primary immunodeficiency in adults.
   Limitation of Use: Safety and efficacy of chronic use of recombinant human hyaluronidase in HyQvia have not been established in conditions other than primary immunodeficiency.
5. Xembify (Immune Globulin Subcutaneous [Human} – klhw, 20% Solution)

Xembify is indicated for treatment of primary humoral immunodeficiency (PI) in patients 2 years of age and older.

B. Compendial Uses

1. Idiopathic thrombocytopenic purpura (ITP)
2. Multifocal motor neuropathy
3. Kawasaki syndrome
4. B-cell chronic lymphocytic leukemia (CLL)
5. Prophylaxis of bacterial infections in pediatric human immunodeficiency virus (HIV) infection
6. Prophylaxis of bacterial infections in bone marrow transplant (BMT)/hematopoietic stem cell transplant (HSCT) recipients
7. Dermatomyositis
8. Polymyositis
9. Myasthenia gravis
10. Guillain-Barré syndrome

11. Lambert-Eaton myasthenic syndrome
12. Fetal/neonatal alloimmune thrombocytopenia
13. Parvovirus B19-induced pure red cell aplasia
14. Stiff-person syndrome
15. Management of immune checkpoint inhibitor-related nervous system adverse events
16. Acquired red cell aplasia
17. Acute disseminated encephalomyelitis
18. Autoimmune mucocutaneous blistering diseases
19. Autoimmune hemolytic anemia
20. Autoimmune neutropenia
21. Birdshot retinochoroidopathy
22. BK virus associated nephropathy
23. Churg-Strauss Syndrome
24. Enteroviral meningoencephalitis
25. Hematophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS)
26. Hemolytic disease of newborn
27. HIV-associated thrombocytopenia
28. Hyperimmunoblobulinemia E Syndrome
29. Hypogammaglobulinemia from chimeric antigen receptor T (CAR-T) therapy
30. Multiple myeloma
31. Neonatal hemochromatosis, prophylaxis
32. Opsoclonus-myoclonus
33. Paraneoplastic opsonus-myoclonus ataxia associated with neuroblastoma
34. Post-transfusion purpura
35. Rasmussen encephalitis
36. Renal transplantation from a live donor with ABO incompatibility or positive cross match
37. Secondary immunosuppression associated with major surgery, hematological malignancy, major burns, and collagen-vascular diseases
38. Solid organ transplantation, for allosensitized members
39. Toxic epidermal necrolysis and Stevens-Johnson syndrome
40. Toxic shock syndrome
41. Systemic lupus erythematosus (SLE)
42. Toxic necrotizing fasciitis due to group A streptococcus

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

A. Primary immunodeficiency
   1. Diagnostic test results (when applicable)
      a. Copy of laboratory report with serum immunoglobulin levels: IgG, IgA, IgM, and IgG subclasses
      b. Vaccine response to pneumococcal polysaccharide vaccine (post-vaccination *Streptococcus pneumoniae* antibody titers)
      c. Pertinent genetic or molecular testing in members with a known genetic disorder
      d. Copy of laboratory report with lymphocyte subset enumeration by flow cytometry
   2. IgG trough level for those continuing with IVIG therapy

B. Myasthenia gravis
   1. Clinical records describing standard treatments tried and failed

C. Secondary hypogammaglobulinemia (CLL, HIV, BMT/HSCT recipients, surgery, malignancy, burns, collagen-vascular disease)
   1. Copy of laboratory report with pre-treatment serum IgG level (when applicable)

D. Chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN)
   1. Pre-treatment electrodiagnostic studies (electromyography [EMG] or nerve conduction studies [NCS])
   2. For CIDP, pre-treatment cerebrospinal fluid (CSF) analysis (when available)
E. Dermatomyositis and polymyositis
   1. Pre-treatment electrodiagnostic studies (EMG/NCS)
   2. Pre-treatment muscle biopsy report (when available)
   3. Clinical records describing standard treatments tried and failed
F. Lambert-Eaton Myasthenic Syndrome (LEMS)
   1. Neurophysiology studies (e.g., electromyography) (when applicable)
   2. A positive anti- P/Q type voltage-gated calcium channel antibody test (when applicable)
G. Idiopathic thrombocytopenic purpura
   1. Laboratory report with pre-treatment/current platelet count
   2. Chronic/persistent ITP: copy of medical records supporting trial and failure with corticosteroid or anti-D therapy (unless contraindicated)
H. Parvovirus B19-indicated Pure Red Cell Aplasia (PRCA)
   1. Copy of test result confirming presence of parvovirus B19
I. Stiff-person syndrome
   1. Anti-glutamic acid decarboxylase (GAD) antibody testing results
   2. Clinical records describing standard treatments tried and failed
J. Toxic shock syndrome or toxic necrotizing fasciitis due to group A streptococcus
   1. Documented presence of fasciitis (when applicable)
   2. Microbiological data (culture or Gram stain)

III. CRITERIA FOR INITIAL APPROVAL

a. Primary Immunodeficiency

Initial authorization of 6 months may be granted for members with any of the following diagnoses:

1. Severe combined immunodeficiency (SCID) or congenital agammaglobulinemia (eg, X-linked or autosomal recessive agammaglobulinemia)
   1. Diagnosis confirmed by genetic or molecular testing, or
   2. Pretreatment IgG level < 200 mg/dL, or
   3. Absence or very low number of T cells (CD3 T cells < 300/microliter) or the presence of maternal T cells in the circulation (SCID only)
2. Wiskott-Aldrich syndrome, DiGeorge syndrome, or ataxia-telangiectasia (or other non-SCID combined immunodeficiency)
   1. Diagnosis confirmed by genetic or molecular testing (if applicable), and
   2. History of recurrent bacterial infections (eg, pneumonia, otitis media, sinusitis, sepsis, gastrointestinal), and
   3. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
3. Common variable immunodeficiency (CVID)
   1. Age 4 years or older, and
   2. Other causes of immune deficiency have been excluded (eg, drug induced, genetic disorders, infectious diseases such as HIV, malignancy), and
   3. Pretreatment IgG level < 500 mg/dL or ≥ 2 SD below the mean for age, and
   4. History of recurrent bacterial infections, and
   5. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
4. Hypogammaglobulinemia (unspecified), IgG subclass deficiency, selective IgA deficiency, selective IgM deficiency, or specific antibody deficiency
   1. History of recurrent bacterial infections
   2. Impaired antibody response to pneumococcal polysaccharide vaccine (see Appendix A)
   3. Any of the following pre-treatment laboratory findings:

i. Hypogammaglobulinemia: IgG < 500 mg/dL or ≥ 2 SD below the mean for age
ii. Selective IgA deficiency: IgA level < 7 mg/dL with normal IgG and IgM levels
iii. Selective IgM deficiency: IgM level < 30 mg/dL with normal IgG and IgA levels
iv. IgG subclass deficiency: IgG1, IgG2, or IgG3 ≥ 2 SD below mean for age assessed on at least 2 occasions; normal IgG (total) and IgM levels, normal/low IgA levels
v. Specific antibody deficiency: normal IgG, IgA and IgM levels

5. Other predominant antibody deficiency disorders must meet a., b., and c.i. in section 4. above.
6. Other combined immunodeficiency must meet criteria in section 2. above.

Re-authorization of 6 months may be granted when the following criteria are met:
1. A reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy, AND
2. IgG trough levels are monitored at least yearly and maintained at or above the lower range of normal for age (when applicable for indication), OR
3. The prescriber will re-evaluate the dose of IVIG and consider a dose adjustment (when appropriate).

B. Myasthenia Gravis

1. Authorization of 1 month may be granted to members who are prescribed IVIG for worsening weakness, acute exacerbation, or in preparation for surgery.
   a. Worsening weakness includes an increase in any of the following symptoms: diplopia, ptosis, blurred vision, difficulty speaking (dysarthria), difficulty swallowing (dysphagia), difficulty chewing, impaired respiratory status, fatigue, and limb weakness. Acute exacerbations include more severe swallowing difficulties and/or respiratory failure
   b. Pre-operative management (eg, prior to thymectomy)
2. Authorization of 6 months may be granted to members with refractory myasthenia gravis who have tried and failed 2 or more of standard therapies (eg, corticosteroids, azathioprine, cyclosporine, mycophenolate mofetil, rituximab).

C. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

1. Initial authorization of 3 months may be granted when the following criteria are met:
   a. Disease course is progressive or relapsing/remitting for 2 months or longer
   b. Moderate to severe functional disability
   c. The diagnosis was confirmed by electrodiagnostic studies and the evaluation of cerebrospinal fluid (CSF)
2. Re-authorization of 6 months may be granted when the following criteria are met:
   a. Significant improvement in disability and maintenance of improvement since initiation of IVIG therapy
   b. IVIG is being used at the lowest effective dose and frequency

D. Dermatomyositis or Polymyositis

1. Initial authorization of 3 months may be granted when the following criteria are met:
   a. Member has at least 4 of the following:
      i. Proximal muscle weakness (upper or lower extremity and trunk)
      ii. Elevated serum creatine kinase (CK) or aldolase level
      iii. Muscle pain on grasping or spontaneous pain
      iv. Myogenic changes on EMG (short-duration, polyphasic motor unit potentials with spontaneous fibrillation potentials)
      v. Positive anti-Jo-1 (histadyl tRNA synthetase) antibody
      vi. Non-destructive arthritis or arthralgias
      vii. Systemic inflammatory signs (fever: more than 37°C at axilla, elevated serum CRP level or accelerated ESR of more than 20 mm/h by the Westergren method,
      viii. Pathological findings compatible with inflammatory myositis (inflammatory infiltration of skeletal evidence of active regeneration may be seen), and

b. Standard first-line treatments (corticosteroids) and second-line treatments (immunosuppressants) have been tried but were unsuccessful or not tolerated, or
c. Member is unable to receive standard first-line and second-line therapy because of a contraindication or other clinical reason.

2. Re-authorization of 6 months may be granted when the following criterion is met:
a. Significant improvement in disability and maintenance of improvement since initiation of IVIG therapy

E. Idiopathic Thrombocytopenic Purpura (Immune Thrombocytopenia)

1. Newly diagnosed ITP (diagnosed within the past 3 months) or initial therapy: authorization of 1 month may be granted when the following criteria are met
a. Children (< 18 years of age)
i. Significant bleeding symptoms (mucosal bleeding or other moderate/severe bleeding) or
ii. High risk for bleeding* (see Appendix B), or
iii. Rapid increase in platelets is required* (eg, surgery or procedure)
b. Adults (≥ 18 years of age)
i. Platelet count < 30,000/mcL, or
ii. Platelet count < 50,000/mcL and significant bleeding symptoms, high risk for bleeding or rapid increase in platelets is required*, and
iii. Corticosteroid therapy is contraindicated and IVIG will be used alone or IVIG will be used in combination with corticosteroid therapy
2. Chronic/persistent ITP (≥ 3 months from diagnosis) or ITP unresponsive to first-line therapy: authorization of 6 months may be granted when the following criteria are met:
a. Platelet count < 30,000/mcL, or
b. Platelet count < 50,000/mcL and significant bleeding symptoms, high risk for bleeding* or rapid increase in platelets is required*, and
c. Relapse after previous response to IVIG or inadequate response/intolerance/contraindication to corticosteroid or anti-D therapy
3. Adults with refractory ITP after splenectomy: authorization of 6 months may be granted when either of the following criteria is met:
a. Platelet count < 30,000/mcL, or
b. Significant bleeding symptoms
4. ITP in pregnant women: authorization through delivery may be granted to pregnant women with ITP.

* The member's risk factor(s) for bleeding (see Appendix B) or reason requiring a rapid increase in platelets must be provided.

F. B-cell Chronic Lymphocytic Leukemia (CLL)

1. Initial authorization of 6 months may be granted when all of the following criteria are met:
a. IVIG is prescribed for prophylaxis of bacterial infections.
b. Member has a history of recurrent sinopulmonary infections requiring intravenous antibiotics or hospitalization.
c. Member has a pretreatment serum IgG level <500 mg/dL.
2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy.

G. Prophylaxis of Bacterial Infections in HIV-Infected Pediatric Patients

1. Initial authorization of 6 months may be granted to pediatric members with HIV infection when any of the following criteria are met:
a. IVIG is prescribed for primary prophylaxis of bacterial infections and pretreatment serum IgG < 400 mg/dL, or
b. IVIG is prescribed for secondary prophylaxis of bacterial infections for members with a history of recurrent bacterial infections (> 2 serious bacterial infections in a 1-year period), or

c. Member has failed to form antibodies to common antigens, such as measles, pneumococcal, and/or Haemophilus influenzae type b vaccine, or
d. Member lives in an area where measles is highly prevalent and who have not developed an antibody response after two doses of measles, mumps, and rubella virus vaccine live, or
e. Member has been exposed to measles and request is for a single dose, or
f. Member has chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy

2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy.

H. Prophylaxis of Bacterial Infections in BMT/HSCT Recipients

1. Initial authorization of 6 months may be granted to members who are BMT/HSCT recipients when the following criteria are met:
   a. IVIG is prescribed for prophylaxis of bacterial infections.
   b. Either of the following:
      i. IVIG is requested within the first 100 days post-transplant.
      ii. Member has a pretreatment serum IgG < 400 mg/dL.
2. Re-authorization of 6 months may be granted when a reduction in the frequency of bacterial infections has been demonstrated since initiation of IVIG therapy.

I. Multifocal Motor Neuropathy (MMN)

1. Initial authorization of 3 months may be granted when the following criteria are met:
   a. Member experienced progressive, multifocal, asymmetrical weakness without objective sensory loss in 2 or more nerves for at least 1 month
   b. The diagnosis was confirmed by electrodiagnostic studies
2. Re-authorization of 6 months may be granted when significant improvement in disability and maintenance of improvement have occurred since initiation of IVIG therapy

J. Guillain-Barre Syndrome (GBS)

Authorization of 2 months total may be granted for GBS when the following criteria are met:

1. Member has severe disease with significant weakness (eg inability to stand or walk without aid, respiratory weakness)
2. Onset of neurologic symptoms occurred less than 4 weeks from the anticipated start of therapy

K. Lambert-Eaton Myasthenic Syndrome (LEMS)

1. Initial authorization of 6 months may be granted for LEMS when the following criteria are met:
   a. Diagnosis has been confirmed by either of the following:
      i. Neurophysiology studies (e.g., electromyography)
      ii. A positive anti- P/Q type voltage-gated calcium channel antibody test
   b. Anticholinesterases (eg pyridostigmine) and amifampridine (eg 3,4-diaminopyridine phosphate, Firdapse) have been tried but were unsuccessful or not tolerated
   c. Weakness is severe or there is difficulty with venous access for plasmapheresis
2. Re-authorization of 6 months may be granted when member is responding to therapy (i.e., there is stability or improvement in symptoms relative to the natural course of LEMS).

L. Kawasaki Syndrome

Authorization of 1 month may be granted for pediatric members with Kawasaki syndrome.

M. Fetal/Neonatal Alloimmune Thrombocytopenia (F/NAIT)

Authorization of 6 months may be granted for treatment of F/NAIT.

N. Parvovirus B19-induced Pure Red Cell Aplasia (PRCA)

Authorization of 6 months may be granted for severe, refractory anemia associated with bone marrow

suppression, with parvovirus B19 viremia.

O. Stiff-person Syndrome

Authorization of 6 months may be granted for stiff-person syndrome when the following criteria are met:

1. Diagnosis has been confirmed by anti-glutamic acid decarboxylase (GAD) antibody testing
2. Member had an inadequate response to first-line treatment (benzodiazepines and/or baclofen)

P. Management of immune checkpoint inhibitor-related nervous system adverse events

Authorization of 1 month may be granted for management of immune checkpoint-inhibitor toxicities when all of the following criteria are met:

1. Member has experienced a moderate or severe adverse event to a PD-1 or PD-L1 inhibitor (eg, pembrolizumab, nivolumab, atezolizumab, avelumab, durvalumab)
2. The offending medication has been held or discontinued
3. Member experienced one or more of the following nervous system adverse events: pneumonitis, myasthenia gravis, peripheral neuropathy, encephalitis, transverse myelitis, or severe inflammatory arthritis

Q. Acquired Red Cell Aplasia

Authorization of 6 months may be granted for acquired red cell aplasia.

R. Acute Disseminated Encephalomyelitis

Authorization of 6 months may be granted for acute disseminated encephalomyelitis in members who have had an insufficient response to intravenous corticosteroid treatment.

S. Autoimmune Mucocutaneous Blistering Disease

Authorization of 6 months may be granted for autoimmune mucocutaneous blistering disease (includes pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid, and epidermolysis bullosa aquisita) when the following criteria are met:

1. Diagnosis has been proven by biopsy and confirmed by pathology report, and
2. Condition is rapidly progressing, extensive or debilitating, and
3. Member has failed or experienced significant complications (eg diabetes, steroid-induced osteoporosis) from standard treatment (corticosteroids, immunosuppressive agents).

T. Autoimmune Hemolytic Anemia

Authorization of 6 months may be granted for warm-type autoimmune hemolytic anemia in members who do not respond or have a contraindication to corticosteroids or splenectomy.

U. Autoimmune Neutropenia

Authorization of 6 months may be granted for autoimmune neutropenia where treatment with G-CSF (granulocyte colony stimulating factor) is not appropriate.

V. Birdshot Retinochoroidopathy

Authorization of 6 months may be granted for birdshot (vitiliginous) retinochoroidopathy that is not responsive to immunosuppressives (eg corticosteroids, cyclosporine).

W. BK Virus Associated Nephropathy

Authorization of 6 months may be granted for BK virus associated nephropathy.

X. Churg-Strauss Syndrome

Authorization of 6 months may be granted for severe, active Churg-Strauss syndrome as adjunctive therapy for members who have experienced failure, intolerance, or are contraindicated to other interventions.

Y. Enteroviral Meningoencephalitis

Authorization of 6 months may be granted for severe cases of enteroviral meningoencephalitis.

Z. Hematophagocytic Lymphohistiocytosis (HLH) or Macrophage Activation Syndrome (MAS)
Authorization of 6 months may be granted for treatment of hypogammaglobulinemia in HLH or MAS when total IgG is less than 400 mg/dL or two standard deviations below the mean for age.

AA. Hemolytic Disease of Newborn
Authorization of 6 months may be granted for isoimmune hemolytic disease in neonates.

BB. HIV-associated Thrombocytopenia
Authorization of 6 months may be granted for HIV-associated thrombocytopenia when the following criteria are met:
1. Pediatric members with IgG < 400 mg/dL and has one of the following:
   a. 2 or more bacterial infections in a 1-year period despite antibiotic chemoprophylaxis with TMP-SMZ or another active agent, or
   b. Received 2 doses or measles vaccine and lives in a region with a high prevalence or measles, or
   c. HIV-associated thrombocytopenia despite anti-retroviral therapy, or
   d. Chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy, or
   e. T4 cell count ≥ 200/mm^3
2. Adult members with significant bleeding, platelet count < 20,000/mcL, and failure of RhIG in Rh-positive patients

CC. Hyperimmunoglobulinemia E Syndrome
Authorization of 6 months may be granted to treat severe eczema in hyperimmunoglobulinemia E syndrome.

DD. Hypogammaglobulinemia from CAR-T therapy
Authorization of 6 months may be granted for members with IgG < 400 mg/dL receiving treatment with CAR-T therapy (tisagenlecleucel [Kymriah] or axicabtagene ciloleucel [Yescarta]).

EE. Multiple Myeloma
Authorization of 6 months may be granted for multiple myeloma in members who have recurrent, serious infections despite the use of prophylactic antibiotics.

FF. Neonatal Hemochromatosis
Authorization of 6 months may be granted for prophylaxis in members who are pregnant with a history of pregnancy ending in documented neonatal hemochromatosis.

GG. Opsoclonus-myoclonus
Authorization of 6 months may be granted for treatment of either of the following:
1. Paraneoplastic opsoclonus-myoclonus-ataxia associated with neuroblastoma
2. Refractory opsoclonus-myoclonus, as last-resort treatment

HH. Post-transfusion Purpura
Authorization of 1 month may be granted for post-transfusion purpura.

II. Rasmussen Encephalitis
Authorization of 6 months may be granted for Rasmussen encephalitis in members whose symptoms do not improve with anti-epileptic drugs and corticosteroids.

JJ. Renal Transplantation
Authorization of 6 months may be granted for a member undergoing renal transplantation from a live donor with ABO incompatibility or positive cross match.

KK. Secondary Immunosuppression Associated with Major Surgery, Hematological Malignancy, Major Burns, and Collagen-Vascular Diseases

Authorization of 6 months may be granted to prevent or modify recurrent bacterial or viral infections in members with secondary immunosuppression (IgG < 400 mg/dL) associated with major surgery, hematological malignancy, extensive burns, or collagen-vascular disease.

LL. Solid Organ Transplantation
Authorization of 6 months may be granted for solid organ transplantation for allosensitized members.

MM. Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome
Authorization of 1 month may be granted for severe cases of toxic epidermal necrolysis or Stevens-Johnson syndrome.

NN. Toxic Shock Syndrome
Authorization of 1 month may be granted for staphylococcal or streptococcal toxic shock syndrome when the infection is refractory to several hours of aggressive therapy, an undrainable focus is present, or the member has persistent oliguria with pulmonary edema.

OO. Systemic Lupus Erythematosus
Authorization of 6 months may be granted for severe, active SLE in members who have experienced inadequate response, intolerance or have a contraindication to first and second line therapies.

PP. Toxic Necrotizing Fasciitis Due To Group A Streptococcus
Authorization of 1 month may be granted for members with fasciitis due to invasive streptococcal infection.

IV. CONTINUATION OF THERAPY

Authorization may be granted for continuation of therapy when either the following criteria is met:
a. For conditions with reauthorization criteria listed under section III: Members who are currently receiving IVIG therapy must meet the applicable reauthorization criteria for the member's condition.
b. For all other conditions, all members (including new members) must meet initial authorization criteria.

V. APPENDICES

Appendix A: Impaired Antibody Response to Pneumococcal Polysaccharide Vaccine
- Age 2 years and older: impaired antibody response demonstrated to vaccination with a pneumococcal polysaccharide vaccine
- Not established for children less than 2 years of age
- Excludes the therapy initiated in the hospital setting

Appendix B: Examples of Risk Factors for Bleeding (not all inclusive)
- Undergoing a medical or dental procedure where blood loss is anticipated
- Comorbidity (eg, peptic ulcer disease, hypertension)
- Mandated anticoagulation therapy
- Profession or lifestyle predisposes patient to trauma (eg, construction worker, fireman, professional athlete)

VI. REFERENCES
1. Cutaquig [package insert]. Hoboken, NJ: Octapharma USA Inc.; December 2018.
2. Cuvitru [package insert]. Lexington, MA: Baxalta US Inc.; February 2019.
3. Hizentra [package insert]. Kankakee, IL: CSL Behring LLC; March 2018.
4. HyQvia [package insert]. Lexington, MA: Baxalta US Inc.; January 2019.

5. Xembify [package insert]. Research Triangle Park, NC: Grifols Therapeutics LLC; July 2019.
6. Asceniv [package insert]. Boca Raton, FL: ADMA Biologics; April 2019.
7. Bivigam [package insert]. Boca Raton, FL: Biotest Pharmaceuticals Corporation; January 2017.
8. Carimune NF [package insert]. Kankakee, IL: CSL Behring LLC; November 2016.
9. Flebogamma 10% DIF [package insert]. Los Angeles, CA: Grifols Biologicals, Inc.; July 2017.
10. Flebogamma 5% DIF [package insert]. Los Angeles, CA: Grifols Biologicals, Inc.; July 2017.
11. Gammagard Liquid [package insert]. Westlake Village, CA: Baxalta US Inc.; June 2016.
12. Gammagard S/D [package insert]. Lexington, MA: Baxalta US Inc.; August 2017.
13. Gammagard S/D IgA less than 1 mcg/mL [package insert]. Westlake Village, CA: Baxalta US Inc.; September 2016.
14. Gammaked [package insert]. Research Triangle Park, NC: Grifols Therapeutics LLC; June 2018.
15. Gammaplex 5% [package insert]. Hertfordshire, United Kingdom: Bio Products Laboratory; December 2016.
16. Gammaplex 10% [package insert]. Hertfordshire, United Kingdom: Bio Products Laboratory; April 2018.
17. Gamunex-C [package insert]. Research Triangle Park, NC: Grifols Therapeutics Inc.; June 2018.
18. Octagam 10% [package insert]. Hoboken, NJ: Octapharma USA, Inc.; April 2015.
19. Octagam 5% [package insert]. Hoboken, NJ: Octapharma USA, Inc.; October 2014.
20. Panzyga [package insert]. Hoboken, NJ: Octapharma USA.; January 2019.
21. Privigen [package insert]. Kankakee, IL: CSL Behring LLC; September 2017.
22. DRUGDEX® System (electronic version). Truven Health Analytics, Ann Arbor, MI. Available at http://www.micromedexsolutions.com [available with subscription]. Accessed June 16, 2019.
23. AHFS Drug Information. http://online.lexi.com/lco. Accessed June 16, 2019.
24. Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: a review of evidence by Work Group Report of the American Academy of Allergy, Asthma, and Immunology. *J Allergy Clin Immunol*. 2017;139:S1-46.
25. Panel on Opportunistic Infections in HIV-Exposed and HIV-Infected Children. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children. Department of Health and Human Services. Available at https://aidsinfo.nih.gov/contentfiles/lvguidelines/oi_guidelines_pediatrics.pdf. Accessed June 18, 2019.
26. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplant recipients: a global perspective. *Biol Blood Marrow Transplant*. 2009;15(10):1143-1238.
27. Feasby T, Banwell B, Bernstead T, et al. Guidelines on the use of intravenous immune globulin for neurologic conditions. *Transfus Med Rev*. 2007;21(2):S57-S107.
28. Donofrio PD, Berger A, Brannagan TH 3rd, et al. Consensus statement: the use of intravenous immunoglobulin in the treatment of neuromuscular conditions report of the AANEM ad hoc committee. *Muscle Nerve*. 2009;40(5):890-900.
29. Elovaara I, Apostolski S, van Doorn P, et al. EFNS guidelines for the use of intravenous immunoglobulin in treatment of neurological diseases: EFNS task force on the use of intravenous immunoglobulin in treatment of neurological diseases. *Eur J Neurol.* 2008;15(9):893-908.
30. Patwa HS, Chaudhry V, Katzberg H, et al. Evidence-based guideline: intravenous immunoglobulin in the treatment of neuromuscular disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology*. 2012;78(13);1009-1015.
31. Anderson D, Kaiser A, Blanchette V, et al. Guidelines on the use of intravenous immune globulin for hematologic conditions. *Transfus Med Rev*. 2007;21(2):S9-S56.
32. Picard C, Al-Herz W, Bousfiha A, et al. Primary immunodeficiency diseases: an update on the classification from the International Union of Immunological Societies Expert Committee for Primary Immunodeficiency. *J Clin Immunol*. 2015; 35(8):696-726.
33. Bonilla FA, Khan DA, Ballas ZK, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. *J Allergy Clin Immunol*. 2015;136(5):1186-205.e1-78.
34. Orange JS, Ballow M, Stiehm ER, et al. Use and interpretation of diagnostic vaccination in primary immunodeficiency: a working group report of the Basic and Clinical Immunology Interest section of the American Academy of Allergy, Asthma and Immunology. *J Allergy Clin Immunol*. 2012;130:S1-S24.
35. Ameratunga R, Woon ST, Gillis D, Koopmans W, Steele R. New diagnostic criteria for common variable immune deficiency (CVID), which may assist with decisions to treat with intravenous or subcutaneous immunoglobulin. *Clin Exp Immunol*. 2013;174(2):203-11.

36. Immune Deficiency Foundation. About primary immunodeficiencies. Specific disease types. http://primaryimmune.org/about-primary-immunodeficiencies/specific-disease-types/. Accessed June 12, 2019.
37. European Society for Immunodeficiencies. Diagnostic criteria for PID. http://esid.org/Working-Parties/Clinical/Resources/Diagnostic-criteria-for-PID2. Accessed June 12, 2019.
38. Immune Deficiency Foundation. *Diagnostic and Clinical Care Guidelines for Primary Immunodeficiency Diseases*. 3rd edition. Towson, MD: Immune Deficiency Foundation; 2015. http://primaryimmune.org/wp-content/uploads/2015/03/2015-Diagnostic-and-Clinical-Care-Guidelines-for-PI.pdf. Accessed June 12, 2019.
39. NCCN Clinical Practice Guidelines in Oncology® Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (Version 5.2019). © 2019 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed June 18, 2019.
40. Van den Bergh PY, Hadden RD, Bouche P, et al. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society - first revision. *Eur J Neurol*. 2010;17(3):356-363.
41. Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Societies guideline on management of multifocal motor neuropathy. *J Peripher Nerv Syst*. 2010;15:295-301.
42. Olney RK, Lewis RA, Putnam TD, Campellone JV. Consensus criteria for the diagnosis of multifocal motor neuropathy. *Muscle Nerve*. 2003;27:117-121.
43. Dalakas M. Inflammatory muscle diseases. *N Engl J Med*. 2015;372(18):1734-1747.
44. Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood.* 2011;117(16):4190-4207.
45. Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood.* 2010;115(2):168-186.
46. Shearer WT, Dunn E, Notarangelo LD, et al. Establishing diagnostic criteria for severe combined immunodeficiency disease (SCID), leaky SCID, and Omenn syndrome: the Primary Immune Deficiency Treatment Consortium experience. *J Allergy Clin Immunol.* 2014;133(4):1092.
47. NCCN Clinical Practice Guidelines in Oncology® Management of Immunotherapy-Related Toxicities (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed June 18, 2019.
48. [HIVPeds]Working Group on Antiretroviral Therapy of the National Pediatric HIV Resource Center. Antiretroviral therapy and medical management of pediatric HIV infection. *Pediatrics*. 1998;102;1005-1063.
49. Center for Medicare and Medicaid Services (CMS). Intravenous immune globulin for autoimmune mucocutaneous blistering diseases. Decision Memorandum. CPG-00109N. Baltimore, MD: CMS; January 22, 2002.
50. Sawinski D, Goral S. BK virus infection: An update on diagnosis and treatment. *Nephrol Dial Transplant*. 2015;30(2):209-217.
51. Groh M, Pagnoux C, Baldini C, et al. Eosinophilic granulomatosis with polyangiitis (Churg–Strauss) (EGPA)Consensus Task Force recommendations for evaluation and management. *Eur J Intern Med*. 2015;26(7):545-553.
52. McKinney RE, Katz SL, Wilfert CM. Chronic enteroviral meningoencephalitis in agammaglobulinemic patients. *Rev Infect Dis*. 1987;9(2):334-56.
53. Sen, E.S., Clarke, SL, Ramanan, A.V. Macrophage Activation Syndrome. *Indian J Pediatr.* 2016;83(3): 248-53.
54. Kimata H. High-dose intravenous gammaglobulin treatment of hyperimmunoglobulinemia E syndrome. *J Allergy Clin Immunol*. 1995;95:771-774.
55. Yescarta [package insert]. Santa Monica, CA: Kite Pharma; October 2017.
56. Kymriah [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2018.
57. Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at https://www.online.lexi.com [available with subscription]. Accessed June 19, 2019.
58. Whitington PF, Kelly S. Outcome of pregnancies at risk for neonatal hemochromatosis is improved by treatment with high-dose intravenous immunoglobulin. *Pediatrics*. 2008;121(6):e1615-e1621.
59. Tate ED, Pranzatelli MR, Verhulst SJ, et al. Active comparator-controlled rater-blinded study of corticotropin-based immunotherapies for opsoclonus-myoclonus syndrome. *J Child Neurol*. 2012; 27:875-884.
60. Mutch LS, Johnston DL. Late presentation of opsoclonus-myoclonus-ataxia syndrome in a child with stage 4S neuroblastoma. *J Pediatr Hematol Oncol*. 2005;27(6):341-343.

61. Sonnenday CJ, Ratner LE, Zachary AA, et al. Preemptive therapy with plasmapheresis/intravenous immunoglobulin allows successful live donor renal transplantation in patients with a positive cross-match. *Transplant Proc*. 2002;34(5):1614-1616.
62. Razonable RR, Humar A. Cytomegalovirus in Solid Organ Transplantation. *Am J Transplant*. 2013;13:93-106.
63. Jordan SC, Toyoda M, Kahwaji J, et al. Clinical Aspects of Intravenous Immunoglobulin Use in Solid Organ Transplant Recipients. *Am J Transplant*. 2011;11:196-202
64. Kimberlin DW, Brady MT, Jackson MA, et al. Staphylococcus aureus. American Academy of Pediatrics. Red Book: 2018 Report of the Committee on Infectious Diseases. 2018:733-746
65. Gordon C, Amissah-Arthur MB, Gayed M, et al. British Society for Rheumatology guideline on management of systemic lupus erythematosus in adults. *Rheumatology (Oxford).* 2018;57:e1-45.

Reference number(s)
2008-A

SPECIALTY GUIDELINE MANAGEMENT

HUMIRA (adalimumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Moderately to severely active rheumatoid arthritis (RA)
2. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)
3. Active psoriatic arthritis (PsA)
4. Active ankylosing spondylitis (AS)
5. Moderately to severely active Crohn's disease (CD)
6. Moderate to severely active ulcerative colitis (UC)
7. Moderate to severe chronic plaque psoriasis (PsO)
8. Moderate to severe Hidradenitis Suppurativa
9. Non-infectious intermediate, posterior and panuveitis

B. Compendial Uses
Axial spondyloarthritis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
1. Authorization of 24 months may be granted for members who have previously received Humira or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
   b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)
1. Authorization of 24 months may be granted for members who have previously received Humira or any other biologic DMARD indicated for moderately to severely active polyarticular juvenile idiopathic arthritis.

2. Authorization of 24 months may be granted for treatment of active pJIA when any of the following criteria is met:

a. Member has experienced an inadequate response to at least a 3-month trial ofmethotrexate.
b. Member has intolerance or contraindication to methotrexate (see Appendix A).

C. Active psoriatic arthritis (PsA)
Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis
1. Authorization of 24 months may be granted for members who have previously received Humira or any other biologic DMARD indicated for active ankylosing spondylitis.

2. Authorization of 24 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
   b. Member has an intolerance or contraindication to two or more NSAIDs.

E. Moderately to severely active Crohn's disease (CD)
1. Authorization of 24 months may be granted for members who have previously received Humira or any other biologic indicated for the treatment of Crohn's disease.

2. Authorization of 24 months may be granted for treatment of moderately to severely active CD if the member has had an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix B).

F. Moderately to severely active ulcerative colitis (UC)
1. Authorization of 24 months may be granted for members who have previously received Humira or any other biologic indicated for moderately to severely active ulcerative colitis.

2. Authorization of 24 months may be granted for treatment of moderately to severely active UC if the member has had an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix C).

G. Moderate to severe chronic plaque psoriasis (PsO)
1. Authorization of 24 months may be granted for members who have previously received Humira, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe chronic plaque psoriasis.

2. Authorization of 24 months may be granted for treatment of moderate to severe chronic plaque psoriasis when all of the following criteria are met:
   a. At least 5% of body surface area (BSA) is affected OR crucial bodyareas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   b. Member meets any of the following criteria:
      i. Member has had an inadequate response or intolerance to either phototherapy (e.g.,UVB, PUVA) or a pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      ii. Member has a clinical reason to avoid pharmacologic treatment withmethotrexate, cyclosporine or acitretin (see Appendix D).
      iii. Member has severe psoriasis that warrants a biologic DMARD as first-linetherapy.

H. Moderate to severe hidradenitis suppurativa
Authorization of 24 months may be granted for treatment of moderate to severe hidradenitis suppurativa.

I. Uveitis (non-infectious intermediate, posterior and panuveitis)

Authorization of 24 months may be granted for treatment of non-infectious intermediate, posterior and panuveitis.

III. CONTINUATION OF THERAPY

A. For ulcerative colitis:
Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve clinical remission by treatment day 56 (week 8) and maintain positive clinical response with Humira thereafter as evidenced by low disease activity or improvement in signs and symptoms of ulcerative colitis.

B. For all other indications:
Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Humira as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB)

Note: Members who have received Humira or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate
1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Conventional Therapy Options for CD
1. Mild to moderate disease – induction of remission:
   a. Oral budesonide, oral mesalamine
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternatives: oral budesonide, methotrexate intramuscularly (IM)
3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenously (IV)
   b. Alternatives: methotrexate IM

4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM
5. Perianal and fistulizing disease – induction of remission
   a. Metronidazole ± ciprofloxacin
6. Perianal and fistulizing disease – maintenance of remission
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM

Appendix C: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
   a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
   b. Rectal mesalamine (e.g., Canasa, Rowasa)
   c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
   d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
   a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
   b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
   a. Prednisone, hydrocortisone IV, methylprednisolone IV
   b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: sulfasalazine
5. Pouchitis: Metronidazole, ciprofloxacin
   a. Alternative: rectal mesalamine

Appendix D: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy (male or female)
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Humira [package insert]. North Chicago, IL: AbbVie Inc.; May 2017.
2. van der Heijde D, Ramiro S, Landewe R, et al. 2016 Update of the international ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis.* 2017;0:1-14.
3. Sieper J, van der Heijde D, Dougados M, et al. Efficacy and safety of adalimumab in patients with non-radiographic axial spondyloarthritis: results of a randomised placebo-controlled trial (ABILITY-1). *Ann Rheum Dis.* 2013;72(6):815-22.
4. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017*;0*:1-18.
5. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guidelinefor the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.

6. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations forthe use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59(6):762-784.
7. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res*. 2011;63(4):465-482.
8. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies; 2015 update. *Ann Rheum Dis*. 2016;75(3):499-510.
9. Gladman DD, Antoni C, P Mease, et al. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis* 2005;64(Suppl II):ii14–ii17.
10. Peluso R, Lervolino S, Vitiello M, et al. Extra-articular manifestations in psoriatic arthritis patients. *Clin Rheumatol*. 2014 May 8. [Epub ahead of print].
11. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
12. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis* 2011;70:896–904.
13. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Associationof America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol.* 2015: 10.1002/art.39298. [Epub ahead of print].
14. Talley NJ, Abreu MT, Achkar J, et al. An evidence-based systematic review on medical therapies for inflammatory bowel disease. *Am J Gastroenterol.* 2011;106(Suppl 1):S2-S25.

Reference number(s)
1726-A

SPECIALTY GUIDELINE MANAGEMENT

IBRANCE (palbociclib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Ibrance is indicated for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:
1. an aromatase inhibitor as initial endocrine based therapy in postmenopausal women, or
2. fulvestrant in women with disease progression following endocrine therapy.

B. Compendial Uses
Soft tissue sarcoma: well-differentiated/dedifferentiated liposarcoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast cancer
Authorization of 12 months may be granted for the treatment of HR-positive HER2-negative breast cancer when one of the following criteria is met:
1. Ibrance is used in combination with an aromatase inhibitor (eg, anastrozole, exemestane, letrozole).
2. Ibrance is used in combination with fulvestrant.

B. Soft tissue sarcoma
Authorization of 12 months may be granted for treatment of well-differentiated/dedifferentiated liposarcoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Ibrance [package insert]. New York, NY: Pfizer Inc.; March 2017.
2. The NCCN Drugs & Biologics Compendium® © 2017 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed January 16, 2018.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 2. 2016. http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed January 16, 2018.

CVS caremark™

Reference number
2538-A

SPECIALTY GUIDELINE MANAGEMENT

ILUMYA (tildrakizumab-asmn)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Moderate to severe plaque psoriasis

A. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Ilumya, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.

B. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis for members who are 18 years of age or older when all of the following criteria are met:
   1. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   2. Member meets any of the following criteria:
      i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix).
      iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Ilumya as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Ilumya or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy (male or female)
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Ilumya [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2018.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol.* 2009;61:451-485.
3. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis andpsoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.

Reference number(s)
2172-A

SPECIALTY GUIDELINE MANAGEMENT

GLEEVEC (imatinib mesylate)
imatinib mesylate (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications[1,2]

1. Treatment of newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase
2. Treatment of patients with Ph+ CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alpha therapy
3. Treatment of adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL)
4. Treatment of pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy
5. Treatment of adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with PDGFR (platelet-derived growth factor receptor) gene re-arrangements as determined with an FDA-approved test
6. Treatment of adult patients with aggressive systemic mastocytosis without the D816V c-Kit mutation as determined with an FDA-approved test or with c-Kit mutational status unknown
7. Treatment of adult patients with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL) who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or FISH demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who areFIP1L1-PDGFRα fusion kinase negative or unknown
8. Treatment of adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP)
9. Treatment of patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST)
10. Adjuvant treatment of adult patients following complete gross resection of Kit (CD117) positiveGIST

B. Compendial Uses[3-5]

1. Treatment of patients with advanced phase CML (accelerated phase or blast phase)
2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
3. Ph+ ALL/lymphoblastic lymphoma
4. GIST (primary, preoperative, postoperative and continued treatment)
5. Desmoid tumors
6. Pigmented villonodular synovitis/tenosynovial giant cell tumor
7. Chordoma
8. C-Kit mutated melanoma
9. AIDS-related Kaposi sarcoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myelogenous Leukemia (CML)[1-4]
Authorization of 12 months may be granted for the treatment of CML when BOTH of the following criteria are met:
1. Diagnosis of CML was confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing
2. Member did not fail (other than due to intolerance) prior therapy with a TKI (e.g., dasatinib, nilotinib, bosutinib, ponatinib)

B. Ph+ Acute Lymphoblastic Leukemia (ALL)/lymphoblastic lymphoma[1-3,5]
Authorization of 12 months may be granted for the treatment of Ph+ ALL/lymphoblastic lymphoma when diagnosis of Ph+ ALL/lymphoblastic lymphoma was confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing

C. Gastrointestinal Stromal Tumor (GIST), Desmoid Tumors, Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor (PVNS/TGCT), Hypereosinophilic Syndrome/Chronic Eosinophilic Leukemia (HES/CEL), Dermatofibrosarcoma Protuberans (DFSP), Chordoma[1-3]
Authorization of 12 months may be granted for the treatment of GIST, desmoid tumors, PVNS/TGCT, HES/CEL, DFSP, or chordoma

D. Myelodysplastic Syndromes and Myeloproliferative Diseases (MDS/MPD)[1,2]
Authorization of 12 months may be granted for the treatment of MDS or MPD when the member's disease is associated with PDGFR gene rearrangements

E. Aggressive Systemic Mastocytosis (ASM)[1,2]
Authorization of 12 months may be granted for the treatment of ASM without the D816V c-Kit mutation or with c-Kit mutational status unknown

F. Melanoma[3]
Authorization of 12 months may be granted for the treatment of c-Kit mutation-positive melanoma

G. AIDS-related Kaposi sarcoma[3]
Authorization of 12 months may be granted for the treatment of AIDS-related Kaposi sarcoma

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL diagnosis-specific authorization criteria below:

A. Chronic Myelogenous Leukemia (CML)[1-4]

Authorization of up to 12 months may be granted for the treatment of CML when ALL of the following criteria are met:

1. Diagnosis of CML was confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing
2. Member did not fail (other than due to intolerance) prior therapy with a TKI (e.g., dasatinib, nilotinib, bosutinib, ponatinib)
3. Member meets ANY of the following criteria:
   a. CML is in chronic phase and member is receiving benefit from therapy(i.e., achieved or maintained a cytogenic or molecular response to therapy).
   b. CML is in accelerated or blast phase CML
   c. Member has received a HSCT for CML (any phase)

B. Ph+ Acute Lymphoblastic Leukemia (ALL)/lymphoblastic lymphoma, Melanoma, Myelodysplastic Syndromes and Myeloproliferative Diseases (MDS/MPD), Aggressive Systemic Mastocytosis (ASM), Gastrointestinal Stromal Tumor (GIST), Desmoid Tumors, Pigmented Villonodular Synovitis/Tenosynovial Giant Cell Tumor (PVNS/TGCT), Hypereosinophilic Syndrome/Chronic Eosinophilic Leukemia (HES/CEL), Dermatofibrosarcoma Protuberans (DFSP), Chordoma, AIDS-related Kaposi sarcoma[1-5]

All members (including new members) requesting authorization for continuation of therapy for Ph+ ALL/lymphoblastic lymphoma, melanoma, MDS/MPD, ASM, GIST, desmoid tumors, PVNS/TGCT, HES/CEL, DFSP, chordoma or AIDS-related Kaposi sarcoma must meet ALL initial authorization criteria

IV. REFERENCES

1. Gleevec [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2017.
2. imatinib [package insert]. Cranbury, NJ: Sun Pharmaceuticals Inc.; October 2017.
3. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed March 30, 2018.
4. The NCCN Clinical Practice Guidelines in Oncology® Chronic Myelogenous Leukemia (Version 4.2018). © 2018 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed March 30, 2018.
5. The NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version1.2018). © 2018 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed March 30, 2018.

Reference number
1997-A

SPECIALTY GUIDELINE MANAGEMENT

IMBRUVICA (ibrutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Mantle Cell Lymphoma (MCL)

Imbruvica is indicated for the treatment of adult patients with MCL who have received at least one prior therapy.

2. Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)
   - Imbruvica is indicated for the treatment of adult patients with CLL/SLL.
   - Imbruvica is indicated for the treatment of adult patients with CLL/SLL with 17p deletion.

3. Waldenström's Macroglobulinemia (WM)

Imbruvica is indicated for the treatment of adult patients with WM.

4. Marginal Zone Lymphoma (MZL)

Imbruvica is indicated for the treatment of adult patients with MZL who require systemic therapy and have received at least one prior anti-CD20-based therapy.

5. Chronic Graft versus Host Disease (cGVHD)

Imbruvica is indicated for the treatment of adult patients with cGVHD after failure of one or more lines of systemic therapy.

B. Compendial Use

1. Mantle cell lymphoma, in combination with rituximab as pretreatment in order to limit the number of cycles of less aggressive induction therapy with RHyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone) regimen
2. Gastric MALT lymphoma, second-line or subsequent therapy for recurrent or progressive disease
3. Non-gastric MALT lymphoma, second-line or subsequent therapy for refractory or progressive disease
4. Hairy cell leukemia, for progression
5. Lymphoplasmacytic lymphoma (LPL)
6. Primary central nervous system lymphoma, for relapsed or refractory disease
7. Follicular lymphoma
8. Nodal marginal zone lymphoma, second-line or subsequent therapy for refractory or progressive disease
9. Splenic marginal zone lymphoma, second-line or subsequent therapy
10. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma in members who have received prior chemoimmunotherapy
11. Diffuse large B-cell lymphoma, second-line or subsequent therapy for refractory or progressive disease
12. High-grade B-cell lymphoma, second-line or subsequent therapy for refractory or progressive disease
13. AIDS-related B-cell lymphoma, for second-line or subsequent therapy for relapsed disease
14. Post-transplant lymphoproliferative disorders, subsequent therapy for members with partial response, persistent, or progressive disease after receiving chemoimmunotherapy

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Mantle Cell Lymphoma (MCL)

Authorization of 12 months may be granted for the treatment of MCL when any of the following criteria is met:

1. The member has received at least one prior therapy when the requested medication is used a as a single agent or in combination with rituximab.
2. The requested medication will be used in combination with rituximab as pretreatment to induction therapy with RHyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone) regimen.

B. Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)

Authorization of 12 months may be granted for the treatment of CLL/SLL.

C. Waldenström's Macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL)

Authorization of 12 months may be granted for the treatment of WM/LPL when the requested medication is used as a single agent or in combination with rituximab.

D. Marginal Zone Lymphoma (MZL)

Authorization of 12 months may be granted for the treatment of MZL, such as gastric or non-gastric MALT lymphoma, nodal marginal zone lymphoma, or splenic marginal zone lymphoma when the member has received at least one prior therapy.

E. Chronic Graft-Versus-Host Disease (cGVHD)

Authorization of 12 months may be granted for the treatment of cGVHD when the member has failed one or more lines of therapy.

F. Hairy Cell Leukemia

Authorization of 12 months may be granted for the treatment of hairy cell leukemia when the requested medication is used as a single agent for disease progression.

G. Primary central nervous system lymphoma

Authorization of 12 months may be granted for the treatment of relapsed or refractory primary central nervous system lymphoma when the requested medication is used as a single agent.

H. Follicular lymphoma (FL)

Authorization of 12 months may be granted for the treatment of follicular lymphoma when the requested medication is used as a single agent.

I. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma

Authorization of 12 months may be granted to members with histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma in members who have received prior chemoimmunotherapy.

J. Diffuse large B-cell lymphoma

Authorization of 12 months may be granted for the treatment of diffuse large B-cell lymphoma when the requested medication is used as second-line or subsequent therapy.

K. High-grade B-cell lymphoma

Authorization of 12 months may be granted for the treatment of high-grade B-cell lymphoma when the requested medication is used as second-line or subsequent therapy.

L. AIDS-related B-cell lymphoma

Authorization for 12 months may be granted for the treatment of relapsed AIDS-related B-cell lymphoma when the requested medication is used as a single agent and as second-line or subsequent therapy.

M. Post-transplant lymphoproliferative disorders

Authorization for 12 months may be granted for the treatment of partial response, persistent, progressive post-transplant lymphoproliferative disorders after receiving chemoimmunotherapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

IV. REFERENCES

1. Imbruvica [package insert]. Sunnyvale, CA: Pharmacyclics LLC; July 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed June 27, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: B-cell Lymphomas. Version 4.2019. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed June 28, 2019.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Hairy Cell Leukemia. Version 4.2018. https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed August 2, 2018.

Reference number
2079-A

SPECIALTY GUIDELINE MANAGEMENT

INLYTA (axitinib)

POLICY

XXVI. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Inlyta is indicated for the treatment of advanced renal cell carcinoma (RCC) after failure of one prior systemic therapy.

B. Compendial Uses
1. Relapsed or surgically unresectable stage IV renal cell carcinoma
2. Papillary, Hürthle cell, or follicular thyroid carcinoma

All other indications are considered experimental/investigational and are not a covered benefit.

XXVII. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma
Authorization of 12 months may be granted for treatment of relapsed, metastatic, or unresectable renal cell carcinoma as a single agent or in combination with pembrolizumab.

B. Papillary, Hürthle cell, or Follicular Thyroid Carcinoma
Authorization of 12 months may be granted for treatment of radioiodine refractory papillary, Hürthle cell, or follicular thyroid carcinoma.

XXVIII. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section II when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

XXIX. REFERENCES

1. Inlyta [package insert]. New York, NY: Pfizer Inc., August 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 24, 2019.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer. Version 4.2019. Accessed May 24, 2019. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Thyroid Carcinoma. Version 1.2019. Accessed May 24, 2019. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf.

Reference number
2079-A

Reference number(s)
1703-A

SPECIALTY GUIDELINE MANAGEMENT

INTRON A (interferon alfa-2b)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Malignant melanoma
2. Condylomata acuminata
3. Hairy cell leukemia
4. AIDS-related Kaposi sarcoma
5. Chronic hepatitis B virus infection
6. Chronic hepatitis C virus infection
7. Follicular non-Hodgkin's lymphoma

B. Compendial Uses
1. Non-Hodgkin's lymphoma
   i. Adult T-cell leukemia/lymphoma (ATLL)
   ii. Mycosis fungoides (MF)/Sezary syndrome (SS)
2. Myeloproliferative neoplasms
   i. Essential thrombocythemia
   ii. Myelofibrosis
   iii. Polycythemia vera
3. Renal cell carcinoma
4. Chronic myelogenous leukemia (CML)
5. Giant cell tumor of the bone
6. Acute hepatitis C virus infection
7. Desmoid tumors (soft tissue sarcoma)
8. Systemic mastocytosis
9. Carcinoid syndrome
10. Hypereosiniphilic syndrome
11. Kasabach-Merritt syndrome
12. Leptomeningeal metastases
13. Life threatening hemangioma of infancy
14. Meningeoma
15. Neuroendocrine tumors of the GI tract, lung, or thymus (carcinoid tumors)
16. Ocular surface neoplasia (conjunctival and corneal neoplasm)
17. Respiratory papillomatosis
18. Vulvar vestibulitis

All other indications are considered experimental/investigational and are not a covered benefit.

I. CRITERIA FOR INITIAL APPROVAL

A. Malignant melanoma
Authorization of 12 months may be granted for treatment of malignant melanoma.

B. Non-Hodgkin's lymphoma (NHL)
Authorization of 12 months may be granted for treatment of NHL with any of the following subtypes:
1. Adult T-cell leukemia/lymphoma (ATLL) when used in combination with either of the following:
   a. Zidovudine, or
   b. Arsenic trioxide
2. Mycosis fungoides (MF)/Sezary syndrome (SS)
3. Hairy cell leukemia when used as a single agent
4. Follicular lymphoma (clinically aggressive)

C. Renal cell carcinoma
Authorization of 12 months may be granted for treatment of renal cell carcinoma when both of the following criteria are met:
1. Intron-A will be used in combination with bevacizumab.
2. The disease is of clear-cell histology.

D. Condylomata acuminata
Authorization of 12 months may be granted for treatment of condylomata acuminata.

E. AIDS-related Kaposi sarcoma
Authorization of 12 months may be granted for treatment of AIDS-related Kaposi sarcoma when both of the following are met:
1. Intron-A is used for subsequent therapy.
2. Intron-A will be given with antiretroviral therapy (ART).

F. Chronic myelogenous leukemia (CML)
Authorization of 6 months may be granted for treatment of CML.

G. Giant cell tumor of the bone
Authorization of 12 months may be granted for treatment of giant cell tumor of the bone when either of the following criteria are met:
1. Intron-A will be used as a single agent, or
2. Intron-A will be used in combination with denosumab.

H. Desmoid tumors (soft tissue sarcoma)
Authorization of 12 months may be granted for treatment of desmoid tumors when used as a single agent.

I. Acute and chronic hepatitis C virus infection
Authorization of up to 48 weeks may be granted for treatment of acute and chronic hepatitis C virus infection.

J. Chronic hepatitis B (including hepatitis D virus co-infection) virus infection
Authorization of 48 weeks may be granted for treatment of chronic hepatitis B (including hepatitis D virus co-infection) virus infection.

K. Myeloproliferative neoplasms
Authorization of 12 months may be granted for treatment of symptomatic low-risk myelofibrosis, essential thrombocythemia, and polycythemia vera.

L. Systemic mastocytosis
Authorization of 12 months may be granted for treatment of systemic mastocytosis when either of the following criteria are met:

1. Intron-A will be used as a single agent, or
2. Intron-A will be used in combination with prednisone.

M. Hypereosinophilic syndrome

Authorization of 12 months may be granted for treatment of hypereosinophilic syndrome when the patient has had an inadequate response or has contraindication to corticosteroids.

N. Kasabach-Merritt syndrome

Authorization of 12 months may be granted for treatment of Kasabach-Merritt syndrome.

O. Leptomeningeal metastases

Authorization of 12 months may be granted for treatment of leptomeningeal metastases.

P. Life threatening hemangioma of infancy

Authorization of 12 months may be granted for treatment of life threatening hemangioma in an infant patient who has had an inadequate response or contraindication to corticosteroids.

Q. Meningeoma

Authorization of 12 months may be granted for treatment of meningioma when either of the following criteria are met:

1. The disease is recurrent, or
2. The disease is surgically inaccessible.

R. Neuroendocrine tumors of the GI tract, lung, or thymus (carcinoid tumors)

Authorization of 12 months may be granted for treatment of neuroendocrine tumors of the GI tract, lung, or thymus.

S. Carcinoid syndrome

Authorization of 12 months may be granted for treatment of carcinoid syndrome.

T. Ocular surface neoplasia (conjunctival and corneal neoplasm)

Authorization of 12 months may be granted for treatment of ocular surface neoplasia (conjunctival and corneal neoplasm).

U. Respiratory papillomatosis

Authorization of 12 months may be granted for treatment of respiratory papillomatosis.

V. Vulvar vestibulitis

Authorization of 12 months may be granted for treatment of vulvar vestibulitis

II. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity.

III. REFERENCES

1. Intron A [package insert]. Whitehouse Station, NJ: Schering Corporation; October 2017.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 28, 2019.
3. Micromedex Solutions [database online]. Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com/. Accessed April 28, 2019.

4. Lexicomp Online®, AHFS® Drug Information, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; http://online.lexi.com [available with subscription]. Accessed April 28, 2019.
5. Clinical Consult. CVS Caremark Clinical Programs Review: Focus on Hematology-Oncology Clinical Programs. September 12, 2012.
6. Roufosse FE, Goldman M, Cogan E. Hypereosinophilic syndromes. *Orphanet J Rare Dis.* 2007;2:37.
7. Wananukul S, Nuchprayoon I, Seksarn P. Treatment of Kasabach-Merritt syndrome: a stepwise regimen of prednisolone, dipyridamole, and interferon. *Int J Dermatol.* 2003;42:741.
8. Gerber S, Bongiovanni, et al. A deficiency in interferon-alpha production in women with vulvar vestibulitis. Obstet Gynecol 2002 Mar;186(3):361-4.
9. Leventhal BG, Kashima HK, Mounts P, et al. Long-term response of recurrent respiratory papillomatosis to treatment with lymphoblastoid interferon alfa-n-1. *N Engl J Med.* 1991;325:613-617.
10. Frieden IJ, Eichenfield LF, Esterly NB, et al. Guidelines of care of hemangiomas of infancy. American Academy of Dermatology/Outcome Committee. *J Am Acad Dermatol.* 1997;37(4):631-637.
11. Shah SU, Kaliki S, Kim HJ, Lally SE, Shields JA, Shields CL. Topical Interferon Alfa-2b for Management of Ocular Surface Squamous Neoplasia in 23 Cases: Outcomes Based on American Joint Committee on Cancer Classification. *Arch Ophthalmol.* 2012;130(2):159–164.
12. Chamberlain MC. A phase II trial of intra-cerebrospinal fluid alpha interferon in the treatment of neoplastic meningitis. *Cancer.* 2002; 94:2675-2680.
13. Kaba SE, De Monte F, Bruner JM et al. The treatment of recurrent unresectable and malignant meningiomas with interferon alpha2B. *Neurosurgery.* 1997;40:271-275.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**ISOTRETINOINS (ALL ORAL)**
BRAND NAME (generic)	
	ABSORICA (isotretinoin)
	AMNESTEEM (isotretinoin)
	CLARAVIS (isotretinoin)
	MYORISAN (isotretinoin)
	ZENATANE (isotretinoin)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Isotretinoin is indicated for the treatment of severe recalcitrant nodular acne. Nodules are inflammatory lesions with a diameter of 5 mm or greater. The nodules may become suppurative or hemorrhagic. "Severe," by definition, means "many" as opposed to "few or several" nodules. Because of significant adverse effects associated with its use, isotretinoin should be reserved for patients with severe nodular acne who are unresponsive to conventional therapy, including systemic antibiotics. In addition, isotretinoin is indicated only for those female patients who are not pregnant, because isotretinoin can cause severe birth defects.

A single course of therapy for 15 to 20 weeks has been shown to result in complete and prolonged remission of disease in many patients. If a second course of therapy is needed, it should not be initiated until at least 8 weeks after completion of the first course, because experience has shown that patients may continue to improve while off isotretinoin. The optimal interval before retreatment has not been defined for patients who have not completed skeletal growth.

Compendial Uses
Acne – refractory[7]
Cutaneous T-cell Lymphoma (CTCL) (e.g., mycosis fungoides, Sézary syndrome)[6]
Keratosis follicularis (Darier Disease) – severe[7]
Lamellar ichthyosis – severe skin involvement[6]
Neuroblastoma[7]
Pityriasis rubra pilaris[6]
Rosacea – severe refractory[7]
Squamous Cell Cancers – to reduce the development of precancers and skin cancers in high risk patients[7]
Transient acantholytic dermatosis (Grover's Disease) – severe[7]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has any of the following diagnoses: A) severe recalcitrant nodular acne vulgaris, B) refractory acne vulgaris, C) rosacea

  AND

  - The patient has tried and had inadequate treatment responses to any topical acne product AND an oral antibiotic

    AND

  - Treatment will be limited to 40 weeks (2 courses) or less AND with at least 8 weeks between each course

OR

- The patient has any of the following diagnoses: A) neuroblastoma, B) cutaneous T-cell lymphoma (CTCL) (e.g., mycosis fungoides, Sézary syndrome), C) is at high risk for developing skin cancer (squamous cell cancers), D) transient acantholytic dermatosis (Grover's Disease), E) keratosis follicularis (Darier Disease), F) lamellar ichthyosis, G) pityriasis rubra pilaris

REFERENCES

1. Absorica [package insert]. Jacksonville, FL: Ranbaxy Laboratories Inc.; December 2017.
2. Amnesteem [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; April 2018.
3. Claravis [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; August 2016.
4. Myorisan [package insert]. Marietta, GA: VersaPharm Incorporated; September 2015.
5. Zenatane [package insert]. Bachupally, India: Dr. Reddy's Laboratories Limited; June 2015.
6. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed June 2018.
7. Micromedex Solutions [database online]. Greenwood Village, CO: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed June 2018.
8. Questions and Answers about Acne. National Institute of Arthritis and Muskuloskeletal and Skin Diseases. http://www.niams.nih.gov/Health_Info/Acne/#acne_g. Accessed June 2018.
9. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016;74:945-73.
10. Questions and Answers about Rosacea. National Institute of Arthritis and Muskuloskeletal and Skin Diseases. http://www.niams.nih.gov/Health_Info/Rosacea/default.asp#6. Accessed June 2018.
11. Granulomatous Rosacea. http://rarediseases.info.nih.gov/gard/6548/granulomatous-rosacea/case/26122/case-questions. Accessed June 2018.
12. Neuroblastoma Treatment. National Cancer Institute at the National Institute of Health. http://www.cancer.gov/types/neuroblastoma/hp/neuroblastoma-treatment-pdq/#link/_661. Accessed June2018.
13. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Squamous Cell Skin Cancer. Version 2.2018. NCCN Guidelines http://www.nccn.org/professionals/physician_gls/pdf/nmsc.pdf. Accessed June 2018.
14. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Non-Hodgkin's Lymphomas. Version 4.2018. Available at: www.nccn.org. Accessed June 2018.
15. National Comprehensive Cancer Network. NCCN Drugs & Biologics Compendium. https://www.nccn.org/professionals/drug_compendium/content/contents.asp. Accessed June 2018.
16. Office of Rare Disease Research. NIH National Center for Advancing Translational Sciences. Transient acantholytic dermatosis. https://rarediseases.info.nih.gov/gard/6551/transient-acantholytic-dermatosis/resources/8#2884. Accessed June 2018.
17. National Organization for Rare Disorders, Inc. Grover's Disease. https://rarediseases.org/rare-diseases/grovers-disease. Accessed June 2018.
18. American Osteopathic College of Dermatology. Grover's Disease. http://www.aocd.org/?page=GroversDisease. Accessed June 2018.
19. Darier disease. Office of Rare Disease Research. https://rarediseases.info.nih.gov/gard/6243/darier-disease/resources/8. Accessed June 2018.
20. Darier Disease. American Osteopathic College of Dermatology. http://www.aocd.org/skin/dermatologic_diseases/darier_disease.html. Accessed June 2018.
21. Lamellar ichthyosis. Office of Rare Disease Research. https://rarediseases.info.nih.gov/gard/10803/lamellar-ichthyosis/resources/8. Accessed June 2018.

22. Pityriasis rubra pilaris. Office of Rare Disease Research. https://rarediseases.info.nih.gov/gard/7401/pityriasis-rubra-pilaris/resources/8. Accessed June 2018.
23. Pityriasis Rubra Pilaris. American Osteopathic College of Dermatology. http://www.aocd.org/?page=PityriasisRubraPil. Accessed June 2018.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

SPORANOX ORAL CAPSULES
(itraconazole)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

Policy

FDA-APPROVED INDICATIONS
Sporanox (itraconazole) Capsules are indicated for the treatment of the following fungal infections in immunocompromised and non-immunocompromised patients:
1. Blastomycosis, pulmonary and extrapulmonary
2. Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and
3. Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy.
Specimens for fungal cultures and other relevant laboratory studies (wet mount, histopathology, serology) should be obtained before therapy to isolate and identify causative organisms. Therapy may be instituted before the results of the cultures and other laboratory studies are known; however, once these results become available, antiinfective therapy should be adjusted accordingly.

Sporanox Capsules are also indicated for the treatment of the following fungal infections in non-immunocompromised patients:
1. Onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (tinea unguium), and
2. Onychomycosis of the fingernail due to dermatophytes (tinea unguium).
Prior to initiating treatment, appropriate nail specimens for laboratory testing (KOH preparation, fungal culture, or nail biopsy) should be obtained to confirm the diagnosis of onychomycosis.

Compendial Uses
- Coccidioidomycosis[2,3]
- Cryptococcosis[2,3]
- Microsporidiosis[2]
- Penicilliosis[2]
- Pityriasis versicolor/Tinea versicolor[2,3]
- Sporotrichosis[2,3]
- Tinea corporis/Tinea cruris, Tinea capitis, Tinea manuum/Tinea pedis[3]

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:
- Patient has one of the following diagnoses: A) Pityriasis versicolor, B) Tinea versicolor, C) Onychomycosis due to tinea that has been confirmed by a fungal diagnostic test
  OR
- Patient has one of the following diagnoses: A) Blastomycosis, B) Histoplasmosis, C) Aspergillosis, D) Coccidioidomycosis, E) Cryptococcosis, F) Sporotrichosis, G) Penicilliosis, H) Microsporidiosis
  OR
- Patient has one of the following diagnoses: A) Tinea corporis, B) Tinea cruris, C) Tinea capitis, D) Tineamanuum, E) Tinea pedis
  AND
  - Patient experienced an inadequate treatment response, adverse event, intolerance, or contraindication to griseofulvin

REFERENCES

1. Sporanox capsule [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; October 2017.
2. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed April 2018.
3. Micromedex Solutions [database online]. Greenwood Village, CO: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed April 2018.
4. Patterson TF, Thompson GR, Denning DW, et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2016;63:112–146.
5. Wheat L, Freifeld A, Kleiman M, et al. Clinical Practice Guidelines for the Management of Patients with Histoplasmosis: 2007 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2007;45:807–25.
6. Chapman S, Dismukes W, Proia L, et al. Clinical Practice Guidelines for the Management of Blastomycosis: 2008 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2008;46:1801–12.
7. Perfect J, Dismukes W, Dromer F, et al. Clinical Practice Guidelines for the Management of Cryptococcal Disease: 2010 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2010;50:291–322.
8. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf. Accessed April 2018.

Reference number(s)
1906-A

SPECIALTY GUIDELINE MANAGEMENT

KADCYLA (ado-trastuzumab emtansine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications[1]
Kadcyla, as a single agent, is indicated for the treatment of patients with human epidermal growth factor receptor 2 (HER2)-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease, or developed disease recurrence during or within six months of completing adjuvant therapy.

B. Compendial Use[2-4]
1. Recurrent HER2-positive breast cancer
2. Non-small cell lung cancer with HER2 mutations

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast cancer[1-3]
Authorization of 12 months may be granted for treatment of HER2-positive breast cancer.

B. Non-small cell lung cancer[2,4]
Authorization of 12 months may be granted for treatment of lung cancer with HER2 mutations.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Kadcyla [package insert]. South San Francisco, CA: Genentech, Inc.; July 2016.
2. The NCCN Drugs & Biologics Compendium™ © 2018 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed January 15, 2018.
3. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: breast cancer. Version 3.2017. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed January 15, 2018.
4. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: non-small cell lung cancer. Version 2.2018 https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed January 15, 2018.

CVS caremark™

Reference number(s)
1609-A

SPECIALTY GUIDELINE MANAGEMENT

KALBITOR (ecallantide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of acute attacks of hereditary angioedema (HAE) in patients 12 years of age and older

All other indications are considered experimental/investigational and are not a covered benefit.

VIII. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. C4 levels and C1 inhibitor functional and antigenic protein levels
B. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
C. Chart notes confirming family history of angioedema, if applicable

IX. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of acute hereditary angioedema attacks when the requested medication will not be used in combination with Berinert, Firazyr, or Ruconest and either of the following criteria is met:
A. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing:
   1. C1 inhibitor (C1-INH) antigenic level is below the lower limit of normal as defined by the laboratory performing the test, or
   2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)

B. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
   1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
   2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

X. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:
A. Member meets the criteria for initial approval.
B. Member has experienced reduction in severity and/or duration of attacks when they use the requested medication to treat an acute attack.

XI. REFERENCES

1. Kalbitor [package insert]. Burlington, MA: Dyax Corp.; March 2015.

2. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
3. Cicardi M, Bork K, Caballero T, et al. Hereditary Angioedema International Working Group. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy.* 2012;67:147-157.
4. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol: In Practice*. 2013; 1(5): 458-467.
5. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. *Allergy Asthma Proc*. 2012; 33(6):S145-S156.
6. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Allergy*. 2018;00:1-22.
7. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109:395-202.
8. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014;69: 602-616.
9. Bowen T. Hereditary angioedema: beyond international consensus – circa December 2010 – The Canadian Society of Allergy and Clinical Immunology Dr. David McCourtie Lecture. *Allergy Asthma Clin Immunol*. 2011;7(1):1.
10. Bernstein J. Update on angioedema: Evaluation, diagnosis, and treatment. *Allergy and Asthma Proceedings.* 2011;32(6):408-412.
11. Longhurst H, Cicardi M. Hereditary angio-edema. *Lancet.* 2012;379:474-481.
12. Farkas H, Martinez-Saguer I, Bork K, et al. International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency. *Allergy*. 2017;72(2):300-313.
13. Henao MP, Kraschnewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management.* 2016; 12: 701-711.

Reference number
1957-A

SPECIALTY GUIDELINE MANAGEMENT

KEVZARA (sarilumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Kevzara is indicated for treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs)

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Moderately to severely active rheumatoid arthritis (RA)

A. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

B. Authorization of 12 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
   1. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
   2. Member has an intolerance or contraindication to methotrexate (see Appendix).

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who are using Kevzara for an indication outlined in section II and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs (e.g., Xeljanz), and repeated yearly for members with risk factors** for TB that are continuing therapy with biologics.

* If the screening testing for TB is positive, there must be documentation of further testing to confirm there is no active disease. Do not administer sarilumab to members with active TB infection. If there is latent disease,
TB treatment must be started before initiation of sarilumab.

** Risk factors for TB include: Persons with close contact to people with infectious TB disease; persons who

have recently immigrated from areas of the world with high rates of TB (e.g., Africa, Asia, Eastern Europe, Latin America, Russia); children less than 5 years of age who have a positive TB test; groups with high rates of TB transmission (e.g., homeless persons, injection drug users, persons with HIV infection); persons who work or reside with people who are at an increased risk for active TB (e.g., hospitals, long-term care facilities, correctional facilities, homeless shelters).

For all indications: Members cannot use Kevzara concomitantly with any other biologic DMARD or targeted synthetic DMARD.

V. APPENDIX: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

VI. REFERENCES

1. Kevzara [package insert]. Bridgewater, NJ: Sanofi-aventis, U.S. LLC /Regeneron Pharmaceuticals, Inc.; April 2018.
2. Genovese MC, Fleischmann R, Kivitz AJ, et al. Sarilumab plus methotrexate in patients with active rheumatoid arthritis and inadequate response to methotrexate: results of a phase III study. *Arthritis Rheumatol.* June 2015;67(6):1424-37.
3. Strand V, Reaney M, Chen C, et al. Sarilumab improves patient-reported outcomes in rheumatoid arthritis patients with inadequate response/intolerance to tumour necrosis factor inhibitors. *RMD Open.* 2017; 3**:**e000416. doi: 10.1136/rmdopen-2016-000416.
4. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on 21 June 2019 from: https://www.cdc.gov/tb/topic/basics/risk.htm.

Reference number
1802-A

SPECIALTY GUIDELINE MANAGEMENT

KINERET (anakinra)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Moderately to severely active rheumatoid arthritis (RA)
2. Cryopyrin-Associated Periodic Syndromes (CAPS)
   a. Neonatal-Onset Multisystem Inflammatory Disease (NOMID)

B. Compendial Uses
1. Systemic juvenile idiopathic arthritis (sJIA)
2. Adult-onset Still's disease
3. B-cell lymphomas – multicentric Castleman's disease
4. Recurrent pericarditis
5. Hyperimmunoglobulin D syndrome [Mevalonate Kinase Deficiency (MKD)]

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to Severely Active Rheumatoid Arthritis (RA)
Authorization of 24 months may be granted for members who meet ANY of the following criteria:
1. Member has experienced an inadequate response to at least a 3-month trial of a biologic DMARD ora targeted synthetic DMARD (e.g., Xeljanz)
2. Member has experienced intolerance to a biologic or targeted synthetic DMARD

B. Adult Onset Still's Disease
Authorization of 24 months may be granted for members with Adult Onset Still's disease.

C. Active Systemic Juvenile Idiopathic Arthritis (sJIA)
1. Authorization of 24 months may be granted for the treatment of sJIA for members who have received Actemra or Ilaris in a paid claim through a pharmacy or medical benefit within the previous 120 days.
2. Authorization of 24 months may be granted for the treatment of active sJIA for members who have had an inadequate response to a trial of corticosteroids, methotrexate, or leflunomide.

D. Neonatal-Onset Multisystem Inflammatory Disease (NOMID)
Authorization of 24 months may be granted for the treatment of cryopyrin-associated periodic syndromes (CAPS), including NOMID (also known as chronic infantile neurologic cutaneous and articular syndrome [CINCA]).

E. Recurrent Pericarditis
Authorization of 12 months may be granted for the treatment of recurrent pericarditis for members who have failed a first-line therapy agent (i.e., colchicine).

F. B-cell Lymphomas – Multicentric Castleman's Disease
Authorization of 12 months may be granted for the treatment of multicentric Castleman's disease.

G. Hyperimmunoglobulin D Syndrome [Mevalonate Kinase Deficiency (MKD)]
Authorization of 24 months may be granted for the treatment of hyperimmunoglobulin D syndrome.

III. CONTINUATION OF THERAPY

A. Adult Onset Still's Disease, Rheumatoid Arthritis and Juvenile Idiopathic Arthritis
Authorization of 24 months may be granted for all members (including new members) who have achieved or maintained a positive clinical response after at least 3 months of therapy with Kineret as evidenced by low disease activity or improvement in signs and symptoms of the condition.

B. Neonatal-Onset Multisystem Inflammatory Disease (NOMID), Castleman's disease, Recurrent Pericarditis, and Hyperimmunoglobulin D Syndrome
All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. APPENDIX: Examples of Contraindications to Methotrexate

1. History of intolerance or adverse event
2. Alcoholic liver disease or other chronic liver disease
3. Elevated liver transaminases
4. Interstitial pneumonitis or clinically significant pulmonary fibrosis
5. Renal impairment
6. Current pregnancy or planning pregnancy
7. Breastfeeding
8. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
9. Myelodysplasia
10. Hypersensitivity
11. Significant drug interaction

V. REFERENCES

1. Kineret [package insert]. Stockholm, Sweden: Swedish Orphan Biovitrum AB (publ); May 2016.
2. DRUGDEX® System (electronic version). Truven Health Analytics, Ann Arbor, MI. Available at http://www.micromedexsolutions.com [available with subscription]. Accessed January 15, 2018.
3. Ringold S, Weiss PF, Beukelman T, et al. 2013 Update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis: Recommendations for the Medical Therapy of Children With Systemic Juvenile Idiopathic Arthritis and Tuberculosis Screening Among Children Receiving Biologic Medications. *Arthritis & Rheumatism.* 2013;65:2499-2512.
4. Laskari K, Tzioufas AG, Moutsopoulos HM. Efficacy and long-term follow-up of IL-1R inhibitor anakinra in adults with Still's disease: a case-series study. *Arthritis Res Ther*. 2011;13(3):R91.
5. Lequerre T, Quartier P, Rosellini D, et al. Interleukin-1 receptor antagonist (anakinra) treatment in patients with systemic-onset juvenile idiopathic arthritis or adult onset Still disease: preliminary experience in France. *Ann Rheum Dis*. 2008;67:302-308.

6. Caremark Clinical Programs Review, Focus on Rheumatology: External consultant recommendations; September 2005.
7. The NCCN Drugs & Biologics Compendium™. National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed January 15, 2018.
8. Smolen JS, Landewé R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. *Rhem Dis.* 2014;73:492-509.
9. Singh JA, Furst DE, Bharat A, et al. 2012 Update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. *Arthritis Care Res.* 2012;64(5):625-639.
10. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59(6):762-784.
11. Aletasha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid Arthritis Classification Criteria. An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative. *Arthritis Rheum.* 2010;62:2569-2581.
12. Anderson J, Caplan L, Yazdany J, et al. Rheumatoid Arthritis Disease Activity Measures: American College of Rheumatology Recommendations for Use in Clinical Practice. *Arthritis Rheum.* 2010;64:640-647.
13. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res*. 2011;63(4):465-482.
14. Quartier P, Allantaz F, Cimaz R, et al. A multicentre, randomized, double-blind, placebo-controlled trial with the interleukin-1 receptor antagonist anakinra in patients with systemic-onset juvenile idiopathic arthritis (ANAJIS trial). *Ann Rheum Dis*. 2011;70:747-754.
15. Clinical Consult. CVS/caremark Clinical Program Review: Focus on Rheumatology Clinical Programs; November 10, 2014.
16. Efthimiou P, Paik P K, Bielory L. Diagnosis and Management of Adult Onset Still's Disease. *Ann Rheum Dis*. 2006 May;65(5):564-72. Epub 2005 Oct 11.
17. National Organization for Rare Disorders. URL: https://www.rarediseases.org/rare-disease-information/rare-diseases/byID/1210/viewFullReport. Accessed January 15, 2018.
18. Adler Y, Charron P, Imazio M, et al. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC) Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2015 Nov 7; 36 (42): 2921-64.
19. Kostjukovits S, Kalliokoski L, Antila K, Korppi M. Treatment of hyperummunoglobulinemia D Syndrome with biologics in children: review of the literature and Finnish experience. Eur J Pediatr. 2015 Jun; 174 (6): 707-14
20. National Organization for Rare Disorders. Hyperiimunoglobulin D Syndrome. http://rarediseases.org/rare-diseases/hyper-igd-syndrome. Accessed January 15, 2018.
21. American College of Rheumatology. Hyperimmunoglobulin D Syndrome. http://www.rheumatology.org/I-AM-A/Patient-Caregiver/Diseases-Conditions/Hyperimmunoglobulin-D-Syndrome-Juvenile. Accessed April 18, 2017.
22. Clinical Consult. CVS/caremark Clinical Program Review: Focus on Rheumatology Clinical Programs; June 27, 2016.

Reference number
1865-A

SPECIALTY GUIDELINE MANAGEMENT

LENVIMA (lenvatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Lenvima is indicated for the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer (DTC).
2. Lenvima is indicated in combination with everolimus, for the treatment of patients with advanced renal cell carcinoma (RCC) following one prior anti-angiogenic therapy.
3. Lenvima is indicated for the first-line treatment of patients with unresectable hepatocellular carcinoma (HCC).
4. Lenvima is indicated in combination with pembrolizumab, for the treatment of patients with advanced endometrial carcinoma that is not microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior systemic therapy and are not candidates for curative surgery or radiation.

B. Compendial Uses

Medullary, follicular, Hurthle cell or papillary thyroid carcinoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review for endometrial carcinoma: Documentation of laboratory report confirming MSI-H or mismatch repair deficient (dMMR) tumor status.

III. CRITERIA FOR INITIAL APPROVAL

A. Thyroid carcinoma (follicular, Hürthle cell, papillary)

Authorization of 12 months may be granted for the treatment of radioiodine refractory follicular, Hürthle cell, or papillary thyroid carcinoma.

B. Medullary thyroid carcinoma

Authorization of 12 months may be granted for the treatment of medullary thyroid carcinoma if the member has progressed on vandetanib (Caprelsa) or cabozantinib (Cometriq) OR these therapies are inappropriate.

C. Renal Cell Carcinoma

Authorization of 12 months may be granted for the treatment of advanced or metastatic renal cell carcinoma when used in combination with everolimus (Afinitor) AND either of the following is met:

1. The disease is predominantly clear cell and the member has used prior therapy OR
2. The disease is non-clear cell

D. Hepatocellular Carcinoma

Authorization of 12 months may be granted for the treatment of unresectable hepatocellular carcinoma.

E. Endometrial Carcinoma

Authorization of 12 months may be granted for the treatment of endometrial carcinoma when used in combination with pembrolizumab for advanced endometrial carcinoma that is not MSI-H or dMMR when the member has disease progression following prior systemic therapy and is not a candidate for curative surgery or radiation.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy for an indication outlined in Section III when there is no evidence of unacceptable toxicity or disease progression on the current regimen.

V. REFERENCES

1. Lenvima [package insert]. Woodcliff Lake, NJ: Eisai Inc.; September 2019.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 16, 2019.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology Thyroid Carcinoma (Version 1.2018). http://www.nccn.org. Accessed November 5, 2018.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology Kidney Cancer (Version 2.2019). http://www.nccn.org. Accessed November 5, 2018.

Reference number(s)
1646-A

SPECIALTY GUIDELINE MANAGEMENT

Letairis (ambrisentan)

POLICY

XXX. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1):

A. To improve exercise ability and delay clinical worsening
B. In combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability.

All other indications are considered experimental/investigational and are not a covered benefit.

XXXI. CRITERIA FOR INITIAL APPROVAL

Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

C. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
D. PAH was confirmed by either criterion (1) or criterion (2) below:
   6. Pretreatment right heart catheterization with all of the following results:
      i. mPAP ≥ 25 mmHg
      ii. PCWP ≤ 15 mmHg
      iii. PVR > 3 Wood units
   7. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      v. Post cardiac surgery
      vi. Chronic heart disease
      vii. Chronic lung disease associated with prematurity
      viii. Congenital diaphragmatic hernia

XXXII. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

XXXIII. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH
1.1 Idiopathic (PAH)

1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
1.4.1 Connective tissue diseases
1.4.2 HIV infection
1.4.3 Portal hypertension
1.4.4 Congenital heart diseases
1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.5 Chronic thromboembolic PH
4.6 Other pulmonary artery obstructions
4.6.1 Sarcoma (high or intermediate grade) or angiosarcoma
4.6.2 Other malignant tumors
Renal carcinoma
Uterine carcinoma
Germ cell tumours of the testis
Other tumours
4.6.3 Non-malignant tumours
Uterine leiomyoma
4.6.4 Arteritis without connective tissue disease
4.6.5 Congenital pulmonary artery stenosis
4.6.6 Parasites
Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.6 Complex congenital heart disease

XXXIV. REFERENCES

1. Letairis [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2018.
2. Ambrisentan [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; December 2018.
3. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
4. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest

Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
5. Badesch DB, Champion HC, Gomez-Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S55-S66.
6. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol.* 2013;62:D34-S41.
7. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
8. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S78-S84.
9. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
10. Abman, SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.
11. Klinger, JR., Elliott, CG, Levine, DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019:155(3): 565-586.
12. Galie, N., McLaughlin, VV, Rubin, LJ, Simonneau, G. An overview of the 6th World Symposium on Pulmonary Hypertension. Eur Respir J 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019

Reference number(s)
1989-A, 1990-A, 2117-A

SPECIALTY GUIDELINE MANAGEMENT

leuprolide acetate injection

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications[1,2]
1. Prostate cancer: Leuprolide acetate is indicated in the palliative treatment of advanced prostate cancer.
2. Central precocious puberty (CPP): Leuprolide acetate is indicated in the treatment of children with central precocious puberty.

B. Compendial Uses
1. Use as a stimulation test to confirm the diagnosis of CPP[3-6]
2. Use in combination with growth hormone for children with growth failure and advancing puberty[9-13]
3. Prostate cancer[14,15]
4. Inhibition of premature luteinizing hormone (LH) surges in women undergoing assisted reproductive technology[16-18]

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Central precocious puberty (CPP)[2-8]
1. Authorization up to age 12 may be granted for the treatment of CPP in a female member when all of the following criteria are met:
   a. The diagnosis of CPP has been confirmed by a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third generation luteinizing hormone (LH) assay
   b. The diagnosis of CPP has been confirmed by assessment of bone age versus chronological age
   c. The member was less than 8 years of age at the onset of secondary sexual characteristics
2. Authorization up to age 13 may be granted for the treatment of CPP in a male member when all of the following criteria are met:
   a. The diagnosis of CPP has been confirmed by a pubertal response to a GnRH agonist test or a pubertal level of a third generation LH assay
   b. The diagnosis of CPP has been confirmed by assessment of bone age versus chronological age
   c. The member was less than 9 years of age at the onset of secondary sexual characteristics

B. Stimulation test for CPP diagnosis[3-6]
Authorization of one dose may be granted for use as a stimulation test to confirm the diagnosis of CPP.

C. Advancing puberty and growth failure[9-13]
Authorization of 12 months may be granted for the treatment of advancing puberty and growth failure in a pediatric member when leuprolide acetate is used in combination with growth hormone.

D. Prostate cancer[1,14,15]
Authorization of 12 months may be granted for treatment of prostate cancer.

E. Inhibition of premature luteinizing hormone (LH) surge‡[16-18]
Authorization of 12 months may be granted for the inhibition of premature LH surge in a member undergoing ovulation induction or assisted reproductive technology (ART).

‡ Specialty Guideline Management coverage review will be bypassed for leuprolide if it is being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements in Section IIIE. A medical authorization number and confirmation of the approved procedure(s) will be required. *NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements in Section IIIE.*

III. CONTINUATION OF THERAPY

A. Central precocious puberty
1. Authorization up to age 12 may be granted for continuation of therapy for CPP in a female memberif the member is currently less than 12 years of age.
2. Authorization up to age 13 may be granted for continuation of therapy for CPP in a male member if the member is currently less than 13 years of age.

B. Prostate cancer, stimulation test for CPP diagnosis, advancing puberty and growth failure, and inhibition of premature LH surge.
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Leuprolide acetate injection [package insert]. Princeton, NJ: Sandoz Inc.; August 2017.
2. Leuprolide acetate injection for pediatric use [package insert]. Princeton, NJ: Sandoz Inc.; May 2017.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, CO. Available at: http://www.micromedexsolutions.com Accessed May 24, 2018.
4. Carel J, Eugster EA, Rogol A, et al. Consensus statement on the use of gonadotropin-releasing hormone analogs in children. *Pediatrics.* 2009;123:e752-e762.
5. Kletter GB, Klein KO, Wong YY. A pediatrician's guide to central precocious puberty. *Clin Pediatr.* 2015;54:414-424.
6. Houk CP, Kunselman AR, Lee PA. Adequacy of a single unstimulated luteinizing hormone level to diagnose central precocious puberty in girls. *Pediatrics*. 2009;123:e1059-e1063.
7. Kaplowitz P, Bloch C, the Section on Endocrinology. Evaluation and referral of children with signs ofearly puberty. *Pediatrics.* 2016;137:e20153732.
8. Clinical Consult: CVS Caremark Clinical Programs Review. Focus on Pediatric Endocrinology Clinical Programs. May 15, 2013.
9. Kamp GA, Mul D, Waelkens JJ, et al. A randomized controlled trial of three years growth hormone and gonadotropin-releasing hormone agonist treatment in children with idiopathic short stature and intrauterine growth retardation. *J Clin Endocrinol Metab*. 2001;86:2969-2975.
10. Mericq V, Cajardo H, Effers M, et al. Effects of treatment with GH alone or in combination with LHRH analog on bone mineral density in pubertal GH-deficient patients*. J Clin Endocrinol Metab.* 2002;87:84-89.
11. Mul D, Wit JM, Oostdijk W, et al. The effect of pubertal delay by GnRH agonist in GH-deficient children on final height. *J Clin Endocrinol Metab.* 2001;86:4655-4656.

12. Quintos JB, Vogiatzi MG, Harbison MD, et al. Growth hormone therapy alone or in combination with gonadotropin-releasing hormone analog therapy to improve the height deficit in children with congenital adrenal hyperplasia. *J Clin Endocrinol Metab*. 2001;86:1511-1517.
13. Tanaka T, Satoh M, Yasunaga T, et al. GH and GnRH analog treatment in children who enter puberty at short stature. *J Pediatr Endocrinol Metab*. 1997;10:623-628.
14. The NCCN Drugs & Biologics Compendium® © 2016 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed November 09, 2016.
15. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: prostate cancer. Version 3.2016. http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed November 09, 2016.
16. Urman B, Yakin K. Ovulatory disorders and infertility. *J Reprod Med*. 2006;51(4):267-282.
17. Clinical Consult. Caremark Clinical Program Review: Focus on Reproductive Endocrinology Clinical Programs. July 2008.
18. National Collaborating Centre for Women's and Children's Health. Fertility: assessment and treatment for people with fertility problems (Clinical guideline no. 156). National Institute for Health and Clinical Excellence (NICE); 2013.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

LIDODERM
(lidocaine patch 5%)

ZTLIDO
(lidocaine topical system)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Quantity Limit

POLICY

FDA-APPROVED INDICATIONS

Lidoderm
Lidoderm is indicated for relief of pain associated with post-herpetic neuralgia. It should be applied only to **intact skin**.

ZTLido
ZTLido (lidocaine topical system) 1.8% is indicated for the relief of pain associated with post-herpetic neuralgia (PHN).

Compendial Uses
Pain associated with diabetic neuropathy
Pain associated with cancer-related neuropathy

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for any of the following:
  - Pain associated with post-herpetic neuralgia
  - Pain associated with diabetic neuropathy
  - Pain associated with cancer-related neuropathy (including treatment-related neuropathy [e.g. neuropathy associated with radiation treatment or chemotherapy])

Quantity Limits apply.
90 patches/30 days
270 patches/90 days

REFERENCES

1. Lidoderm [package insert]. Chadds Ford, PA: Endo Pharmaceuticals Inc.; January 2015.
2. ZTLido [package insert]. San Diego, CA: Scilex Pharmaceuticals Inc.; August 2018
3. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed September 2018.
4. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed September 2018.
5. Barbano RL, Herrmann DN, Hart-Gouleau S, et al: Effectiveness, tolerability, and impact on quality of life of the 5% lidocaine patch in diabetic polyneuropathy. Arch Neurol 2004; 61:914-918.
6. Dworkin RH, O'Connor AB, Backonja M, et al. Pharmacologic Management of Neuropathic Pain: Evidence-based recommendations. *Pain* 2007; 132(3):237-251.

7. National Comprehensive Cancer Network: Adult Cancer Pain V.1.2018. National Comprehensive Cancer Network. Fort Washington, PA. 2008. Available from URL: http://www.nccn.org/professionals/physician_gls/PDF/pain.pdf. Accessed September 2018.
8. Vadalouca A, Raptis E, Moka E, et al. Pharmacological Treatment of Neuropathic Cancer Pain: A Comprehensive Review of Current Literature. World Institute of Pain. *Pain Practice.* 2011; 12(3):219-251.
9. Derry S, Wiffen PJ, Moore RA, et al. Topical lidocaine for neuropathic pain in adults (Review). *Cochrane Database Syst Rev* 2014. doi: 10.1002/14651858.CD010958.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

LOTRONEX
(alosetron)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Lotronex is indicated only for women with severe diarrhea-predominant irritable bowel syndrome (IBS) who have:

- chronic IBS symptoms (generally lasting six months or longer),
- had anatomic or biochemical abnormalities of the gastrointestinal tract excluded, and
- not responded adequately to conventional therapy

Diarrhea-predominant IBS is severe if it includes diarrhea and one or more of the following:

- frequent and severe abdominal pain/discomfort
- frequent bowel urgency or fecal incontinence
- disability or restriction of daily activities due to IBS

Because of infrequent but serious gastrointestinal adverse events associated with Lotronex, the indication is restricted to those patients for whom the benefit-to-risk balance is most favorable.

Clinical studies have not been performed to adequately confirm the benefits of Lotronex in men.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for a biological female or a person that self-identifies as a female with a diagnosis of severe diarrhea-predominant irritable bowel syndrome (IBS) AND all of the following apply: A) Chronic IBS symptoms lasting at least 6 months, B) Gastrointestinal tract abnormalities have been ruled out, C) Inadequate response to conventional therapy

REFERENCES

1. Lotronex [package insert]. San Diego, CA: Prometheus Laboratories Inc.; July 2016.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/.Accessed September 2018.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed September 2018.

Reference number(s)
2415-A

SPECIALTY GUIDELINE MANAGEMENT

MEPSEVII (vestronidase alfa-vjbk)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Mepsevii is indicated in pediatric and adult patients for the treatment of Mucopolysaccharidosis VII (MPS VII, Sly syndrome).

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Mucopolysaccharidosis VII (MPS VII, Sly syndrome)
Indefinite authorization may be granted for treatment of MPS VII (Sly syndrome) when the diagnosis of MPS VII was confirmed by enzyme assay demonstrating a deficiency of beta-glucuronidase enzyme activity or by genetic testing.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Mepsevii [package insert]. Novato, CA: Ultragenyx; November 2017.

PRIOR AUTHORIZATION CRITERIA

BRAND NAME
(generic)

NAMENDA (all dosage forms)
(memantine hydrochloride)

Prior Authorization applies only to patients less than 30 years of age.

Status: CVS Caremark Criteria
Type: Initial Prior Authorization with Age Edit

POLICY

FDA-APPROVED INDICATIONS
Namenda and Namenda XR are indicated for the treatment of moderate to severe dementia of the Alzheimer's type.

COVERAGE CRITERIA
The requested drug will be covered with prior authorization for patients less than 30 years of age when the following criteria are met:

- The patient has a diagnosis of moderate to severe dementia of the Alzheimer's type

REFERENCES

1. Namenda [package insert]. Irvine, CA: Allergan USA, Inc.; August 2016.
2. Namenda XR [package insert]. Irvine, CA: Allergan USA, Inc.; October 2016.
3. Micromedex Solutions [database online]. Greenwood Village, CO: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed May 2018.
4. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed May 2018.
5. Rabins P, Blacker D, Rovner B. Practice Guideline for the Treatment of Patients with Alzheimer's Disease and Other Dementias, Second Edition. *Am J Psychiatry*. 2007; 164(12S):1-56.
6. Qaseem A, Snow V, Cross T, et al. Current Pharmacological Treatment of Dementia: A Clinical Practice Guideline from the American College of Physicians and the American Academy of Family Physicians. *An Intern Med* 2008; 148:370-378.
7. Goldman JS, Hahn SE, Catania JW, et. al. ACMG Practice Guidelines. Genetic counseling and testing for Alzheimer disease: Joint practice guidelines of the American College of Medical Genetics and the National Society of Genetic Counselors. *Genetics in Medicine* June 2011; 13:597-605.

Reference number(s)
1931-A

SPECIALTY GUIDELINE MANAGEMENT

NEULASTA (pegfilgrastim)
FULPHILA (pegfilgrastim-jmdp)
UDENYCA (pegfilgrastim-cbqv)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication

Neulasta
Neulasta is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Fulphila
Fulphila is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia

Udenyca
Udenyca is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

B. Compendial Use
Stem cell transplantation-related indications

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Prevention of neutropenia in cancer patients receiving myelosuppressive chemotherapy
Authorization of 6 months may be granted for prevention of febrile neutropenia when both of thefollowing criteria are met:
1. Member has a non-myeloid malignancy and is currently receiving, or willbe receiving myelosuppressive anti-cancer therapy
2. The requested product will not be administered less than 24 hours before or after chemotherapy or radiotherapy

B. Stem cell transplantation-related indications

Authorization of 6 months may be granted for stem cell transplantation-related indications.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Neulasta [package insert]. Thousand Oaks, CA: Amgen Inc.; December 2017.
2. Fulphila [package insert]. Zurich, Switzerland: Mylan; June 2018.
3. Udenyca [package insert]. Redwood City, California: Coherus BioSciences, Inc: November 2018.
4. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed June 15, 2018.
5. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed June 15, 2018.
6. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloid Growth Factors. Version 1.2018. http://www.nccn.org/professionals/physican_gls/pdf/myeloid_growth.pdf. Accessed June 15, 2018.
7. Aapro MS, Bohlius J, Cameron DA, et al. 2010 update of EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphoproliferative disorders and solid tumors. *Eur J Cancer*. 2011;47(1):8-32.
8. Smith TJ, Bohlke K, Lyman GH, et al. Recommendations for the use of white blood cell growth factors: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2015;33(28):3199-3212.

Reference number(s)
1930-A

SPECIALTY GUIDELINE MANAGEMENT

NEUPOGEN (filgrastim)
GRANIX (tbo-filgrastim)
ZARXIO (filgrastim-sndz)
NIVESTYM (filgrastim-aafi)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Neupogen

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
   Neupogen is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.

2. Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy
   Neupogen is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia.

3. Patients with Cancer Receiving Bone Marrow Transplant
   Neupogen is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation.

4. Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy
   Neupogen is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

5. Patients With Severe Chronic Neutropenia
   Neupogen is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

Nivestym

1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
   Nivestym is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.

2. Patients With Acute Myeloid Leukemia Receiving Induction or ConsolidationChemotherapy

Nivestym is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia.

3. Patients with Cancer Receiving Bone Marrow Transplant
   Nivestym is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation.

4. Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy
   Nivestym is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.

5. Patients With Severe Chronic Neutropenia
   Nivestym is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

Granix
Granix is indicated to reduce the duration of severe neutropenia in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

Zarxio
1. Patients with Cancer Receiving Myelosuppressive Chemotherapy
   a. Zarxio is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever.
2. Patients With Acute Myeloid Leukemia Receiving Induction or Consolidation Chemotherapy
   a. Zarxio is indicated for reducing the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of adults with acute myeloid leukemia.
3. Patients with Cancer Undergoing Bone Marrow Transplant
   a. Zarxio is indicated to reduce the duration of neutropenia and neutropenia-related clinical sequelae, (e.g., febrile neutropenia) in patients with non-myeloid malignancies undergoing myeloablative chemotherapy followed by marrow transplantation.
4. Patients Undergoing Autologous Peripheral Blood Progenitor Cell Collection and Therapy
   a. Zarxio is indicated for the mobilization of autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis.
5. Patients With Severe Chronic Neutropenia
   a. Zarxio is indicated for chronic administration to reduce the incidence and duration of sequelae of neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.

B. Compendial Uses (Neupogen/Granix/Zarxio/Nivestym)
1. Treatment of chemotherapy-induced febrile neutropenia in patients with non-myeloid malignancies
2. Treatment of anemia in patients with myelodysplastic syndromes (MDS)
3. Treatment of neutropenia in patients with MDS
4. Following chemotherapy for acute lymphocytic leukemia (ALL)
5. Stem cell transplantation-related indications
6. Agranulocytosis
7. Aplastic anemia
8. Neutropenia related to HIV/AIDS

9. Neutropenia related to renal transplantation

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Neutropenia in cancer patients receiving myelosuppressive chemotherapy

Authorization of 6 months may be granted for prevention or treatment of febrile neutropenia when both of the following criteria are met:

1. Member has a non-myeloid malignancy and has received, is currentlyreceiving, or will be receiving myelosuppressive anti-cancer therapy
2. The requested drug will not be administered less than 24 hours before or after chemotherapy or radiotherapy

B. Other indications

Authorization of 6 months may be granted for members with any of the following indications:

1. Agranulocytosis
2. Aplastic anemia
3. Neutropenia related to HIV/AIDS
4. Neutropenia related to renal transplantation
5. Acute myeloid leukemia
6. Stem cell transplantation-related indications
7. Severe chronic neutropenia (congenital, cyclic, or idiopathic)
8. Myelodysplastic syndrome (anemia or neutropenia)

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Neupogen [package insert]. Thousand Oaks, CA: Amgen Inc.; June 2018.
2. Nivestym [package insert]. Lake Forest, IL: Pfizer Inc.; July 2018.
3. Granix [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; June 2017.
4. Zarxio [package insert]. Princeton, NJ: Sandoz Inc.; December 2017.
5. The NCCN Drugs & Biologics Compendium® © 2017 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed June 29, 2018.
6. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed June 29, 2018.
7. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed July 29, 2018.
8. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloid Growth Factors. Version 1.2018. http://www.nccn.org/professionals/physican_gls/pdf/myeloid_growth.pdf. Accessed June 29, 2018.
9. Aapro MS, Bohlius J, Cameron DA, et al. 2010 update of EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphoproliferative disorders and solid tumors. *Eur J Cancer.* 2011;47(1):8-32.

10. Smith TJ, Bohlke K, Lyman GH, et al. Recommendations for the use of white blood cell growth factors: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol*. 2015;33(28):3199-3212.

Reference number
2027-A

SPECIALTY GUIDELINE MANAGEMENT

NEXAVAR (sorafenib)

POLICY

XXXV. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Hepatocellular carcinoma

Nexavar is indicated for the treatment of patients with unresectable hepatocellular carcinoma (HCC).

2. Renal cell carcinoma

Nexavar is indicated for the treatment of patients with advanced renal cell carcinoma (RCC).

3. Differentiated thyroid carcinoma

Nexavar is indicated for the treatment of locally recurrent or metastatic, progressive, differentiated thyroid carcinoma (DTC) that is refractory to radioactive iodine treatment.

B. Compendial Uses

1. Hepatocellular carcinoma (Child-Pugh Class A or B7)
   a. Patients who have unresectable disease and are not a transplant candidate
   b. Patients who are inoperable by performance status or comorbidity, or have local disease or local disease with minimal extrahepatic disease only
   c. Patients who have metastatic disease or extensive liver tumor burden
   d. Subsequent treatment as a single-agent for patients who have progressed after first-line lenvatinib
2. Acute myeloid leukemia
   a. In combination with azacitidine or decitabine in patients age ≥ 60 years with FLT3-ITD mutation as low-intensity treatment induction when not a candidate for intensive induction therapy or declines intensive therapy
   b. In combination with azacitidine or decitabine in patients age ≥ 60 years with FLT3-ITD mutation, as post-remission therapy following response to previous lower intensity therapy with the same regimen
   c. A component of repeating the initial successful induction if late relapse (greater than or equal to 12 months) for relapsed or refractory disease
   d. In combination with azacitidine or decitabine for relapsed or refractory disease
3. Soft tissue sarcoma subtypes
   a. Angiosarcoma, as single agent therapy
   b. Desmoid tumors (aggressive fibromatosis), primary, recurrent, or progressive disease
   c. Solitary fibrous tumor, as single-agent therapy
   d. Hemangiopericytoma, as single-agent therapy
   e. Leiomyosarcoma
4. Gastrointestinal stromal tumors (GIST), treatment for disease progression after single-agent therapy with imatinib, sunitinib and regorafenib
5. Thyroid carcinoma (medullary carcinoma, papillary carcinoma, Hürthle cell carcinoma, or follicular)
6. Relapsed/refractory bone cancer, as second-line therapy as a single agent for the following subtypes:
   a. Osteosarcoma
   b. Dedifferentiated chondrosarcoma
   c. High-grade undifferentiated pleomorphic sarcoma (UPS)
7. Recurrent chordoma

8. Epithelial ovarian cancer, fallopian tube cancer, and primary peritoneal cancer; if platinum-resistant, in combination with topotecan for persistent disease or recurrence

All other indications are considered experimental/investigational and are not a covered benefit.

XXXVI. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: FLT3-ITD mutation testing results (where applicable)

XXXVII. CRITERIA FOR INITIAL APPROVAL

A. Hepatocellular Carcinoma

1. Authorization of 12 months may be granted for treatment of unresectable or metastatic hepatocellular carcinoma.
2. Authorization of 12 months may be granted for treatment of hepatocellular carcinoma for subsequent treatment as a single agent for members who progressed after first-line lenvatinib.

B. Acute Myeloid Leukemia

Authorization of 12 months may be granted for treatment of acute myeloid leukemia when either of the following criteria are met:

1. Nexavar will be used in combination with azacitidine or decitabine in members age 60 or older with FLT3-ITD mutation as low-intensity treatment induction or post-remission therapy; **OR**

2. **Nexavar will be used** for relapsed/refractory disease as either:
   - **a.** A component of repeating the initial successful induction if late relapse (greater than or equal to 12 months); **OR**
   - b. In combination with azacitidine or decitabine if the member is FLT3-ITD mutation positive.

C. Soft Tissue Sarcoma

1. Authorization of 12 months may be granted for treatment of leiomyosarcoma.
2. Authorization of 12 months may be granted for treatment of angiosarcoma, solitary fibrous tumor, or hemangiopericytoma as single agent therapy.
3. Authorization of 12 months may be granted for treatment of primary, recurrent, or progressive desmoid tumor/aggressive fibromatosis.

D. Gastrointestinal Stromal Tumor (GIST)

Authorization of 12 months may be granted for treatment of gastrointestinal stromal tumor for disease progression after single-agent therapy with imatinib, sunitinib, and regorafenib.

E. Renal Cell Carcinoma

Authorization of 12 months may be granted for treatment of advanced renal cell carcinoma.

F. Differentiated Thyroid Carcinoma

Authorization of 12 months may be granted for treatment of progressive and/or symptomatic radioiodine refractory papillary, Hürthle cell, or follicular thyroid carcinoma.

G. Medullary Thyroid Carcinoma

Authorization of 12 months may be granted for treatment of medullary thyroid carcinoma when either of the following criteria are met:

1. Member has an intolerance or contraindication to vandetanib (Caprelsa) AND cabozantinib (Cometriq), OR
2. Member has disease progression while on vandetanib (Caprelsa) or cabozantinib (Cometriq).

H. Bone Cancer

1. Authorization of 12 months may be granted for treatment as second-line therapy for relapsed/refractory or metastatic disease as a single agent for the following types of bone cancer:
   a. Osteosarcoma
   b. Dedifferentiated chondrosarcoma
   c. High-grade undifferentiated pleomorphic sarcoma (UPS)

I. Chordoma

Authorization of 12 months may be granted for treatment of recurrent chordoma as a single agent.

J. Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

Authorization of 12 months may be granted for treatment of epithelial ovarian, fallopian tube, or primary peritoneal cancer if the disease is platinum-resistant and Nexavar is given in combination with topotecan for persistent disease or recurrence.

XXVIII. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who are clinically benefiting from therapy or who have not experienced an unacceptable toxicity.

XXXIX. REFERENCES

1. Nexavar [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; December 2018.
2. The NCCN Drugs & Biologic Compendium 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 28, 2019.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Hepatobiliary Cancers. Version 2.2019. Accessed May 30, 2019. https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Acute Myeloid Leukemia. Version 3.2019. Accessed May 30, 2019. https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf.
5. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Kidney Cancer. Version 4.2019. Accessed May 30, 2019. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.
6. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Thyroid Carcinoma. Version 1.2019. Accessed May 30, 2019. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf.
7. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Soft Tissue Sarcoma. Version 2.2019. Accessed May 30, 2019. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf.
8. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Bone Cancer. Version 2.2019. Accessed May 30, 2019. https://www.nccn.org/professionals/physician_gls/pdf/bone.pdf.
9. Santoro A, Comandone A, et al. Phase II prospective study with sorafenib in advanced soft tissue sarcomas after anthracycline-based therapy. Ann Oncol. 2013. 24 (4): 1093-8.
10. Bramwell, VH, Steward WP, et al. Neoadjuvant chemotherapy with doxorubicin and cisplatin in malignant fibrous histiocytoma of bone: A European Osteosarcoma Intergroup study. J Clin Oncol. 1999. 17 (10): 3260-9.

Reference number
1734-A

SPECIALTY GUIDELINE MANAGEMENT

SANDOSTATIN (octreotide acetate injection)
SANDOSTATIN LAR DEPOT (octreotide acetate for injectable suspension)
octreotide acetate injection

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. octreotide acetate/Sandostatin:
   a. Indicated to reduce blood levels of growth hormone and IGF-1 (somatomedin C) in acromegaly patients who have had inadequate response to or cannot be treated with surgical resection, pituitary irradiation, and bromocriptine mesylate at maximally tolerated doses.
   b. Indicated for the symptomatic treatment of patients with metastatic carcinoid tumors where it suppresses or inhibits the severe diarrhea and flushing episodes associated with the disease.
   c. Indicated for the treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors.

2. Sandostatin LAR: Sandostatin LAR Depot is indicated in patients in whom initial treatment with Sandostatin injection has been shown to be effective and tolerated.
   a. Indicated for long-term maintenance therapy in acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option.
   b. Indicated for long-term treatment of the severe diarrhea and flushing episodes associated with metastatic carcinoid tumors.
   c. Indicated for long-term treatment of the profuse watery diarrhea associated with vasoactive intestinal peptide (VIP)-secreting tumors.

B. Compendial Uses

1. Neuroendocrine tumors (NETs):
   a. Adrenal gland tumors
   b. Tumors of the gastrointestinal (GI) tract, lung, and thymus (carcinoid tumors)
   c. Tumors of the pancreas
2. Meningiomas
3. Thymomas and thymic carcinomas
4. Congenital hyperinsulinism (CHI)/persistent hyperinsulinemic hypoglycemia of infancy(PHHI) (octreotide and Sandostatin only)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Acromegaly

Authorization of 24 months may be granted for the treatment of acromegaly when all of the following criteria are met:

1. Member has a high pretreatment insulin-like growth factor-1 (IGF-1) level for age and/or gender based on the laboratory reference range.
2. Member had an inadequate or partial response to surgery or radiotherapy OR there is a clinical reason why the member has not had surgery or radiotherapy

B. Neuroendocrine tumors (NETs)/carcinoid syndrome

1. Tumors of the gastrointestinal (GI) tract (carcinoid tumor)
   Authorization of 24 months may be granted for treatment of metastatic or unresectable NETs of the GI tract.
2. Tumors of the thymus (carcinoid tumor)
   Authorization of 24 months may be granted for treatment of metastatic or unresectable NETs of the thymus.
3. Tumors of the lung (carcinoid tumor)
   Authorization of 24 months may be granted for treatment of metastatic or unresectable NETs of the lung.
4. Tumors of the pancreas
   Authorization of 24 months may be granted for treatment of NETs of the pancreas.
5. Tumors of the adrenal gland
   Authorization of 24 months may be granted for treatment of NETs of the adrenal gland.

C. Meningiomas

Authorization of 24 months may be granted to members for treatment of unresectable meningioma.

D. Thymomas and thymic carcinomas

Authorization of 24 months may be granted for treatment of thymomas and thymic carcinomas.

E. Congenital hyperinsulinism (CHI)/persistent hyperinsulinemic hypoglycemia of infancy (octreotide and Sandostatin only)

Authorization of 6 months may be granted for treatment of CHI and persistent hyperinsulinemic hypoglycemia in an infant.

III. CONTINUATION OF THERAPY

A. Acromegaly

Authorization of 24 months may be granted for continuation of therapy for acromegaly when the member's IGF-1 level has decreased or normalized since initiation of therapy.

B. All other indications

Members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Octreotide acetate [package insert]. Rockford, IL: Mylan Institutional LLC; May 2015.
2. Sandostatin [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March2012.
3. Sandostatin LAR Depot [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2016.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Availableat: http://www.nccn.org. Accessed February 8, 2018.
5. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2014;99:3933-3951.

6. American Association of Clinical Endocrinologists Acromegaly Guidelines Task Force. Medical guidelines for clinical practice for the diagnosis and treatment of acromegaly – 2011 update. *Endocr Pract*. 2011;17(suppl 4):1-44.
7. The NCCN Clinical Practice Guidelines in Oncology® Neuroendocrine Tumors (Version 3.2017). © 2017 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed February 8, 2018.
8. Rinke A, Muller H, Schade-Brittinger C, et al. Placebo-controlled, double-blind, prospective, randomized study on the effect of octreotide LAR in the control of tumor growth in patients with metastatic neuroendocrine midgut tumors: a report from the PROMID study group. *J Clin Oncol*. 2009;27:4656-4663.
9. The NCCN Clinical Practice Guidelines in Oncology® Central Nervous System Cancers (Version1.2017). © 2017 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed February 8, 2018.
10. The NCCN Clinical Practice Guidelines in Oncology® Thymomas and Thymic Carcinomas. (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed February 8, 2018.

Reference number
2597-A

SPECIALTY GUIDELINE MANAGEMENT

OLUMIANT (baricitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Olumiant is indicated for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Moderately to severely active rheumatoid arthritis (RA)

A. Authorization of 24 months may be granted for treatment of moderately to severely active RA for members who have previously received treatment with Olumiant.

B. Authorization of 24 months may be granted for treatment of moderately to severely active RA for members who have experienced an inadequate response or intolerance to at least one tumor necrosis factor (TNF) inhibitor.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Olumiant as evidenced by low disease activity or improvement in signs and symptoms of RA.

IV. OTHER

Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Olumiant or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. REFERENCES

1. Olumiant [package insert]. Indianapolis, IN: Lilly USA, LLC; May 2018.

Reference number(s)
2138-A, 2679-A

SPECIALTY GUIDELINE MANAGEMENT

OLYSIO (simeprevir)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Olysio is indicated for the treatment of adults with chronic hepatitis C virus (HCV) infection:

A. in combination with sofosbuvir in patients with HCV genotype 1 without cirrhosis or with compensated cirrhosis

B. in combination with peginterferon alfa (PEG-IFN) and ribavirin (RBV) in patients with HCV genotype 1 or 4 without cirrhosis or with compensated cirrhosis

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Decompensated cirrhosis/moderate or severe hepatic impairment (Child Turcotte Pugh Class B or C)

Note: When the requested drug is being used in a combination therapy regimen, exclusions to the other antiviral drugs also apply.

III. INITIAL CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus infection, in combination with PEG-IFN and RBV

1. Genotype 1 or 4 infection

Authorization of up to 6 weeks total may be granted for initiation of therapy in members who are treatment-naïve or failed prior treatment with PEG-IFN and RBV AND meet one of the following criteria:

a. Genotype 1a infection without the NS3 Q80K polymorphism
b. Genotype 1b infection
c. Genotype 4 infection

B. Chronic hepatitis C virus infection, in combination with Sovaldi

1. Genotype 1a infection

a. Authorization of up to 12 weeks total may be grantedfor members without cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
b. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis without the NS3 Q80K polymorphism who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.

2. Genotype 1b infection

a. Authorization of up to 12 weeks total may be grantedfor members without cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.
b. Authorization of up to 24 weeks total may be granted for members with compensated cirrhosis who are treatment-naïve or failed prior treatment with PEG-IFN and RBV.

3. Recurrent HCV infection post liver transplantation
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have recurrent HCV genotype 1 or 4 infection post liver transplantation.

C. Chronic hepatitis C virus infection, in combination with Sovaldi and RBV
Recurrent HCV infection post liver transplantation
Authorization of up to 12 weeks total may be granted for members without cirrhosis or with compensated cirrhosis who have recurrent HCV genotype 1 or 4 infection post liver transplantation.

D. HCV and HIV Coinfection
Authorization may be granted for members with HCV and HIV coinfection when the criteria for approval of the requested regimen in Section A, B or C above are met.

IV. CONTINUATION OF THERAPY

A. Chronic hepatitis C virus infection, in combination with PEG-IFN and RBV
Genotype 1 or 4 infection at week 4 assessment
Authorization of up to 12 weeks total for Olysio and up to 48 weeks total for PEG-IFN and RBV may be granted for members with HCV-RNA < 25 IU/mL at week 4 of treatment.

V. REFERENCES

1. Olysio [package insert]. Titusville, NJ: Janssen Products, LP; May 2017.
2. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Last changes made September 21, 2017. Accessed September 22,2017.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**OMEGA-3 FATTY ACIDS**
BRAND NAME (generic)	**EPANOVA (omega-3-carboxylic acids)**
	LOVAZA (omega-3-acid ethyl esters)
	VASCEPA (icosapent ethyl)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Epanova

Epanova (omega-3-carboxylic acids) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500mg/dL) hypertriglyceridemia.

Usage Considerations: Patients should be placed on an appropriate lipid-lowering diet before receiving Epanova and should continue this diet during treatment with Epanova.

Laboratory studies should be done to ascertain that the triglyceride levels are consistently abnormal before instituting Epanova therapy. Every attempt should be made to control serum lipids with appropriate diet, exercise, weight loss in obese patients, and control of any medical problems such as diabetes mellitus and hypothyroidism that are contributing to the lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (such as beta blockers, thiazides, estrogens) should be discontinued or changed if possible prior to consideration of triglyceride-lowering drug therapy.

Limitations of Use

The effect of Epanova on the risk for pancreatitis has not been determined.

The effect of Epanova on cardiovascular mortality and morbidity has not been determined.

Lovaza

Lovaza (omega-3-acid ethyl esters) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.

Usage Considerations: Patients should be placed on an appropriate lipid-lowering diet before receiving Lovaza and should continue this diet during treatment with Lovaza.

Laboratory studies should be done to ascertain that the lipid levels are consistently abnormal before instituting Lovaza therapy. Every attempt should be made to control serum lipids with appropriate diet, exercise, weight loss in obese patients, and control of any medical problems such as diabetes mellitus and hypothyroidism that are contributing to the lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (such as beta blockers, thiazides, estrogens) should be discontinued or changed if possible prior to consideration of triglyceride-lowering drug therapy.

Limitations of Use

The effect of Lovaza on the risk for pancreatitis has not been determined.

The effect of Lovaza on cardiovascular mortality and morbidity has not been determined.

Vascepa

Vascepa (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.
Usage Considerations: Patients should be placed on an appropriate lipid-lowering diet and exercise regimen before receiving Vascepa and should continue this diet and exercise regimen with Vascepa.
Attempts should be made to control any medical problems such as diabetes mellitus, hypothyroidism, and alcohol intake that may contribute to lipid abnormalities. Medications known to exacerbate hypertriglyceridemia (such as beta blockers, thiazides, estrogens) should be discontinued or changed, if possible, prior to consideration of TG-lowering drug therapy.
Limitations of Use
The effect of Vascepa on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.
The effect of Vascepa on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has, or did have prior to the start of a triglyceride lowering drug, a triglyceride level greater than or equal to 500 mg/dL
  AND
- The patient will be on an appropriate lipid-lowering diet and exercise regimen during treatment

REFERENCES

1. Epanova [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; March 2017.
2. Lovaza [package insert]. Research Triangle Park, NC: GlaxoSmithKline; September 2015.
3. Vascepa [package insert]. Bedminster, NJ: Arnarin Pharma Inc.; February 2017.
4. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed November 2017.
5. Micromedex Solutions [database online]. Greenwood Village, CO: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed November 2017.
6. Stone NJ, Robinson J, Lichtenstein AH, et al. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013. [Epub Ahead of Print].
7. Miller, M., Stone, N.J., Ballantyne, C., et al. Triglycerides and Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation.* 2011;123:2293-2333.
8. Berglund L, Brunzell JD, Goldberg AC, et al, "Evaluation and Treatment of Hypertriglyceridemia: An Endocrine Society Clinical Practice Guideline," *J Clin Endocrinol Metab,* September 2012, 97: 2969–2989.
9. Grundy, SM, Cleeman JI, Merz NB, et al. Implications of Recent Clinical Trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. *Circulation*. July 13, 2004;110:227-239.

Reference number
2291-A

SPECIALTY GUIDELINE MANAGEMENT

ONCASPAR (pegaspargase)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

C. FDA-Approved Indications

Acute lymphoblastic leukemia (ALL):

1. Oncaspar is indicated as a component of a multi-agent chemotherapeutic regimen for the first line treatment of pediatric and adult patients with ALL.
2. Oncaspar is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of pediatric and adult patients with ALL and hypersensitivity to native forms of L-asparaginase.

D. Compendial Uses

1. Extranodal natural killer/T-cell lymphoma, nasal type: as a component of multi-agent chemotherapeutic regimen
2. Lymphoblastic lymphoma (managed in the same manner as ALL)
3. Acute lymphoblastic leukemia (ALL) as a component of multi-agent chemotherapeutic regimen or central nervous system directed therapy as systemic therapy (IV/IM route)
4. Pediatric acute lymphoblastic leukemia (ALL) as a component of a multi-agent chemotherapeutic regimen[2,4]

All other indications are considered experimental/investigational and are not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

1. Acute Lymphoblastic Leukemia (ALL) and Lymphoblastic Lymphoma
Authorization of 12 months may be granted for the treatment of ALL or lymphoblastic lymphoma when the requested medication is used in conjunction with multi-agent chemotherapy.

2. **Extranodal Natural Killer/T-cell Lymphoma, nasal type**
Authorization of 12 months may be granted for the treatment of extranodal natural killer/T-cell lymphoma, nasal type when the requested medication is used in conjunction with multi-agent chemotherapy.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced disease progression or an unacceptable toxicity while on the current regimen.

IV. REFERENCES

1. Oncaspar [package insert]. Westlake Village, CA: Baxalta US Inc.; January 2019.
2. National Comprehensive Cancer Network. The NCCN Drugs & Biologics Compendium. http://www.nccn.org. Accessed July 15, 2019.

3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia. Version 2.2019. http://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed July 15, 2019.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Pediatric Acute Lymphoblastic Leukemia. Version 1.2020. https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed July 15, 2019.

Reference number
2127-A

SPECIALTY GUIDELINE MANAGEMENT

ORENCIA (abatacept)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Moderately to severely active rheumatoid arthritis in adults
2. Moderately to severely active polyarticular juvenile idiopathic arthritis in patients 2 years of age or older
3. Active psoriatic arthritis in adults

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 24 months may be granted for members who have previously received Orencia or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for the treatment of moderately to severely active rheumatoid arthritis.

2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
   b. Member has an intolerance or contraindication to methotrexate (see Appendix).

B. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)

1. Authorization of 24 months may be granted for members who have previously received Orencia or Actemra.

2. Authorization of 24 months may be granted for treatment of active pJIA when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial of a TNF inhibitor.
   b. Member has intolerance or contraindication to a TNF inhibitor.

C. Active psoriatic arthritis (PsA)

Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Orencia as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Orencia or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDIX: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

VI. REFERENCES

1. Orencia [package insert]. Princeton, NJ: Bristol-Myers Squibb; June 2017.
2. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017*;0*:1-18.
3. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guidelinefor the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
4. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59(6):762-784.
5. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res*. 2011;63(4):465-482.

Reference number(s)
1643-A

SPECIALTY GUIDELINE MANAGEMENT

Orenitram
(treprostinil extended-release tablets)

POLICY

XL. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Orenitram is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity.

All other indications are considered experimental/investigational and are not a covered benefit.

XLI. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

E. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
F. PAH was confirmed by either criterion (1) or criterion (2) below:
   8. Pretreatment right heart catheterization with all of the following results:
      i. mPAP ≥ 25 mmHg
      ii. PCWP ≤ 15 mmHg
      iii. PVR > 3 Wood units
   9. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      ix. Post cardiac surgery
      x. Chronic heart disease
      xi. Chronic lung disease associated with prematurity
      xii. Congenital diaphragmatic hernia

XLII. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

XLIII. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH

1.4. PAH associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.7 Chronic thromboembolic PH
4.8 Other pulmonary artery obstructions
- 4.8.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.8.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma
  - Germ cell tumours of the testis
  - Other tumours
- 4.8.3 Non-malignant tumours
  - Uterine leiomyoma
- 4.8.4 Arteritis without connective tissue disease
- 4.8.5 Congenital pulmonary artery stenosis
- 4.8.6 Parasites
  - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.7 Complex congenital heart disease

XLIV. REFERENCES

1. Orenitram [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; January 2017.
2. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
3. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.

4. Badesch DB, Champion HC, Gomez-Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S55-S66.
5. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol.* 2013;62:D34-S41.
6. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
7. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S78-S84.
8. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
9. Abman, SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.
10. Klinger, JR., Elliott, CG, Levine, DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019:155(3): 565-586.
11. Galie, N., McLaughlin, VV, Rubin, LJ, Simonneau, G. An overview of the 6th World Symposium on Pulmonary Hypertension. Eur Respir J 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.

Reference number(s)
2002-A

SPECIALTY GUIDELINE MANAGEMENT

OTEZLA (apremilast)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

E. FDA-Approved Indications
1. Moderate to severe plaque psoriasis
2. Active psoriatic arthritis
3. Oral ulcers associated with Behçet's disease

All other indications are considered experimental/investigational and are not a covered benefit.

XII. CRITERIA FOR INITIAL APPROVAL

D. Moderate to severe plaque psoriasis

1. Authorization of 24 months may be granted for members who have previously received Otezla or any biologic disease-modifying antirheumatic drug (DMARD) indicated for the treatment of moderate to severe plaque psoriasis.

2. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis when all of the following criteria are met:
   1. At least 5% of BSA is affected OR crucial body areas (i.e., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   2. Member meets any of the following criteria:
      i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix A).

F. Active psoriatic arthritis (PsA)

Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

G. Behcet's syndrome

Authorization of 24 months may be granted for members who have previously received Otezla or any biologic indicated for the treatment of Behcet's syndrome.

Authorization of 24 months may be granted for the treatment of oral ulcers associated with Behçet's syndrome when the member has had an inadequate response to at least one nonbiologic medication for Behçet's disease (e.g., colchicine, systemic glucocorticoids, azathioprine).

XIII. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Otezla as evidenced by low disease activity or improvement in signs and symptoms of the condition.

XIV. Appendix A: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease, or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

XV. REFERENCES

7. Otezla [package insert]. Summit, NJ: Celgene Corporation; July 2019.
8. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol.* 2009;61:451-485.
9. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
10. Coates LC, Kavanaugh A, Mease PJ, et al. Group for research and assessment of psoriasis and psoriatic arthritis 2015 treatment recommendation for psoriatic arthritis. *Arthritis Rheumatol*. 2016 May;68(5):1060-71.

Reference number(s)
2019-A

SPECIALTY GUIDELINE MANAGEMENT

OTREXUP (methotrexate injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Rheumatoid Arthritis (RA) including Polyarticular Juvenile Idiopathic Arthritis (pJIA)
   Otrexup is indicated in the management of selected adults with severe, active rheumatoid arthritis (RA) or children with active polyarticular juvenile idiopathic arthritis (pJIA), who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs).
2. Psoriasis
   Otrexup is indicated in adults for the symptomatic control of severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy, but only when the diagnosis has been established, as by biopsy and/or after dermatologic consultation. It is important to ensure that a psoriasis "flare" is not due to an undiagnosed concomitant disease affecting immune responses.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 24 months may be granted for treatment of RA, pJIA, or psoriasis when BOTH of the following criteria are met:

A. Member has tried and had an inadequate response or intolerance to generic oral methotrexate.
B. Member has inability to prepare and administer generic injectable methotrexate.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet ALL initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Otrexup as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. REFERENCES

1. Otrexup [package insert]. Ewing, NJ: Antares Pharma, Inc.; December 2016.
2. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
3. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017;*0*:1-18.

4. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res*. 2011;63(4):465-482.
5. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol.* 2009;61:451-485.

Reference number(s)
2139-A

SPECIALTY GUIDELINE MANAGEMENT

PEGASYS (peginterferon alfa-2a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Chronic Hepatitis C
   Pegasys, as part of a combination regimen with other hepatitis C virus (HCV) antiviral drugs, is indicated for the treatment of adults with chronic hepatitis C (CHC) with compensated liver disease. Pegasys in combination with ribavirin is indicated for treatment of pediatric patients 5 years of age and older with CHC and compensated liver disease. Pegasys monotherapy is only indicated for the treatment of patients with CHC with compensated liver disease if there are contraindications or significant intolerance to other HCV antiviral drugs.
2. Chronic Hepatitis B
   Pegasys is indicated for the treatment of adult patients with HBeAg-positive and HBeAg-negative chronic hepatitis B infection who have compensated liver disease and evidence of viral replication and liver inflammation. Pegasys is indicated for the treatment of HBeAG-positive CHB in non-cirrhotic pediatric patients 3 years of age and older with evidence of viral replication and elevations in serum alanine.

B. Compendial Uses
Myeloproliferative neoplasm (essential thrombocythemia, polycythemia vera, primary myelofibrosis and post-polycythemia vera or post-essential thrombocythemia myelofibrosis)

All other indications are considered experimental/investigational and are not a covered benefit.

II. INITIAL CRITERIA FOR APPROVAL

A. Chronic hepatitis C virus (HCV) infection
Refer to the SGM of requested regimen for the specific criteria for approval and approval durations.

B. Chronic hepatitis B virus (HBV) infection (including HDV coinfection)
Authorization of up to 48 weeks total may be granted for the treatment of chronic HBV infection, including HDV coinfection.

C. Myeloproliferative neoplasm
Authorization of 12 months may be granted for the treatment of myeloproliferative neoplasm (essential thrombocythemia, polycythemia vera, primary myelofibrosis and post-polycythemia vera or post-essential thrombocythemia myelofibrosis).

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Pegasys [package insert]. South San Francisco, CA: Genentech, Inc; October 2017.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed March 23, 2018.
3. Olysio [package insert]. Titusville, NJ: Janssen Products, LP; November 2017.
4. Sovaldi [package insert]. Foster City, CA: Gilead Sciences, Inc.; November 2017.
5. AASLD/IDSA/IAS–USA. Recommendations for testing, managing, and treating hepatitis C. http://www.hcvguidelines.org. Last changes made September 21, 2017. Accessed March 26,2018.
6. Terrault NA, Bzowej NH, Chang KM, et al. AASLD guidelines for treatment of chronic hepatitis B. *Hepatology*. 2015;1-23.
7. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Myeloproliferative Neoplasms (Version 2.2018). http://www.nccn.org. Accessed March 26,2018.

Reference number(s)
2121-A

SPECIALTY GUIDELINE MANAGEMENT

BUPHENYL (sodium phenylbutyrate)
sodium phenylbutyrate (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Buphenyl is indicated as adjunctive therapy in the chronic management of patients with urea cycle disorders involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS). It is indicated in all patients with neonatal-onset deficiency (complete enzymatic deficiency, presenting within the first 28 days of life). It is also indicated in patients with late-onset disease (partial enzymatic deficiency, presenting after the first month of life) who have a history of hyperammonemic encephalopathy. It is important that the diagnosis be made early and treatment initiated immediately to improve survival. Any episode of acute hyperammonemia should be treated as a life-threatening emergency.

All other indications are considered experimental/investigational and not medically necessary.

II. REQUIRED DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: enzyme assay, biochemical, or genetic testing results supporting diagnosis.

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for chronic management of urea cycle disorder (UCD) when the diagnosis is confirmed by enzymatic, biochemical, or genetic testing.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for chronic management of a urea cycle disorder (UCD), who are experiencing benefit from therapy as evidenced by a reduction in plasma ammonia levels from baseline.

V. REFERENCES

1. Buphenyl [package insert]. Lake Forest, IL: Horizon Pharma USA, Inc.; April 2016.
2. Mew NA, Lanpher BC. Urea Cycle Disorders Overview. In: Pagon RA, Adam MP, Ardinger HH, et. al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017 [updated April 9, 2015]. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1217/?report=printable.
3. Häberle J, Boddaert N, Burlina A, et al. Suggested guidelines for the diagnosis and management of urea cycle disorders. *Orphanet J Rare Dis*. 2012;7:32.

Reference number(s)
2026-A

SPECIALTY GUIDELINE MANAGEMENT

PROLIA (denosumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

H. FDA-Approved Indications
1. Treatment of postmenopausal women with osteoporosis at high risk for fracture
2. Treatment to increase bone mass in men with osteoporosis at high risk for fracture
3. Treatment of men and women with glucocorticoid-induced osteoporosis at high risk for fracture
4. Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy (ADT) for non-metastatic prostate cancer
5. Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

I. Compendial Uses
Prevention or treatment of osteoporosis during androgen deprivation therapy for prostate cancer in patients with high fracture risk

All other indications are considered experimental/investigational and are not a covered benefit.

XVI. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fractures, T-score, and FRAX fracture probability as applicable to Sections III.A, III.B, and III.C.

XVII. CRITERIA FOR INITIAL APPROVAL

E. Postmenopausal osteoporosis

Authorization of 12 months may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:
1. Member has a history of fragility fractures
2. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
   a. Member has indicators of higher fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3.5], or increased fall risk)
   b. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., zoledronic acid [Reclast], teriparatide [Forteo])
   c. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

F. Osteoporosis in men

Authorization of 12 months may be granted to male members with osteoporosis when ANY of the following criteria are met:

1. Member has a history of an osteoporotic vertebral or hip fracture
2. Member meets criteria BOTH of the following criteria:
   a. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)
   b. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

G. Glucocorticoid-induced osteoporosis

Authorization of 12 months may be granted to members with glucocorticoid-induced osteoporosis when ALL of the following criteria are met:

1. Member is currently receiving or will be initiating glucocorticoid therapy
2. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)
3. Member meets ANY of the following criteria:
   a. Member has a history of a fragility fracture
   b. Member has a pre-treatment T-score less than or equal to -2.5
   c. Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)

H. Breast cancer

Authorization of 12 months may be granted to members who are receiving adjuvant aromatase inhibitor therapy for breast cancer.

I. Prostate cancer

Authorization of 12 months may be granted to members who are receiving androgen deprivation therapy for prostate cancer.

XVIII. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria and experiences clinical benefit after at least 24 months of therapy with Prolia as evidenced by improvement or stabilization in T-score.

XIX. APPENDIX

Appendix A. Clinical reasons to avoid oral bisphosphonate therapy

- Esophageal abnormality that delays emptying such as stricture of achalasia
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance <35 mL/min)
- History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool

- High FRAX fracture probability: 10 year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%.
- 10-year probability; calculation tool available at: https://www.sheffield.ac.uk/FRAX/

- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg per day.

XX. REFERENCES

1. Prolia [package insert]. Thousand Oaks, CA: Amgen Inc.; April 2019.
2. The NCCN Drugs & Biologics Compendium™ © 2018 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed October 25, 2018.
3. Bisphosphonates. *Drug Facts and Comparisons.* Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health Inc; March 21, 2019. Accessed April 10, 2019.
4. Cosman F, de Beur SJ, LeBoff MS, et al. National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int.* 2014;25(10): 2359-2381.
5. Jeremiah MP, Unwin BK, Greenwald MH, et al. Diagnosis and management of osteoporosis. *Am Fam Physician*. 2015;92(4):261-268.
6. Watts NB, Bilezikian JP, Camacho PM, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of postmenopausal osteoporosis. *Endocr Pract*. 2016;22 (Suppl 4):1-42.
7. ACOG Practice Bulletin Number 129: Osteoporosis. *Obstet Gynecol*. 2012;120(3):718-734.
8. National Institute for Health and Care Excellence. Osteoporosis Overview. Last updated February 2018. Available at: http://pathways.nice.org.uk/pathways/osteoporosis. Accessed April 10, 2019.
9. Treatment to prevent osteoporotic fractures: an update. Department of Health and Human Services, Agency for Healthcare Research and Quality. 2012; Publication No. 12-EHC023-EF. Available at www.effectivehealthcare.ahrq.gov/lbd.cfm.
10. Watts NB, Adler RA, Bilezikian JP, et al. Osteoporosis in men : an Endocrine Society clinical practice guideline. *J Clin Endocr Metab*. 2012;97(6):1802-1822.
11. Gralow JR, Biermann S, Farooki A, et al. NCCN Task Force Report: Bone Health in Cancer Care. *JNCCN*. 2013; 11(Suppl 3):S1-50.
12. FRAX® WHO fracture risk assessment tool. © World Health Organization Collaborating Centre for Metabolic Bone Diseases: University of Sheffield, UK. Available at: https://www.sheffield.ac.uk/FRAX/. Accessed April 10, 2019.
13. Fink HA, Gordon G, Buckley L, et al. 2017 American College of Rheumatology Guidelines for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis. *Arthritis Care Res*. 2017;69:1521-1537.
14. Ensrud KE, Crandall CJ. Osteoporosis. Ann Intern Med 2017;167(03):ITC17–ITC32.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**NARCOLEPSY AGENTS**
BRAND NAME (generic)	**PROVIGIL (modafinil)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Provigil is indicated to improve wakefulness in adult patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea, and shift work disorder.

In OSA, Provigil is indicated as an adjunct to standard treatment(s) for the underlying obstruction. If continuous positive airway pressure (CPAP) is the treatment of choice for a patient, a maximal effort to treat with CPAP for an adequate period of time should be made prior to initiating Provigil. If Provigil is used adjunctively with CPAP, the encouragement of and periodic assessment of CPAP compliance is necessary.

Compendial Uses/ Limited Treatment Option
Fatigue related to multiple sclerosis[7-9]

COVERAGE CRITERIA
The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has a diagnosis of narcolepsy confirmed by sleep labevaluation

OR

- The patient has a diagnosis of Shift Work Disorder (SWD).

OR

- The patient has a diagnosis of obstructive sleep apnea (OSA) confirmed by polysomnography.

OR

- The patient has a diagnosis of fatigue related to multiple sclerosis
  AND
- The patient has experienced an inadequate treatment response, intolerance or contraindication toamantadine

REFERENCES

1. Provigil [package insert]. Frazer, PA: Cephalon, Inc.; December 2016.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed April 2018.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed April 2018.
4. Morgenthaler TJ, Kapur VK, Brown T, et al. Practice parameters for the treatment of narcolepsy and other hypersomnias of central origin. *Sleep* 2007;30(12):1705-11.

5. Kushida, C, Morgenthaler, T, et al. Practice parameters for the treatment of snoring and obstructive sleep apnea with oral appliances: an update for 2005. *Sleep* 2006;29(2):240-243.
6. Czeisler, CA et al. Modafinil for excessive sleepiness associated with shift work sleep disorder. *New England Journal of Medicine*. 2005: 353; 476-486.
7. Pucci, E, Branas P, D'Amico R, et al. Amantadine for fatigue in multiple sclerosis. *Cochrane Database Syst Rev* 2007;:CD002818
8. Brown JN, Howard CA, Kemp DW. Modafinil for the treatment of multiplesclerosis-related fatigue. *Ann Pharmacother*. 2010 Jun;44(6):1098-103.
9. Zifko UA, Rupp M, Schwarz S, et al. Modafinil in treatment of fatigue in multiple sclerosis. Results of an open-label study. *J Neurol*. 2002;249:983-987.

Reference number(s)
2018-A

SPECIALTY GUIDELINE MANAGEMENT

RASUVO (methotrexate injection)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Rheumatoid Arthritis including Polyarticular Juvenile Idiopathic Arthritis
   Rasuvo is indicated in the management of selected adults with severe, active rheumatoid arthritis (RA) or children with active polyarticular juvenile idiopathic arthritis, who have had an insufficient therapeutic response to, or are intolerant of, an adequate trial of first-line therapy including full dose non-steroidal anti-inflammatory agents (NSAIDs).
2. Psoriasis
   Rasuvo is indicated in adults for the symptomatic control of severe, recalcitrant, disabling psoriasis that is not adequately responsive to other forms of therapy, but only when the diagnosis has been established, as by biopsy and/or after dermatologic consultation. It is important to ensure that a psoriasis “flare” is not due to an undiagnosed concomitant disease affecting immune responses.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 24 months may be granted for treatment of RA, pJIA, or psoriasis when BOTH of the following criteria are met:

A. Member has tried and had an inadequate response or intolerance to generic oralmethotrexate.
B. Member has inability to prepare and administer generic injectablemethotrexate.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet ALL initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Rasuvo as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. REFERENCES

1. Rasuvo [package insert]. Chicago, IL: Medac Pharma Inc.; November 2014.
2. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guidelinefor the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
3. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017;*0*:1-18.

4. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res*. 2011;63(4):465-482.
5. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol.* 2009;61:451-485.

Reference number(s)
1839-A

SPECIALTY GUIDELINE MANAGEMENT

REBIF (interferon beta-1a)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication: Rebif is indicated for the treatment of patients with relapsing forms of multiple sclerosis to decrease the frequency of clinical exacerbations and delay the accumulation of physical disability.

Compendial Use: First clinical episode of multiple sclerosis with magnetic resonance imaging features consistent with multiple sclerosis

All other indications are considered experimental/investigational and are not covered benefits.

II. CRITERIA FOR INITIAL APPROVAL

A. Relapsing forms of multiple sclerosis
Authorization of 24 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis.

B. First clinical episode of multiple sclerosis
Authorization of 24 months may be granted to members for the treatment of a first clinical episode of multiple sclerosis.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Rebif [package insert]. Rockland, MA; EMD Serono Inc.; November 2015.
2. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed April 19, 2018.
3. Clinical Pharmacology. [database online.] Tampa, FL: Gold Standard, Inc.; http://www.clinicalpharmacology-ip.com/default.aspx [available with subscription]. Accessed April 19, 2018.

Reference number(s)
2380-A

SPECIALTY GUIDELINE MANAGEMENT

RECLAST (zoledronic acid)
zoledronic acid

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

J. FDA-Approved Indications
1. Treatment and prevention of osteoporosis in postmenopausal women
2. Treatment to increase bone mass in men with osteoporosis
3. Treatment and prevention of glucocorticoid-induced osteoporosis
4. Treatment of Paget's disease of bone in men and women

All other indications are considered experimental/investigational and are not a covered benefit.

XXI. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: Supporting chart notes or medical record indicating a history of fractures, T-score, and FRAX fracture probability as applicable to Sections III.A, III.B, and III.C.

XXII. CRITERIA FOR INITIAL APPROVAL

J. Postmenopausal osteoporosis

Authorization of 12 months may be granted to postmenopausal members with osteoporosis when ANY of the following criteria are met:
3. Member has a history of fragility fractures
4. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B) and meets ANY of the following criteria:
   a. Member has indicators of higher fracture risk (e.g., advanced age, frailty, glucocorticoid use, very low T-scores [less than or equal to -3.5], or increased fall risk)
   b. Member has failed prior treatment with or is intolerant to previous injectable osteoporosis therapy (e.g., denosumab [Prolia], teriparatide [Forteo])
   c. Member has had an oral bisphosphonate trial of at least 1-year duration or there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

K. Osteoporosis in men

Authorization of 12 months may be granted to male members with osteoporosis when ANY of the following criteria are met:
3. Member has a history of an osteoporotic vertebral or hip fracture

4. Member meets criteria BOTH of the following criteria:
   c. Member has a pre-treatment T-score less than or equal to -2.5 OR member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)
   d. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)

L. Glucocorticoid-induced osteoporosis

Authorization of 12 months may be granted for members with glucocorticoid-induced osteoporosis when ALL of the following criteria are met:

4. Member has had an oral bisphosphonate trial of at least 1-year duration OR there is a clinical reason to avoid treatment with an oral bisphosphonate (See Appendix A)
5. Member is currently receiving or will be initiating glucocorticoid therapy
6. Member meets ANY of the following criteria:
   a. Member has a history of a fragility fracture
   b. Member has a pre-treatment T-score of less than or equal to -2.5
   c. Member has osteopenia (i.e., pre-treatment T-score greater than -2.5 and less than -1) with a high pre-treatment FRAX fracture probability (See Appendix B)

M. Paget's disease of bone

Authorization of one dose (5 mg) may be granted for the treatment of Paget's disease of bone.

XXIII. CONTINUATION OF THERAPY

A. Paget's disease of bone

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

B. All other indications

Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria and experiences clinical benefit after at least 24 months of therapy with zoledronic acid or Reclast as evidenced by improvement or stabilization in T-score.

XXIV. APPENDIX

Appendix A. Clinical reasons to avoid oral bisphosphonate therapy

- Esophageal abnormality that delays emptying such as stricture of achalasia
- Active upper gastrointestinal problem (e.g., dysphagia, gastritis, duodenitis, erosive esophagitis, ulcers)
- Inability to stand or sit upright for at least 30 to 60 minutes
- Inability to take at least 30 to 60 minutes before first food, drink, or medication of the day
- Renal insufficiency (creatinine clearance <35 mL/min)
- History of intolerance to an oral bisphosphonate

Appendix B. WHO Fracture Risk Assessment Tool

- High FRAX fracture probability: 10 year major osteoporotic fracture risk ≥ 20% or hip fracture risk ≥ 3%
- 10-year probability; calculation tool available at: https://www.sheffield.ac.uk/FRAX/
- The estimated risk score generated with FRAX should be multiplied by 1.15 for major osteoporotic fracture and 1.2 for hip fracture if glucocorticoid treatment is greater than 7.5 mg per day.

XXV. REFERENCES

1. Reclast [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2017.
2. Zoledronic acid injection [package insert]. Schaumburg, IL: Sagent Pharmaceuticals, Inc.; May 2018
3. Bisphosphonates. *Drug Facts and Comparisons.* Facts & Comparisons [database online]. St. Louis, MO: Wolters Kluwer Health Inc; March 21, 2019. Accessed April 10, 2019.
4. Cosman F, de Beur SJ, LeBoff MS, et al. National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int.* 2014;25(10)*: 2359-2381.*
5. Jeremiah MP, Unwin BK, Greenwald MH, et al. Diagnosis and management of osteoporosis. *Am Fam Physician*. 2015;92(4):261-268.
6. *Wat*ts NB, Bilezikian JP, Camacho PM, et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of postmenopausal osteoporosis. *Endocr Pract*. 2016;22 (Suppl 4):1-42.
7. ACOG Practice Bulletin Number 129: Osteoporosis. *Obstet Gynecol*. 2012;120(3):718-734.
8. National Institute for Health and Care Excellence. Osteoporosis Overview. Last updated February 2018. Available at: http://pathways.nice.org.uk/pathways/osteoporosis. Accessed April 10, 2019.
9. Treatment to prevent osteoporotic fractures: an update. Department of Health and Human Services, Agency for Healthcare Research and Quality. 2012; Publication No. 12-EHC023-EF. Available at www.effectivehealthcare.ahrq.gov/lbd.cfm.
10. Watts NB, Adler RA, Bilezikian JP, et al. Osteoporosis in men : an Endocrine Society clinical practice guideline. *J Clin Endocr Metab*. 2012;97(6):1802-1822.
11. Fink HA, Gordon G, Buckley L, et al. 2017 American College of Rheumatology Guidelines for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis. *Arthritis Care Res*. 2017;69:1521-1537.
12. Singer FR, Bone HG, Hosking DJ, et al. Paget's Disease of Bone: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2014; 99(12): 4408-22.
13. FRAX® WHO fracture risk assessment tool. © World Health Organization Collaborating Centre for Metabolic Bone Diseases: University of Sheffield, UK. Available at: https://www.sheffield.ac.uk/FRAX/. Accessed April 10, 2019.
14. Ensrud KE, Crandall CJ. Osteoporosis. Ann Intern Med 2017;167(03):ITC17–ITC32.

Reference number
2182-A

SPECIALTY GUIDELINE MANAGEMENT

REMICADE (infliximab)
INFLECTRA (infliximab-dyyb)
RENFLEXIS (infliximab-abda)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Moderately to severely active Crohn's disease (CD)
2. Moderately to severely active ulcerative colitis (UC)
3. Moderately to severely active rheumatoid arthritis (RA) in combination with methotrexate
4. Active ankylosing spondylitis (AS)
5. Active psoriatic arthritis (PsA)
6. Chronic severe plaque psoriasis (PsO)

B. Compendial Uses
1. Axial spondyloarthritis
2. Behçet's syndrome
3. Granulomatosis with polyangiitis (Wegener's granulomatosis)
4. Hidradenitis suppurativa
5. Juvenile idiopathic arthritis
6. Pyoderma gangrenosum
7. Sarcoidosis
8. Takayasu's arteritis
9. Uveitis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active Crohn's disease (CD)
1. Authorization of 24 months may be granted for members who have previously received Remicade, Inflectra, Renflexis, or any other biologic indicated for the treatment of Crohn's disease.

2. Authorization of 24 months may be granted for treatment of moderately to severely active CD when any of the following criteria is met:
   a. Member has fistulizing disease.
   b. Member has an inadequate response, intolerance or contraindication to at least one conventional therapy option (see Appendix A).

B. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 24 months may be granted for members who have previously received Remicade, Inflectra, Renflexis, or any other biologic or targeted synthetic drug (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.

2. Authorization of 24 months may be granted for treatment of moderately to severely active UC when the member has an inadequate response, intolerance or contraindication to at least ONE conventional therapy option (see Appendix B).

C. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 24 months may be granted for members who have previously received Remicade, Inflectra, Renflexis, or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis. Remicade, Inflectra, or Renflexis must be prescribed in combination with methotrexate or leflunomide unless the member has a clinical reason not to use methotrexate or leflunomide.

2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
   a. Member is prescribed Remicade, Inflectra, or Renflexis in combination with methotrexate or leflunomide, or has a clinical reason not to use methotrexate or leflunomide.
   b. Member meets any of the following criteria:
      i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
      ii. Member has an intolerance or contraindication to methotrexate (see Appendix C).

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis

1. Authorization of 24 months may be granted for members who have previously received Remicade, Inflectra, Renflexis, or any other biologic DMARD indicated for active ankylosing spondylitis.

2. Authorization of 24 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
   b. Member has an intolerance or contraindication to two or more NSAIDs.

E. Active psoriatic arthritis (PsA)

Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

F. Chronic severe plaque psoriasis

1. Authorization of 24 months may be granted for members who have previously received Remicade, Inflectra, Renflexis, Otezla, or any other biologic DMARD indicated for the treatment of chronic, severe plaque psoriasis.

2. Authorization of 24 months may be granted for treatment of chronic severe plaque psoriasis whenall of the following criteria are met:
   a. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   b. Member meets any of the following criteria:
      i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.

ii. Member has a clinical reason to avoid pharmacologic treatment withmethotrexate, cyclosporine or acitretin (see Appendix D).
iii. Member has severe psoriasis that warrants a biologic DMARD as first-linetherapy.

G. Behçet's syndrome
Authorization of 24 months may be granted for treatment of Behçet's syndrome.

H. Granulomatosis with polyangiitis (Wegener's granulomatosis)
Authorization of 24 months may be granted for treatment of granulomatosis with polyangiitis.

I. Hidradenitis suppurativa
Authorization of 24 months may be granted for treatment of severe, refractory hidradenitis suppurativa.

J. Juvenile Idiopathic arthritis (JIA)
1. Authorization of 24 months may be granted for members who have previously received Remicade, Inflectra, or Renflexis or any other biologic DMARD indicated for juvenile idiopathicarthritis.

2. Authorization of 24 months may be granted for treatment of JIA when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial ofmethotrexate.
   b. Member has intolerance or contraindication to methotrexate (see AppendixC).

K. Pyoderma gangrenosum
Authorization of 24 months may be granted for treatment of pyoderma gangrenosum.

L. Sarcoidosis
Authorization of 24 months may be granted for treatment of sarcoidosis.

M. Takayasu's arteritis
Authorization of 24 months may be granted for treatment of Takayasu's arteritis.

N. Uveitis
Authorization of 24 months may be granted for treatment of uveitis in members who have experienced an inadequate response or intolerance or have a contraindication to a trial of immunosuppressive therapy for uveitis (e.g., methotrexate, azathioprine, or mycophenolate mofetil).

.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Remicade, Inflectra, or Renflexis as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Remicade, Inflectra, Renflexis or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDICES

Appendix A: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
   a. Oral budesonide
   b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine
3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenously (IV)
   b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC
5. Perianal and fistulizing disease – induction of remission
   a. Metronidazole ± ciprofloxacin, tacrolimus
6. Perianal and fistulizing disease – maintenance of remission
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

Appendix B: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
   a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
   b. Rectal mesalamine (e.g., Canasa, Rowasa)
   c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
   d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
   a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
   b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
   a. Prednisone, hydrocortisone IV, methylprednisolone IV
   b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: sulfasalazine
5. Pouchitis: Metronidazole, ciprofloxacin
   a. Alternative: rectal mesalamine

Appendix C: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity

7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix D: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Remicade [package insert]. Horsham, PA: Janssen Biotech, Inc.; June 2018.
2. Inflectra [package insert]. Lake Forest, IL: Hospira, a Pfizer Company; July 2018.
3. Renflexis [package insert]. Kenilworth, NJ. Merck &Co., Inc; November 2017.
4. van der Heijde D, Ramiro S, Landewe R, et al. 2016 Update of the international ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis.* 2017;0:1-14.
5. DRUGDEX® System [Internet database]. Ann Arbor, MI: Truven Health Analytics. Updated periodically. Accessed August 17, 2018.
6. Talley NJ, Abreu MT, Achkar J, et al. An evidence-based systematic review on medical therapies for inflammatory bowel disease. Am J Gastroenterol. 2011;106(Suppl 1):S2-S25.
7. Lichtenstein GR, Loftus Jr EV, Isaacs KI, et al. ACG Clinical Guideline: Management of Crohn's Diseasein Adults. Am J Gastroenterol. 2018;113:481-517.
8. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59(6):762-784.
9. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017*;0*:1-18.
10. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guidelinefor the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
11. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
12. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies; 2015 update. *Ann Rheum Dis*. 2016;75(3):499-510.
13. Gladman DD, Antoni C, P Mease, et al. Psoriatic arthritis: epidemiology, clinicalfeatures, course, and outcome. *Ann Rheum Dis* 2005;64(Suppl II):ii14–ii17.
14. Peluso R, Lervolino S, Vitiello M, et al. Extra-articular manifestations in psoriatic arthritis patients. Clin Rheumatol. 2014 May 8. [Epub ahead of print].
15. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis* 2011;70:896–904.

16. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res*. 2011;63(4):465-482.
17. Ringold S, Weiss PF, Beukelman T, et al. 2013 Update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis: Recommendations for the Medical Therapy of Children With Systemic Juvenile Idiopathic Arthritis and Tuberculosis Screening Among Children Receiving Biologic Medications. *Arthritis & Rheumatism.* 2013;65:2499-2512.
18. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Associationof America/Spondyloarthritis Research and Treatment Network 2015 recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol.* 2015: 10.1002/art.39298. [Epub ahead of print].

Reference number(s)
2232-A

SPECIALTY GUIDELINE MANAGEMENT

REVLIMID (lenalidomide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Multiple myeloma in combination with dexamethasone.
2. Multiple myeloma, as maintenance following autologous hematopoietic stem cell transplantation (auto-HSCT).
3. Transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.
4. Mantle cell lymphoma whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib.
5. Previously treated follicular lymphoma, in combination with a rituximab product
6. Previously treated marginal zone lymphoma, in combination with a rituximab product

B. Compendial Uses
1. Multiple myeloma
2. Systemic light chain amyloidosis
3. Classical Hodgkin lymphoma
4. Myelodysplastic syndrome without the 5q deletion cytogenetic abnormality
5. Myelofibrosis-associated anemia
6. POEMS Syndrome
7. Non-Hodgkin lymphoma (NHL) with any of the following subtypes:
   a. AIDS-related diffuse large B-cell lymphoma
   b. Primary central nervous system (CNS) lymphoma
   c. Post-transplant lymphoproliferative disorder
   d. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
   e. Diffuse large B-cell lymphoma
   f. Follicular lymphoma
   g. Nongastric/Gastric mucosa associated lymphoid tissue (MALT) lymphoma
   h. Primary cutaneous B-cell lymphoma
   i. Nodal/splenic marginal zone lymphoma
   j. Multicentric Castleman's disease
   k. Adult T-cell leukemia/lymphoma
   l. Mycosis fungoides (MF)/Sezary syndrome (SS)
   m. Angioimmunoblastic T-cell lymphoma (AITL)
   n. Peripheral T-cell lymphoma not otherwise specified (PTCL NOS)
   o. Enteropathy-associated T-cell lymphoma
   p. Monomorphic epithelotropic intestinal T-cell lymphoma
   q. Nodal peripheral T-cell lymphoma
   r. Follicular T-cell lymphoma
   s. Primary cutaneous anaplastic large cell lymphoma (ALCL)
   t. Hepatosplenic gamma-delta T-cell lymphoma
   u. High-grade B-cell lymphomas

All other indications are considered experimental/investigational and are not medically necessary.

Reference number(s)
2232-A

II. CRITERIA FOR INITIAL APPROVAL

A. Multiple myeloma

Authorization of 12 months may be granted for treatment of multiple myeloma.

B. Non-Hodgkin lymphoma (NHL)

Authorization of 12 months may be granted for treatment of NHL with any of the following subtypes:

2.1.1.1. Second-line or subsequent therapy for relapse of AIDS-related diffuse large B-cell lymphoma
2.1.1.2. Relapsed or refractory primary central nervous system (CNS) lymphoma as a single agent or in combination with rituximab
2.1.1.3. Second-line or subsequent therapy of post-transplant lymphoproliferative disorder (non-germinal center B-cell type)
4. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
5. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma after multiple lines of chemoimmunotherapy
6. Second-line or subsequent therapy for non-germinal center diffuse large B-cell lymphoma in non-candidates for transplant
7. Follicular lymphoma
8. Mantle cell lymphoma
9. Refractory or progressive nongastric MALT lymphoma as a single agent or in combination with rituximab
10. Second-line or subsequent therapy for recurrent or progressive gastric MALT lymphoma
11. Primary cutaneous B-cell lymphoma
12. Second-line or subsequent therapy for refractory or progressive nodal marginal zone lymphoma
13. Second-line or subsequent therapy for splenic marginal zone lymphoma
14. Relapsed, refractory or progressive multicentric Castleman's disease
15. Relapsed or refractory primary cutaneous anaplastic large cell lymphoma (ALCL) or cutaneous ALCL as a single agent
16. Second-line or subsequent therapy for adult T-cell leukemia/lymphoma (acute or lymphoma subtypes)
17. Mycosis fungoides (MF)/Sezary syndrome (SS)
18. Second line or subsequent therapy for relapsed or refractory angioimmunoblastic T-cell lymphoma (AITL)
19. Second-line or subsequent therapy for relapsed or refractory peripheral T-cell lymphoma not otherwise specified (PTCL NOS)
20. Second-line or subsequent therapy for relapsed or refractory enteropathy-associated T-cell lymphoma
21. Second-line or subsequent therapy for relapsed or refractory monomorphic epitheliotropic intestinal T-cell lymphoma
22. Second-line or subsequent therapy for relapsed or refractory nodal peripheral T-cell lymphoma with TFH phenotype
23. Second-line or subsequent therapy for relapsed or refractory follicular T-cell lymphoma
24. Second-line or subsequent therapy for refractory hepatosplenic gamma-delta T-cell lymphoma
25. Second line or subsequent therapy for high-grade B-cell lymphomas

C. Myelodysplastic syndrome

Authorization of 12 months may be granted for treatment of low- to intermediate-1 risk myelodysplastic syndrome (IPSS scale) for those with symptomatic anemia.

D. Myelofibrosis-associated anemia

Authorization of 12 months may be granted for treatment of myelofibrosis-associated anemia when all of the following criteria are met:

3. The requested medication will be given as a single agent or in combination with prednisone.
4. The member has serum erythropoietin levels of either of the following:
   a. 500 mU/mL or greater
   b. Less than 500 mU/mL and no response or loss of response to erythropoietin stimulating agents

E. Systemic light chain amyloidosis

Authorization of 12 months may be granted for treatment of systemic light chain amyloidosis in combination with dexamethasone.

F. Classical Hodgkin lymphoma

Authorization of 12 months may be granted for treatment of relapsed or refractory classical Hodgkin lymphoma as a single agent.

G. POEMS Syndrome

Authorization of 12 months may be granted for treatment of POEMS syndrome in combination with dexamethasone.

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced unacceptable toxicity or disease progression while on the current regimen.

IV. REFERENCES

1. Revlimid [package insert]. Summit, NJ: Celgene Corporation; December 2017.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 25, 2019.
3. DRUGDEX® System (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com (cited: 03/25/2019).
4. The Clinical NCCN Practice Guidelines in Oncology® Multiple Myeloma (Version 1.2019). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed October 8, 2018.
5. The Clinical NCCN Practice Guidelines in Oncology® B-cell Lymphoma (Version 5.2018) © 2018 National Comprehensive Cancer Network, Inc. Available at: www.nccn.org. Accessed October 8, 2018.
6. The Clinical NCCN Practice Guidelines in Oncology® Myelodysplastic Syndromes (Version 1.2019). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed October 8, 2018.
7. The Clinical NCCN Practice Guidelines in Oncology® Myeloproliferative Neoplasms (Version 1.2019) © 2018 National Comprehensive Cancer Network, Inc. Available at: www.nccn.org. Accessed October 8, 2018.
8. The Clinical NCCN Practice Guidelines in Oncology® Systemic Light Chain Amyloidosis (Version 1.2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: www.nccn.org. Accessed October 8, 2018.
9. The Clinical NCCN Practice Guidelines in Oncology® Hodgkin Lymphoma (Version 3.2018) © 2018 National Comprehensive Cancer Network, Inc. Available at: www.nccn.org. Accessed October 8, 2018.
10. The Clinical NCCN Practice Guidelines in Oncology T-cell Lymphomas (Version 5.2018) © 2018 National Comprehensive Cancer Network, Inc. Available at: www.nccn.org. Accessed October 8, 2018.

Reference number(s)
1704-A

SPECIALTY GUIDELINE MANAGEMENT

RITUXAN (rituximab)
Treatment of Hematologic and Oncologic Conditions

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications[1]

1. Non-Hodgkin's lymphoma (NHL) in patients with:
   a. Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent
   b. Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to Rituxan in combination with chemotherapy, as single-agent maintenance therapy
   c. Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL, as a single agent after first-line CVP (cyclophosphamide, vincristine, and prednisone) chemotherapy
   d. Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens
2. Chronic lymphocytic leukemia (CLL), in combination with fludarabine and cyclophosphamide (FC), for the treatment of patients with previously untreated and previously treated CD20-positive CLL.
3. Granulomatosis with polyangiitis (Wegener's Granulomatosis) and microscopic polyangiitis (MPA) (Not addressed in this policy –Refer to Rituxan-RA+Other SGM)
4. Moderately to severely active rheumatoid arthritis (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)
5. Moderate to severe pemphigus vulgaris in adult patients (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)

B. Compendial Uses[2-10]

1. Sjögren's syndrome[2] (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)
2. Multiple sclerosis[2] (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)
3. Neuromyelitis optica (Devic disease)[11,12] (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)
4. Idiopathic inflammatory myopathy, refractory[2] (Not addressed in this policy – Refer to Rituxan-RA+Other SGM)
5. Non-Hodgkin's lymphoma[2,3]
   a. Small lymphocytic lymphoma (SLL)[3]
   b. Mantle cell lymphoma[2,3]
   c. Marginal zone lymphomas (nodal, splenic, gastric MALT, nongastric MALT)[3]
   d. Burkitt lymphoma[2,3]
   e. Primary cutaneous B-cell lymphoma[3]
   f. Castleman's disease[3]
   g. Acquired immunodeficiency syndrome (AIDS)-related B-cell lymphoma[3]
   h. Hairy cell leukemia[3]
   i. Post-transplant lymphoproliferative disorder (PTLD)[2,3]
   j. Lymphoblastic lymphoma[4,5]

6. Relapsed/refractory immune or idiopathic thrombocytopenic purpura (ITP)[2,6]
7. Autoimmune hemolytic anemia[2,7]
8. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (LPL)[2,3]
9. Thrombotic thrombocytopenic purpura[2,8]
10. Myasthenia gravis, refractory[2]
11. Hodgkin's lymphoma, nodular lymphocyte-predominant[2,3]
12. Chronic graft-versus-host disease (GVHD)[2,9]
13. Central nervous system (CNS) cancers[3]
    a. Leptomeningeal metastases from lymphomas
    b. Primary CNS lymphoma
14. Acute lymphoblastic leukemia (ALL)[3]
15. Prevention of Epstein-Barr virus (EBV)-related PTLD in high risk patients[2,8,10]
16. Immune checkpoint inhibitor-related toxicities[3]

All other indications are considered experimental/investigational and are not a covered benefit.

CRITERIA FOR INITIAL APPROVAL

A. Oncologic indications[1-5]

Authorization of 12 months may be granted for treatment of any of the following oncologic disorders that are CD20-positive as confirmed by testing or analysis:

1. Non-Hodgkin's lymphoma (NHL) with any of the following subtypes:
    a. Diffuse large B-cell lymphoma
    b. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
    c. Follicular lymphoma
    d. Mantle cell lymphoma
    e. Marginal zone lymphomas (nodal, splenic, gastric/non-gastric MALT)
    f. Burkitt lymphoma
    g. Primary cutaneous B-cell lymphoma
    h. Castleman's disease
    i. AIDS-related B-cell lymphoma
    j. Hairy cell leukemia
    k. Post-transplant lymphoproliferative disorder (PTLD)
    l. Lymphoblastic lymphoma
2. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (LPL)
3. Hodgkin's lymphoma, nodular lymphocyte-predominant
4. Central nervous system (CNS) cancers with either of the following:
    a. Leptomeningeal metastases from lymphomas
    b. Primary CNS lymphoma
5. Acute lymphoblastic leukemia (ALL)

B. Hematologic indications[2,6-10]

Authorization of 12 months may be granted for treatment of any of the following indications:

1. Refractory immune or idiopathic thrombocytopenic purpura (ITP)
2. Autoimmune hemolytic anemia
3. Thrombotic thrombocytopenic purpura
4. Chronic graft-versus-host disease (GVHD)
5. Prevention of Epstein-Barr virus (EBV)-related PTLD

C. Myasthenia gravis[2]

Authorization of 12 months may be granted for treatment of refractory myasthenia gravis.

D. Immune checkpoint inhibitor-related toxicities[3]
Authorization of 3 months may be granted for treatment of immune checkpoint inhibitor-related toxicities.

II. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

III. REFERENCES

1. Rituxan [package insert]. South San Francisco, CA: Genentech, Inc.; June 2018.
2. Micromedex Solutions [database online]. Truven Health Analytics, Greenwood Village, Colorado, USA. Available at: http://www.micromedexsolutions.com/. Accessed March 30, 2018.
3. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed March 30, 2018.
4. Arber D, Orazi A, Vardiman J, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*. May 19, 2016;127(20):2391-2405.
5. The NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version1.2018). © 2018 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed March 30, 2018.
6. Lexicomp Online®, AHFS® Drug Information, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; http://online.lexi.com [available with subscription]. Accessed March 30, 2018.
7. Clinical Consult: CVS Caremark Clinical Programs Review. Focus on Hematology-Oncology Clinical Programs. April 2008.
8. Clinical Consult: CVS Caremark Clinical Programs Review. Focus on Hematology-Oncology Clinical Programs. July 2013.
9. Clinical Consult: CVS Caremark Clinical Programs Review. Focus on Hematology-Oncology Clinical Programs. July 2009.
10. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant.* 2009; 15(10):1143-1238. URL: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3103296/pdf/nihms205400.pdf. Accessed August 2, 2013.
11. Scott, T.F., Frohman, E.M., DeSeze, J., (2011). Evidence-based guideline: Clinical evaluation and treatment of transverse myelitis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. American Academy of Neurology. 77: 2128-2134.
12. Trebst, C., Jarius, S., et al. (2014). Update on the diagnosis and treatment of neuromyelitis optica: Recommendations of the Neuromyelitis Optica Study Group (NEMOS). J Neurol 261: 1-16.

Reference number(s)
1704-A

SPECIALTY GUIDELINE MANAGEMENT

RITUXAN (rituximab)
Treatment of Rheumatoid Arthritis and Other Conditions

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Moderately to severely active rheumatoid arthritis (RA)
   In combination with methotrexate in patients who have inadequate response to one or more TNF antagonist therapies
2. Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA)
   In combination with glucocorticoids
3. Moderate to severe pemphigus vulgaris
4. Other FDA-approved indications (not addressed in this policy – Refer to Rituxan–OncologySGM)
   a. Non-Hodgkin's lymphoma (NHL)
   b. Chronic lymphocytic leukemia (CLL)

B. Compendial Uses
1. Sjögren's syndrome
2. Multiple sclerosis, relapsing remitting
3. Neuromyelitis optica (Devic disease)
4. Idiopathic inflammatory myopathy, refractory
5. For other compendial uses, refer to Rituxan–Oncology SGM

All other indications are considered experimental/investigational and are not a covered benefit.

II. EXCLUSIONS

Coverage will not be provided for requests for the treatment of rheumatoid arthritis when planned date of administration is less than 16 weeks since date of last dose received.

III. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)
1. Authorization of 24 months may be granted to members who have previously received any biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for the treatment of moderately to severely active rheumatoid arthritis OR have received at least two full doses of Rituxan for the treatment of RA, where the most recent dose was given within 6 months of the request. Rituxan must be prescribed in combination with methotrexate (MTX) unless the member has a contraindication or intolerance to MTX (see Appendix A).

2. Authorization of 24 months may be granted for treatment of moderately to severely active RA whenall of the following criteria are met:
   a. Member is prescribed Rituxan in combination with MTX or has a contraindication or intolerance to MTX.
   b. Member meets any of the following criteria:
      i. Member has experienced an inadequate response to at least a 3-month trial of MTXdespite adequate dosing (i.e., titrated to 20 mg/week)
      ii. Member has an intolerance or contraindication to MTX (see Appendix A)

B. Granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis) and microscopic polyangiitis (MPA)
Authorization of 24 months may be granted for treatment of GPA or MPA.

C. Sjögren's syndrome
Authorization of 24 months may be granted for treatment of Sjögren's syndrome.

D. Multiple sclerosis
Authorization of 24 months may be granted for treatment of multiple sclerosis (MS) when both of the following criteria are met:
1. Member has a diagnosis of relapsing remitting MS
2. Member has had an inadequate response to two or more disease-modifying drugs indicated for MS despite adequate duration of treatment (see Appendix B)

E. Neuromyelitis optica
Authorization of 24 months may be granted for treatment of neuromyelitis optica.

F. Idiopathic inflammatory myopathy
Authorization of 24 months may be granted for treatment of refractory polymyositis or dermatomyositis.

G. Pemphigus vulgaris
Authorization of 24 months may be granted for treatment of moderate to severe pemphigus vulgaris.

IV. CONTINUATION OF THERAPY

A. Rheumatoid arthritis
Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least two doses of therapy with rituximab as evidenced by low disease activity or improvement in signs and symptoms of the condition.

B. Other indications
Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria.

V. APPENDICES

Appendix A: Examples of contraindications to methotrexate
1. Alcoholism, alcoholic liver disease or other chronic liver disease

2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

Appendix B: Disease-modifying drugs indicated for multiple sclerosis

1. Aubagio (teriflunomide)
2. Avonex (interferon beta-1a)
3. Betaseron (interferon beta-1a)
4. Copaxone/Glatopa (glatiramer acetate)
5. Extavia (interferon beta-1a)
6. Gilenya (fingolimod)
7. Tecfidera (dimethyl fumarate)
8. Plegridy (peginterferon beta-1a)
9. Rebif (interferon beta-1a)
10. Tysabri (natalizumab)

VI. REFERENCES

1. Rituxan [package insert]. South San Francisco, CA: Genentech, Inc.; June 2018.
2. DRUGDEX® System [Internet database]. Ann Arbor, MI: Truven Health Analytics. Updated periodically. Accessed February 22, 2018.
3. Dass S, Bowman SJ, Vital EM, et al. Reduction of fatigue in Sjögren syndrome with rituximab: results of a double blind, placebo-controlled study. *Ann Rheum Dis*. 2008;67:1541-1544.
4. Meijer JM, Meiners PM, Vissink A, et al. Effectiveness of rituximab treatment in primary Sjögren's syndrome: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum*. 2010;62(4):960-8.
5. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017*;0*:1-18.
6. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guidelinefor the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
7. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59(6):762-784.
8. Hauser SL, Waubant E, Arnold DL, et al. B-cell depletion with rituximab in relapsing-remittingmultiple sclerosis. *N Engl J Med*. 2008;358:676-688.
9. Scott, T.F., Frohman, E.M., DeSeze, J., (2011). Evidence-based guideline: Clinical evaluation and treatment of transverse myelitis: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. American Academy of Neurology. 77: 2128-2134.
10. Trebst, C., Jarius, S., et al. (2014). Update on the diagnosis and treatment of neuromyelitis optica: Recommendations of the Neuromyelitis Optica Study Group (NEMOS). J Neurol 261: 1-16.

Reference number(s)
1612-A

SPECIALTY GUIDELINE MANAGEMENT

RUCONEST (recombinant C1 esterase inhibitor)

POLICY

XLV. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of acute attacks in adults and adolescent patients with hereditary angioedema (HAE)

All other indications are considered experimental/investigational and are not a covered benefit.

XLVI. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

G. C4 levels and C1 inhibitor functional and antigenic protein levels
H. F12, angiopoietin-1 or plasminogen gene mutation testing, if applicable
I. Chart notes confirming family history of angioedema, if applicable

XLVII. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of acute hereditary angioedema attacks when Ruconest will not be used in combination with Berinert, Firazyr, or Kalbitor and either of the following criteria is met:

E. Member has C1 inhibitor deficiency or dysfunction as confirmed by laboratory testing.
1. C1 inhibitor (C1-INH) antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
2. Normal C1-INH antigenic level and a low C1-INH functional level (functional C1-INH less than 50% or C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)

F. Member has normal C1 inhibitor as confirmed by laboratory testing and meets one of the following criteria:
1. Member has an F12, angiopoietin-1, or plasminogen gene mutation as confirmed by genetic testing, or
2. Member has a documented family history of angioedema and the angioedema was refractory to a trial of high-dose antihistamine (e.g., cetirizine) for at least one month.

XLVIII. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continuation of therapy when all of the following criteria are met:

E. Member meets the criteria for initial approval.
F. Member has experienced reduction in severity, and/or duration of attacks when they use the requested medication to treat an acute attack.

XLIX. REFERENCES

1. Ruconest [package insert]. Raleigh, NC: Santarus, Inc.; March 2018.

2. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy, and management of hereditary angioedema. *Allergy Asthma Clin Immunol*. 2010;6(1):24.
3. Cicardi M, Bork K, Caballero T, et al. Hereditary Angioedema International Working Group. Evidence-based recommendations for the therapeutic management of angioedema owing to hereditary C1 inhibitor deficiency: consensus report of an International Working Group. *Allergy.* 2012;67:147-157.
4. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. *J Allergy Clin Immunol: In Practice*. 2013; 1(5): 458-467.
5. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: consensus of an international expert panel. *Allergy Asthma Proc*. 2012; 33(6):S145-S156.
6. Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. *Allergy*. 2018;00:1-22.
7. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. *Ann Allergy Asthma Immunol*. 2012; 109:395-202.
8. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. *Allergy*. 2014;69: 602-616.
9. Bowen T. Hereditary angioedema: beyond international consensus – circa December 2010 – The Canadian Society of Allergy and Clinical Immunology Dr. David McCourtie Lecture. *Allergy Asthma Clin Immunol*. 2011;7(1):1.
10. Bernstein J. Update on angioedema: Evaluation, diagnosis, and treatment. *Allergy and Asthma Proceedings.* 2011;32(6):408-412.
11. Longhurst H, Cicardi M. Hereditary angio-edema. *Lancet.* 2012;379:474-481.
12. Farkas H, Martinez-Saguer I, Bork K, et al. International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency. *Allergy*. 2017;72(2):300-313.
13. Henao MP, Kraschnewski J, Kelbel T, Craig T. Diagnosis and screening of patients with hereditary angioedema in primary care. *Therapeutics and Clin Risk Management.* 2016; 12: 701-711.

Reference number(s)
1651-A

SPECIALTY GUIDELINE MANAGEMENT

Revatio (sildenafil tablets and oral suspension)
sildenafil tablets (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Sildenafil/Revatio is indicated for the treatment of pulmonary arterial hypertension (WHO Group I) in adults to improve exercise ability and delay clinical worsening.

Limitation of use: Adding sildenafil to bosentan therapy does not result in any beneficial effect on exercise capacity.

B. Compendial Use
Secondary Raynaud's phenomenon *(Tablets only)*

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Pulmonary Arterial Hypertension
Authorization of 24 months may be granted for treatment of PAH when ALL of the following criteria are met:
1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
2. PAH was confirmed by either criterion (i) or criterion (ii) below:
   i. Pretreatment right heart catheterization with all of the following results:
      a. mPAP ≥ 25 mmHg
      b. PCWP ≤ 15 mmHg
      c. PVR > 3 Wood units
   ii. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      a. Post cardiac surgery
      b. Chronic heart disease
      c. Chronic lung disease associated with prematurity
      d. Congenital diaphragmatic hernia

B. Secondary Raynaud's Phenomenon
Authorization of 24 months may be granted for treatment of secondary Raynaud's phenomenon when the patient has had an inadequate response to one of the following medications:
1. Calcium channel blockers

2. Angiotensin receptor blockers
3. Selective serotonin reuptake inhibitors
4. Alpha blockers
5. Topical nitrates

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for members with PAH or secondary Raynaud's phenomenon who are currently receiving sildenafil/Revatio therapy through a paid pharmacy or medical benefit.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

WHO Group 1. Pulmonary Arterial Hypertension (PAH)

1.1 Idiopathic (IPAH)
1.2 Heritable PAH
- 1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2(BMPR2)
- 1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3(KCNK3)
- 1.2.3 Unknown

1.3 Drug- and toxin-induced
1.4. Associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1'. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
1". Persistent pulmonary hypertension of the newborn (PPHN)

WHO Group 2. Pulmonary Hypertension Owing to Left Heart Disease

2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

WHO Group 3. Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia

3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

WHO Group 4. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

WHO Group 5. Pulmonary Hypertension with Unclear Multifactorial Mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders

5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

V. REFERENCES

1. Revatio [package insert]. New York, NY: Pfizer Inc.; February 2018.
2. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
3. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
4. Badesch DB, Champion HC, Gomez-Sanchez MA, et al. Diagnosis and assessment of pulmonaryarterial hypertension. *J Am Coll Cardiol.* 2009;54:S55-S66.
5. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol.* 2013;62:D34-S41.
6. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1Suppl):7S-10S.
7. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S78-S84.
8. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
9. Barst RJ, Ivy DD, Gaitan G, et al. A randomized, double-blind, placebo-controlled, dose-ranging study of oral sildenafil citrate in treatment-naïve children with pulmonary arterial hypertension. *Circulation.* 2012;125:324-334.
10. FDA Drug Safety Communication: FDA recommends against use of Revatio in children with pulmonary hypertension. Available at: http://www.fda.gov/Drugs/DrugSafety/ucm317123.htm. Accessed April 28, 2015.
11. Abman SH, Kinsella JP, Rosenzweig EB, et al. Implications of the U.S. Food and Drug Administration warning against the use of sildenafil for the treatment of pediatric pulmonary hypertension. *Am J Respir Crit Care Med*. 2013;187(6):572-575.
12. FDA Drug Safety Communication: FDA clarifies Warning about Pediatric Use of Revatio (sildenafil) for Pulmonary Arterial Hypertension. Available at: http://www.fda.gov/Drugs/DrugSafety/ucm390876.htm. Accessed April 28, 2015.
13. Abman, SH, Hansmann G, Archer SL, et al. Pediatric pulmonaryhypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.
14. Galiè N, Ghofrani HA, Torbicki A, et al. Sildenafil citrate therapy for pulmonary arterial hypertension. *N Engl J Med*. 2005;353:2148-2157.
15. Rubin LJ, Badesch DB, Fleming RT, et al. Long-term treatment with sildenafil citrate in pulmonary arterial hypertension. *Chest*. 2011;140(5):1274-1283.
16. DRUGDEX® System (electronic version). Truven Health Analytics, Greenwood Village, Colorado. Available at http://www.micromedexsolutions.com. Accessed April 20, 2017.
17. Hughes M, Ong VH, Anderson ME, et al. Consensus best practice pathway of the UK Scleroderma Study Group: digital vasculopathy in systemic sclerosis. *Rheumatology*. 2015;54:2015-2024.
18. Roustit M, Blaise S, Allanore Y, et al. Phosphodiesterase-5 inhibitors for the treatment of secondary Raynaud's phenomenon: systematic review and meta-analysis of randomized trials. *Ann Rheum Dis*. 2013;72(10):1696-1699.
19. Walker KM, Pope J, et al. Treatment of systemic sclerosis complications: what to use when first-line treatment fails – a consensus of systemic sclerosis experts. *Semin Arthritis Rheum*. 2012;42(1):42-55.
20. Raynaud Phenomenon (5-Minute Clinical Consult). Lexi-Drugs. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Available at: http://online.lexi.com. Accessed April 13, 2018.

Reference number
1731-A

SPECIALTY GUIDELINE MANAGEMENT

SILIQ (brodalumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy and have failed to respond or have lost response to other systemic therapies

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Moderate to severe plaque psoriasis

A. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Siliq, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.

B. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis for members who are 18 years of age or older when all of the following criteria are met:
   1. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet,face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   2. Member meets any of the following criteria:
      a. Member has had an inadequate response or intolerance to pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix).

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Siliq as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB)

Note: Members who have received Siliq or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy (male or female)
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Siliq [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; February 2017.
2. Lebwohl M, Strober B, Menter A, et al. Phase 3 studies comparing brodalumab with ustekinumab in psoriasis. *N Engl J Med*. 2015;373(14):1318-1328.
3. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.

Reference number
2015-A

SPECIALTY GUIDELINE MANAGEMENT

SIMPONI ARIA (golimumab injection for intravenous use)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Moderately to severely active rheumatoid arthritis (RA) in combination withmethotrexate
2. Active psoriatic arthritis (PsA)
3. Active ankylosing spondylitis (AS)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 24 months may be granted for members who have previously received Simponi Aria or any other biologic DMARD or targeted synthetic DMARD (e.g. Xeljanz) indicated for the treatment of moderate to severe RA. Simponi Aria must be prescribed in combination with methotrexate unless the member has a contraindication or intolerance to methotrexate (see Appendix A).

2. Authorization of 24 months may be granted for treatment of moderately to severely active RA whenall of the following criteria are met:
   a. Member is prescribed Simponi Aria in combination with methotrexate or has a contraindication or intolerance to methotrexate.
   b. Member meets any of the following criteria:
      i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
      ii. Member has an intolerance or contraindication to methotrexate (See Appendix A).

B. Active psoriatic arthritis (PsA)

Authorization of 24 months may be granted for treatment of active psoriatic arthritis (PsA).

C. Active ankylosing spondylitis (AS)

1. Authorization of 24 months may be granted for members who have previously received Simponi Aria or any other biologic DMARD indicated for active ankylosing spondylitis.

2. Authorization of 24 months may be granted for treatment of active ankylosing spondylitis when any of the following criteria ismet:
   a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs) over a 4-week period in total at maximum recommended or tolerated anti-inflammatory dose.
   b. Member has an intolerance and/or contraindication to two or more NSAIDs (see Appendix B).

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Simponi Aria as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Simponi Aria or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Contraindications to the Use of NSAIDs

1. Allergic-type reaction following aspirin or other NSAID administration
2. Asthma
3. Gastrointestinal bleeding
4. History of intolerance or adverse event
5. Significant drug interaction
6. Urticaria

VI. REFERENCES

1. Simponi Aria [package insert]. Horsham, PA: Janssen Biotech, Inc.; October 2017.
2. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017*;0*:1-18.
3. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guidelinefor the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
4. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59(6):762-784.

Reference number
2092-A

SPECIALTY GUIDELINE MANAGEMENT

SOMATULINE DEPOT (lanreotide)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Somatuline Depot is indicated for the long-term treatment of acromegalic patients who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option.
2. Somatuline Depot is indicated for the treatment of patients with unresectable, well- or moderately-differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.
3. Somatuline Depot is indicated for the treatment of adults with carcinoid syndrome; when used, it reduces the frequency of short-acting somatostatin analog rescue therapy.

B. Compendial Uses

Neuroendocrine tumors (NETs):

1. Tumors of the gastrointestinal (GI) tract, lung, and thymus (carcinoid tumors)
2. Tumors of the pancreas

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Acromegaly

Authorization of 24 months may be granted for the treatment of acromegaly when all of the following criteria are met:

1. Member has a high pretreatment insulin-like growth factor-1 (IGF-1) level for age and/or gender based on the laboratory reference range.
2. Member had an inadequate or partial response to surgery or radiotherapy OR there is a clinical reason why the member has not had surgery or radiotherapy.

B. Neuroendocrine tumors (NETs)

1. Tumors of the gastrointestinal (GI) tract (carcinoid tumor)
   Authorization of 24 months may be granted for treatment of NETs of the GI tract.
2. Tumors of the thymus (carcinoid tumor)
   Authorization of 24 months may be granted for treatment of NETs of the thymus.
3. Tumors of the lung (carcinoid tumor)
   Authorization of 24 months may be granted for treatment of NETs of the lung.
4. Tumors of the pancreas
   Authorization of 24 months may be granted for treatment of NETs of the pancreas.

C. Carcinoid syndrome
Authorization of 24 months may be granted for treatment of carcinoid syndrome.

III. CONTINUATION OF THERAPY

A. Acromegaly
Authorization of 24 months may be granted for continuation of therapy for acromegaly when the member's IGF-1 level has decreased or normalized since initiation of therapy.

B. All other indications
Members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Somatuline Depot [package insert]. Basking Ridge, NJ: Ipsen Biopharmaceuticals, Inc.; December 2018.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Availableat: http://www.nccn.org. Accessed January 29, 2019.
3. Katznelson L, Laws ER, Melmed S, et al. Acromegaly: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab.* 2014;99:3933-3951.
4. American Association of Clinical Endocrinologists Acromegaly Guidelines Task Force. Medical guidelines for clinical practice for the diagnosis and treatment of acromegaly – 2011 update. *Endocr Pract*. 2011;17(suppl 4):1-44.
5. The NCCN Clinical Practice Guidelines in Oncology® Neuroendocrine and Adrenal Tumors (Version 4.2018). © 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed January 29, 2019.
6. Caplin ME, Pavel M, Cwikla JB, et al. Lanreotide in metastatic enteropancreatic neuroendocrine tumors. *N Engl J Med.* 2014;371:224-233.

Reference number
1782-A

SPECIALTY GUIDELINE MANAGEMENT

SPRYCEL (dasatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Newly diagnosed adults with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase
2. Adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib
3. Adults with Ph+ acute lymphoblastic leukemia (ALL) with resistance or intolerance to prior therapy
4. Pediatric patients with Ph+ CML in chronic phase
5. Pediatric patients with newly diagnosed Ph+ ALL in combination with chemotherapy

B. Compendial Uses
1. Primary treatment of advanced phase CML (accelerated phase or blast phase)
2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
3. Ph+ ALL as a single agent or in combination with chemotherapy or corticosteroids
4. Induction therapy for Ph+ ALL in adults aged ≥ 65 years
5. Metastatic chondrosarcoma
6. Recurrent chordoma
7. Gastrointestinal stromal tumor (GIST) in patients with PDGFRA D842V mutation and disease progression on imatinib, sunitinib, or regorafenib

All other indications are considered experimental/investigational and are not a covered benefit.

XXVI. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:

A. Prior to initiation of therapy for treatment of CML or Ph+ ALL: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene

B. For members requesting initiation of Sprycel therapy for treatment of CML or ALL after experiencing resistance to prior tyrosine kinase inhibitor (TKI) therapy: results of T315I mutation testing

XXVII. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)

Authorization of 6 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:
1. Member has not received prior therapy with a TKI (e.g., bosutinib, imatinib, nilotinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of mutational testing are negative for T315I mutation

4. Member has received HSCT for CML

B. Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)
Authorization of 12 months may be granted for treatment of Ph+ ALL or LL that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:
1. Member has not received prior therapy with a TKI (e.g., bosutinib, imatinib, nilotinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of mutational testing are negative for T315I mutation

C. Gastrointestinal Stromal Tumor (GIST)
Authorization of 12 months may be granted for treatment of GIST in members with PDGFRA D842V mutation who have experienced disease progression on imatinib, sunitinib, or regorafenib.

D. Bone Cancer
Authorization of 12 months may be granted for treatment of metastatic chondrosarcoma or recurrent chordoma.

XXVIII. CONTINUATION OF THERAPY

a. CML
Authorization of 12 months may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when any of the following criteria are met:
i. BCR-ABL1 ≤ 10% for members who have been receiving Sprycel for ≤ 12 months
ii. No evidence of disease progression for members who have been receiving Sprycel for > 12 months
iii. Member has received HSCT

b. Ph+ ALL/LL
Authorization of 12 months may be granted for continued treatment of Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing in members who have not experienced disease progression or an unacceptable toxicity.

c. GIST and Bone Cancer
Authorization of 12 months may be granted for continued treatment of GIST, metastatic chondrosarcoma, or recurrent chordoma in members who have not experienced disease progression or an unacceptable toxicity.

XXIX. REFERENCES

1. Sprycel [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; December 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 18, 2019.
3. NCCN Clinical Practice Guidelines in Oncology® Chronic Myelogenous Leukemia (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 16, 2019.
4. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 17, 2019.
5. NCCN Clinical Practice Guidelines in Oncology® Soft Tissue Sarcoma (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 18, 2019.
6. NCCN Clinical Practice Guidelines in Oncology® Bone Cancer (Version 2.2019). © 2019 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 18, 2019.

Reference number(s)
2010-A

SPECIALTY GUIDELINE MANAGEMENT

STELARA (ustekinumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Moderate to severe plaque psoriasis (PsO)
2. Active psoriatic arthritis (PsA)
3. Moderately to severely active Crohn's disease (CD)
4. Moderately to severely active ulcerative colitis (UC)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderate to severe plaque psoriasis (PsO)

1. Authorization of 24 months may be granted for members who are 12 years of age or older who have previously received Stelara, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.

2. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis in members who are 12 years of age or older when all of the following criteria are met:
   a. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   b. Member meets any of the following criteria:
      i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix A).
      iii. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.

B. Active psoriatic arthritis (PsA)

Authorization of 24 months may be granted for treatment of active psoriatic arthritis in members who are 18 years of age or older.

C. Moderately to severely active Crohn's disease (CD)

1. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Stelara or any other biologic indicated for the treatment of Crohn's disease.

2. Authorization of 24 months may be granted for treatment of moderately to severely active CD in members who are 18 years of age or older who have had an inadequate response, intolerance or contraindication to EITHER of the following:

a. At least ONE conventional therapy option (see Appendix B)
b. At least ONE TNF-alpha inhibitor indicated for CD:

i. Cimzia (certolizumab)
ii. Humira (adalimumab)
iii. Remicade (infliximab)

D. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 24 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.

2. Authorization of 24 months may be granted for the treatment of moderately to severely active UC for members who had an inadequate response, intolerance or contraindication to at least one conventional therapy option (See Appendix C).

3. Authorization of 24 months may be granted for members who have been hospitalized for fulminant UC (e.g., continuous bleeding, severe toxic symptoms, including fever and anorexia).

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Stelara as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Stelara or any other biologic DMARD or targeted synthetic DMARD (e.g. Xeljanz) are exempt from requirements related to TB screening in this Policy.

Stelara for intravenous administration is FDA-approved for the treatment of Crohn's disease and ulcerative colitis and will only be authorized for these conditions.

V. APPENDICES

Appendix A: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

Appendix B: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
   a. Oral budesonide

   b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine
3. Moderate to severe disease – induction of remission:
   a. Prednisone, methylprednisolone intravenously (IV)
   b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC
5. Perianal and fistulizing disease – induction of remission:
   a. Metronidazole ± ciprofloxacin, tacrolimus
6. Perianal and fistulizing disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: methotrexate IM or SC

Appendix C: Examples of conventional therapy options for UC

1. Mild to moderate disease – induction of remission:
   a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
   b. Rectal mesalamine (e.g., Canasa, Rowasa)
   c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
   d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
   a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
   b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
   a. Prednisone, hydrocortisone IV, methylprednisolone IV
   b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: sulfasalazine
5. Pouchitis: Metronidazole, ciprofloxacin
   a. Alternative: rectal mesalamine

VI. REFERENCES

1. Stelara [package insert]. Horsham, PA: Janssen Biotech, Inc.; June 2018.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
3. Clinical Consult. CVS Caremark Clinical Programs Review: Focus on Dermatology Programs. April 2015.
4. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis.* 2016;75(3):499-510.
5. Gladman DD, Antoni C, P Mease, et al. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis* 2005;64(Suppl II):ii14–ii17.
6. Talley NJ, Abreu MT, Achkar J, et al. An evidence-based systematic review on medical therapies for inflammatory bowel disease. *Am J Gastroenterol.* 2011;106(Suppl 1):S2-S25.
7. Lichtenstein GR, Loftus Jr EV, Isaacs KI, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018;113:481-517.

Reference number
2022-A

SPECIALTY GUIDELINE MANAGEMENT

SUTENT (sunitinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Advanced renal cell carcinoma (RCC)
2. Adult patients at high risk of recurrent RCC following nephrectomy
3. Gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib
4. Progressive, well-differentiated pancreatic neuroendocrine tumors (PNETs) in patients with unresectable, locally advanced or metastatic disease

B. Compendial Uses
1. Relapsed or surgically unresectable stage IV RCC
2. Soft tissue sarcoma subtypes:
   a. Angiosarcoma
   b. Solitary fibrous tumor
   c. Hemangiopericytoma
3. Thymic carcinoma
4. Thyroid carcinoma (medullary, papillary, Hürthle cell, or follicular)
5. Chordoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma
Authorization of 12 months may be granted for treatment of RCC when either of the following criteria is met:
1. Disease is relapsed, metastatic or unresectable
2. Member is at high risk of recurrent RCC following nephrectomy

B. Soft Tissue Sarcoma
Authorization of 12 months may be granted for treatment of the following subtypes of STS: gastrointestinal stromal tumor, angiosarcoma, solitary fibrous tumor, and hemangiopericytoma.

C. Pancreatic Neuroendocrine Tumor
Authorization of 12 months may be granted for treatment of pancreatic neuroendocrine tumors.

D. Thymic Carcinoma
Authorization of 12 months may be granted for treatment of thymic carcinoma.

E. Thyroid Carcinoma
Authorization of 12 months may be granted for treatment of medullary, papillary, Hurthle cell, or follicular thyroid carcinoma.

F. Chordoma
Authorization of 12 months may be granted for treatment of chordoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Sutent [package insert]. New York, NY: Pfizer Labs.; November 2017.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 18, 2018.
3. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Kidney Cancer. Version 4.2018. Accessed May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Soft Tissue Sarcoma. Version 2.2018. Accessed May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf.
5. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Neuroendocrine and Adrenal Tumors. Version 2.2018. Accessed May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf.
6. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Thymomas and Thymic Carcinomas. Version 2.2018. Accessed May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/thymic.pdf.
7. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Thyroid Carcinoma. Version 1.2018. Accessed May 22, 2018. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf.

Reference number(s)
2013-A

SPECIALTY GUIDELINE MANAGEMENT

TALTZ (ixekizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
1. Moderate to severe plaque psoriasis
2. Active psoriatic arthritis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderate to severe plaque psoriasis

1. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Taltz, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.

2. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis in members who are 18 years of age and older when all of the following criteria are met:
   a. At least 5% of body surface area (BSA) is affected OR crucial bodyareas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   b. Member meets any of the following criteria:
      i. Member has had an inadequate response or intolerance to either phototherapy (e.g.,UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      ii. Member has a clinical reason to avoid pharmacologic treatment withmethotrexate, cyclosporine or acitretin (see Appendix).
      iii. Member has severe psoriasis that warrants a biologic DMARD as first-linetherapy.

B. Active psoriatic arthritis (PsA)

Authorization of 24 months may be granted for treatment of active psoriatic arthritis in members who are 18 years of age or older.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Taltz as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Taltz or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy (male or female)
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Taltz [package insert]. Indianapolis, IN: Eli Lilly and Company; December 2017.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
3. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol.* 2009;61:451-485.
4. Griffiths CE, Reich K, Lebwohl M, et al. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. *Lancet.* 2015;386(9993):541-51.
5. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis*. 2016;75(3):499-510.
6. McInnes IB, Mease PJ, Kirkham B, et al. Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2015;386(9999):1137-46.

Reference number(s)
1664-A

SPECIALTY GUIDELINE MANAGEMENT

TARCEVA (erlotinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Non-Small Cell Lung Cancer (NSCLC)
   Tarceva is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations as detected by an FDA-approved test receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen.

   Limitations of use:
   a. Safety and efficacy of Tarceva have not been established in patients with NSCLC whose tumors have other EGFR mutations.
   b. Tarceva is not recommended for use in combination with platinum-based chemotherapy.

2. Pancreatic cancer
   Tarceva in combination with gemcitabine is indicated for the first-line treatment of patients with locally advanced, unresectable or metastatic pancreatic cancer.

B. Compendial Uses

1. NSCLC, recurrent, advanced or metastatic sensitizing EGFR mutation-positive
2. Recurrent bone cancer – recurrent chordoma
3. Renal cell carcinoma, relapsed or stage IV disease with non-clear cell histology
4. Recurrent brain metastases from EGFR sensitizing mutation-positive NSCLC
5. Vulvar cancer

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: EGFR mutation testing results (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Non-small cell lung cancer (NSCLC)

Authorization of 12 months may be granted for treatment of recurrent, advanced or metastatic NSCLC (including brain metastases from NSCLC) when the member has sensitizing EGFR mutation-positive disease.

B. Pancreatic cancer
Authorization of 12 months may be granted for treatment of locally advanced, unresectable or metastatic pancreatic cancer.

C. Renal cell carcinoma (RCC)
Authorization of 12 months may be granted for treatment of relapsed or stage IV renal cell carcinoma with non-clear cell histology.

D. Chordoma
Authorization of 12 months may be granted for treatment of recurrent chordoma.

E. Vulvar cancer
Authorization of 12 months may be granted for treatment of vulvar cancer.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced an unacceptable toxicity.

V. REFERENCES

1. Tarceva [package insert]. South San Francisco, CA: Genentech USA, Inc.; October 2016.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Non-Small Cell Lung Cancer (Version 3.2019). 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology Pancreatic Adenocarcinoma (Version 1.2019). 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.
5. The NCCN Clinical Practice Guidelines in Oncology Bone Cancer (Version 1.2019). 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.
6. The NCCN Clinical Practice Guidelines in Oncology Kidney Cancer (Version 3.2019). 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.
7. The NCCN Clinical Practice Guidelines in Oncology Central Nervous System Cancers (Version 1.2019). 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.
8. The NCCN Clinical Practice Guidelines in Oncology Vulvar Cancer (Squamous Cell Carcinoma) (Version 2.2019). 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.

Reference number(s)
1665-A

SPECIALTY GUIDELINE MANAGEMENT

Temodar (temozolomide)
temozolomide (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Newly Diagnosed Glioblastoma Multiforme
   Temodar is indicated for the treatment of adult patients with newly diagnosed glioblastoma multiforme concomitantly with radiotherapy and then as maintenance treatment.

2. Refractory Anaplastic Astrocytoma
   Temodar is indicated for the treatment of adult patients with refractory anaplastic astrocytoma, i.e., patients who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine.

B. Compendial Uses

1. Central nervous system (CNS) cancer
2. Ewing sarcoma
3. Neuroendocrine tumors of pancreas, gastrointestinal tract, lung, and thymus
4. Pheochromocytoma/paraganglioma
5. Melanoma
6. Mycosis fungoides/Sézary syndrome
7. Small cell lung cancer
8. Soft tissue sarcoma
9. Uterine sarcoma

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Central nervous system (CNS) cancer
Authorization of 12 months may be granted for treatment of CNS cancers.

B. Ewing sarcoma
Authorization of 12 months may be granted for treatment of Ewing sarcoma.

C. Neuroendocrine tumors of pancreas, gastrointestinal tract, lung, and thymus
Authorization of 12 months may be granted for treatment of neuroendocrine tumors of pancreas, gastrointestinal tract, lung, or thymus.

D. Pheochromocytoma/paraganglioma
Authorization of 12 months may be granted for treatment of pheochromocytoma or paraganglioma.

E. Melanoma
Authorization of 12 months may be granted for treatment of metastatic or unresectable melanoma.

F. Mycosis fungoides/Sezary syndrome
Authorization of 12 months may be granted for treatment of mycosis fungoides/Sezary syndrome.

G. Small cell lung cancer (SCLC)
Authorization of 12 months may be granted for treatment of SCLC.

H. Soft tissue sarcoma (STS)
Authorization of 12 months may be granted for treatment of STS.

I. Uterine sarcoma
Authorization of 12 months may be granted for treatment of uterine sarcoma.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Temodar [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; October 2017.
2. The NCCN Drugs & Biologics Compendium® © 2018 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed September 28, 2018.
3. The NCCN Clinical Practice Guidelines in Oncology® Central Nervous System Cancers (Version1.2018). © 2018 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed September 28, 2018.
4. The NCCN Clinical Practice Guidelines in Oncology® Soft Tissue Sarcoma (Version 2.2018). © 2018 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed September 28, 2018.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**TESTOSTERONE PRODUCTS - INJECTABLE**
BRAND NAME (generic)	**DEPO-TESTOSTERONE (testosterone cypionate injection)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS

Depo-Testosterone Injection is indicated for replacement therapy in the male in conditions associated with symptoms of deficiency or absence of endogenous testosterone:
Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.
Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or LHRH deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation.

Limitations of Use
Safety and efficacy of Depo-Testosterone in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.

Compendial Uses
Gender Dysphoria in transgender male patients [2-3, 6-9]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]
  AND
  - Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard male lab reference values **OR**
  - For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard male lab reference values

OR

- The requested drug is being prescribed for gender dysphoria in a transgender male patient who is 14 years of age or older and able to make an informed, mature decision to engage in therapy

REFERENCES

1. Depo-Testosterone [package insert]. New York, NY: Pharmacia and Upjohn Company; November 2017.
2. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed February 2018.
3. Micromedex Solutions [database online]. Greenwood Village, CO: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed February 2018.

4. Petak S, Nankin H, Spark R, et al. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients – 2002 update. *Endocrine Practice* 2002;8(6):439-456.
5. Bhasin S, Cunningham G, Hayes F, et al. Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism* 2010 95(6):2536-2559.
6. Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, et al; Endocrine Society. Endocrine Treatment of Gender Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism* 2017;102(11):3869-3903.
7. Knezevich EL, Viereck LK, Drincic AT. Medical Management of Adult Transsexual Persons. Pharmacotherapy. 2012;32(1):54-66.
8. Coleman E, Bockting W, Botzer M, et al. Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People. World Professional Association for Transgender Health. Last Updated 2012. Available at: https://s3.amazonaws.com/amo_hub_content/Association140/files/Standards%20of%20Care%20V7%20-%202011%20WPATH%20(2)(1).pdf. Accessed February 2018.
9. American Psychiatric Association. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V). 2013. Available at http://dsm.psychiatryonline.org/book.aspx?bookid=556.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**TESTOSTERONE PRODUCTS – INJECTABLE**
BRAND NAME (generic)	**DELATESTRYL (testosterone enanthate injection)** **XYOSTED (testosterone enanthate injection)**
Status: CVS Caremark Criteria	
Type: Initial Prior Authorization	

POLICY

FDA-APPROVED INDICATIONS

Delatestryl

Males

Delatestryl (Testosterone Enanthate Injection) is indicated for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone.

Primary hypogonadism (congenital or acquired) - testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, or orchiectomy.

Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency, or pituitary-hypothalamic injury from tumors, trauma, or radiation. (Appropriate adrenal cortical and thyroid hormone replacement therapy are still necessary, however, and are actually of primary importance).

If the above conditions occur prior to puberty, androgen replacement therapy will be needed during the adolescent years for development of secondary sexual characteristics. Prolonged androgen treatment will be required to maintain sexual characteristics in these and other males who develop testosterone deficiency after puberty.

Safety and efficacy of Delatestryl in men with “age-related hypogonadism” (also referred to as “late-onset hypogonadism”) have not been established.

Delayed puberty - Delatestryl (Testosterone Enanthate Injection) may be used to stimulate puberty in carefully selected males with clearly delayed puberty. These patients usually have a familial pattern of delayed puberty that is not secondary to a pathological disorder; puberty is expected to occur spontaneously at a relatively late date. Brief treatment with conservative doses may occasionally be justified in these patients if they do not respond to psychological support. The potential adverse effect on bone maturation should be discussed with the patient and parents prior to androgen administration. An X-ray of the hand and wrist to determine bone age should be obtained every six months to assess the effect of treatment on the epiphyseal centers.

Females

Metastatic Mammary Cancer - Delatestryl (Testosterone Enanthate Injection) may be used secondarily in women with advancing inoperable metastatic (skeletal) mammary cancer who are one to five years postmenopausal. Primary goals of therapy in these women include ablation of the ovaries. Other methods of counteracting estrogen activity are adrenalectomy, hypophysectomy, and/or anti-estrogen therapy. This treatment has also been used in pre-menopausal women with breast cancer who have benefited from oophorectomy and are considered to a have a hormone-responsive tumor. Judgment concerning androgen therapy should be made by an oncologist with expertise in this field.

Xyosted

Xyosted (testosterone enanthate) injection is an androgen indicated for testosterone replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone:

- Primary hypogonadism (congenital or acquired): testicular failure due to cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter’s syndrome, chemotherapy, or toxic damage from alcohol or

heavy meals. These men usually have low serum testosterone concentrations and gonadotropins (follicle-stimulating hormone [FSH], luteinizing hormone [LH]) above the normal range.
- Hypogonadotropic hypogonadism (congenital or acquired): gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the low or normal range.

Limitations of Use
- Safety and efficacy of Xyosted in adult males with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.
- Safety and efficacy of Xyosted in males less than 18 years of age have not been established.

Compendial Uses
Gender Dysphoria in transgender male patients[7-10]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:
- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]
  AND
  - Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard male lab reference values **OR**
  - For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard male lab reference values

  OR
- The requested drug is being prescribed for gender dysphoria in a transgender male patient who is 14 years of age or older and able to make an informed, mature decision to engage in therapy
  OR
- Testosterone enanthate injection (generic Delatestryl) is being prescribed for delayed puberty
  OR
- Testosterone enanthate injection (generic Delatestryl) is being prescribed for inoperable metastatic breast cancer in a patient who is 1 to 5 years postmenopausal AND the patient had an incomplete response to other therapy for metastatic breast cancer
  OR
- Testosterone enanthate injection (generic Delatestryl) is being prescribed for a pre-menopausal patient with breast cancer who has benefited from oophorectomy and is considered to have a hormone-responsive tumor

REFERENCES

1. Delatestryl [package insert]. Malvern, PA: Endo Pharmaceuticals Solutions Inc.; October 2016.
2. Xyosted [package insert]. Ewing, NJ: Antares Pharma, Inc; September 2018.
3. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed February 2018.
4. Micromedex Solutions [database online]. Greenwood Village, CO: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed February 2018.
5. Petak S, Nankin H, Spark R, et al. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients – 2002 update. *Endocrine Practice* 2002;8(6):439-456.
6. Bhasin S, Cunningham G, Hayes F, et al. Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism* 2010 95(6):2536-2559.

7. Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, et al; Endocrine Society. Endocrine Treatment of Gender Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism* 2017;102(11):3869-3903.
8. Knezevich EL, Viereck LK, Drincic AT. Medical Management of Adult Transsexual Persons. Pharmacotherapy. 2012;32(1):54-66.
9. Coleman E, Bockting W, Botzer M, et al. Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People. World Professional Association for Transgender Health. Last Updated 2012. Available at: http://admin.associationsonline.com/uploaded_files/140/files/Standards%20of%20Care,%20V7%20Full%20Book.pdf. Accessed February 2018.
10. American Psychiatric Association. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V). 2013. Available at http://dsm.psychiatryonline.org/book.aspx?bookid=556.

PRIOR AUTHORIZATION CRITERIA

DRUG CLASS	**TESTOSTERONE PRODUCTS – TOPICAL/BUCCAL/NASAL**
BRAND NAME (generic)	**ANDRODERM (testosterone transdermal patch)** **ANDROGEL (testosterone topical gel)** **AXIRON (testosterone topical solution)** **FORTESTA (testosterone topical gel)** **NATESTO (testosterone nasal gel)** **STRIANT (testosterone mucoadhesive buccal system)** **TESTIM (testosterone topical gel)** **VOGELXO (testosterone topical gel)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization

POLICY

FDA-APPROVED INDICATIONS
Topical, buccal, and nasal testosterone products are indicated for replacement therapy in adult males for conditions associated with a deficiency or absence of endogenous testosterone.
Primary hypogonadism (congenital or acquired) - testicular failure due to conditions such as cryptorchidism, bilateral torsion, orchitis, vanishing testis syndrome, orchiectomy, Klinefelter Syndrome, chemotherapy, or toxic damage from alcohol or heavy metals. These men usually have low serum testosterone concentrations and gonadotropins (FSH, LH) above the normal range.
Hypogonadotropic hypogonadism (congenital or acquired) - gonadotropin or luteinizing hormone-releasing hormone (LHRH) deficiency or pituitary-hypothalamic injury from tumors, trauma, or radiation. These men have low testosterone serum concentrations but have gonadotropins in the normal or low range.

Limitations of Use

Safety and efficacy of topical, buccal, and nasal testosterone products in men with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.

Safety and efficacy of topical, buccal, and nasal testosterone products in males less than 18 years old have not been established.

Topical testosterone products may have different doses, strengths or application instructions that may result in different systemic exposure.

Compendial Uses
Gender Dysphoria in transgender male patients[14-17]

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for primary or hypogonadotropic hypogonadism [Note: Safety and efficacy of testosterone products in patients with "age-related hypogonadism" (also referred to as "late-onset hypogonadism") have not been established.]
  AND
  - Before the start of testosterone therapy, the patient has at least two confirmed low testosterone levels according to current practice guidelines or your standard male lab reference values **OR**
  - For continuation of testosterone therapy: before the patient started testosterone therapy, the patient had a confirmed low testosterone level according to current practice guidelines or your standard male lab reference values

OR

- The requested drug is being prescribed for gender dysphoria in a transgender male patient who is 14 years of age or older and able to make an informed, mature decision to engage in therapy

REFERENCES

1. Androderm [package insert]. Parsippany, NJ: Actavis Pharma, Inc.; October 2016.
2. Androgel 1% [package insert]. North Chicago, IL: Abbvie Inc; October 2016.
3. Androgel 1.62% [package insert]. North Chicago, IL: Abbvie Inc; October 2016.
4. Axiron [package insert]. Indianapolis, IN: Lilly USA, LLC; July 2017.
5. Fortesta [package insert]. Malvern, PA: Endo Pharmaceuticals Inc.; July 2017.
6. Natesto [package insert]. Malvern, PA: Endo Pharmaceuticals; October 2016.
7. Striant [package insert]. Malvern, PA: Endo Pharmaceuticals.; October 2016.
8. Testim [package insert]. Chesterbrook, PA: Auxilium Pharmaceuticals, Inc.; October 2016.
9. Vogelxo [package insert]. Maple Grove, MN: Upsher-Smith Laboratories, Inc.; August 2017.
10. AHFS DI (Adult and Pediatric) [database online]. Hudson, OH: Lexi-Comp, Inc.; http://online.lexi.com/lco/action/index/dataset/complete_ashp [available with subscription]. Accessed February 2018.
11. Micromedex Solutions [database online]. Greenwood Village, CO: Truven Health Analytics Inc. Updated periodically. www.micromedexsolutions.com [available with subscription]. Accessed February 2018.
12. Petak S, Nankin H, Spark R, et al. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients – 2002 update. *Endocrine Practice* 2002;8(6):439-456.
13. Bhasin S, Cunningham G, Hayes F, et al. Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism* 2010 95(6):2536-2559. Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, et al; Endocrine Society. Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2009 Sep;94(9):3132-54.
14. Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, et al; Endocrine Society. Endocrine Treatment of Gender Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *Journal of Clinical Endocrinology & Metabolism* 2017;102(11):3869-3903.
15. Knezevich EL, Viereck LK, Drincic AT. Medical Management of Adult Transsexual Persons. Pharmacotherapy. 2012;32(1):54-66.
16. Coleman E, Bockting W, Botzer M, et al. Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People. World Professional Association for Transgender Health. Last Updated 2012. Availableat:

https://s3.amazonaws.com/amo_hub_content/Association140/files/Standards%20of%20Care%20V7%20-%202011%20WPATH%20(2)(1).pdf. Accessed February 2018.
17. American Psychiatric Association. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V). 2013. Available at http://dsm.psychiatryonline.org/book.aspx?bookid=556.

Reference number(s)
2266-A

SPECIALTY GUIDELINE MANAGEMENT

XENAZINE (tetrabenazine)
tetrabenazine (generic)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Treatment of chorea associated with Huntington's disease[1]

B. Compendial Uses
1. Chronic tics
2. Tardive dyskinesia
3. Hemiballismus
4. Chorea not associated with Huntington's disease

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR APPROVAL

A. Chorea
Authorization of 12 months may be granted for treatment of chorea.

B. Chronic tics
Authorization of 12 months may be granted for treatment of chronic tics.

C. Tardive dyskinesia
Authorization of 12 months may be granted for the treatment of tardive dyskinesia.

D. Hemiballismus
Authorization of 12 months may be granted for the treatment of hemiballismus.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Xenazine [package insert]. Deerfield, IL: Lundbeck Inc.; September 2017.
2. Micromedex® (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. Available at:

http://www.micromedexsolutions.com. Accessed August 03, 2018.
3. AHFS Drug Information. http://online.lexi.com/lco. Accessed August 03, 2018.
4. Clinical Consult. CVS Caremark Clinical Program Review: Focus on Parkinson's Disease and Movement Disorders Programs. October 14, 2009.
5. Clinical Consult. CVS Caremark Clinical Program Review: Focus on Xenazine Programs. November 10, 2008.
6. Clinical Consult. CVS Caremark Clinical Program Review: Focus on Parkinson's Disease and Movement Disorders Programs. October 18, 2010.
7. Guay DR. Tetrabenazine, a monoamine-depleting drug used in the treatment of hyperkinetic movement disorders. *Am J Geriatr Pharmacother*. 2010; 8:331-373.
8. Armstrong MJ, Miyasaki JM. Evidence-based guideline: pharmacologic treatment of chorea in Huntington disease: Report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2012; 79(6):597-603.
9. Clinical Consult. CVS Caremark Clinical Program Review: Focus on Parkinson's Disease and Movement Disorders Programs. October 13, 2016.
10. Kenney C, Hunter C, Jankovic J. Long-term tolerability of tetrabenazine in the treatment of hyperkinetic movement disorders. Movement Disorders. 2007; 22(2): 193-7.
11. Tetrabenazine [package insert]. Baltimore, MD: Lupin Pharmaceuticals Inc.; April 2018.

Reference number(s)
1887-A

SPECIALTY GUIDELINE MANAGEMENT

tobramycin inhalation solution/TOBI
TOBI Podhaler (tobramycin inhalationpowder)
Bethkis (tobramycin inhalation solution)
Kitabis Pak (tobramycin inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Management of cystic fibrosis patients with *Pseudomonas aeruginosa*

B. Compendial Uses
Pseudomonas aeruginosa lower respiratory tract infection in patients with non-cystic fibrosis bronchiectasis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Cystic Fibrosis
Authorization of 24 months may be granted for members with cystic fibrosis when Pseudomonas aeruginosa is present in airway cultures OR the member has a history of Pseudomonas aeruginosa infection or colonization in the airways.

B. Bronchiectasis (Non-Cystic Fibrosis)
Authorization of 24 months may be granted for members with non-cystic fibrosis bronchiectasis when Pseudomonas aeruginosa is present in airway cultures OR the member has a history of Pseudomonas aeruginosa infection or colonization in the airways.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Tobramycin inhalation solution [package insert]. Sellersville, PA: Teva Pharmaceuticals USA; December 2015.
2. TOBI [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2015.
3. TOBI Podhaler [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; October 2015.
4. Bethkis [package insert]. Woodstock, IL: Chiesi USA, Inc.; July 2017; 2014.
5. Kitabis Pak [package insert]. Midlothian, VA: PARI Respiratory Equipment, Inc.; November 2014.
6. DRUGDEX® System (electronic version). Truven Health Analytics, Greenwood Village, Colorado. Available at http://www.micromedexsolutions.com. Accessed November 28, 2016.

7. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med.* 2013;187:680-689.
8. Rosen, MJ. Chronic cough due to bronchiectasis: ACCP Evidence-Based Clinical Practice Guidelines. *Chest*. 2006;129:122S-131S.

Reference number(s)
1649-A

SPECIALTY GUIDELINE MANAGEMENT

TRACLEER (bosentan)

POLICY

L. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1):
A. In adults to improve exercise ability and to decrease clinical worsening.
B. In pediatric patients aged 3 years and older with idiopathic or congenital PAH to improve pulmonaryvascular resistance (PVR), which is expected to result in an improvement in exercise ability.

All other indications are considered experimental/investigational and are not a covered benefit.

Compendial Use
Eisenmenger's syndrome, WHO functional class III PAH

LI. CRITERIA FOR INITIAL APPROVAL

B. Pulmonary Arterial Hypertension (PAH)
Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
10. Pretreatment right heart catheterization with all of the following results:
i. mPAP ≥ 25 mmHg
ii. PCWP ≤ 15 mmHg
iii. PVR > 3 Wood units
11. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
xiii. Post cardiac surgery
xiv. Chronic heart disease
xv. Chronic lung disease associated with prematurity
xvi. Congenital diaphragmatic hernia

C. Eisenmenger's Syndrome
Authorization of 12 months may be granted for treatment of members with WHO functional class III Eisenmenger's syndrome (refer to Appendix).

LII. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

LIII. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH

1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease

2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia

3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction

4.9 Chronic thromboembolic PH
4.10 Other pulmonary artery obstructions
- 4.10.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.10.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma
  - Germ cell tumours of the testis
  - Other tumours
- 4.10.3 Non-malignant tumours
  - Uterine leiomyoma
- 4.10.4 Arteritis without connective tissue disease
- 4.10.5 Congenital pulmonary artery stenosis
- 4.10.6 Parasites
  - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.8 Complex congenital heart disease

WHO Functional Assessment for Pulmonary Hypertension

Class I
Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain or near syncope.

Class II
Patients with pulmonary hypertension resulting in a slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.

Class III
Patients with pulmonary hypertension resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnea or fatigue, chest pain or near syncope.

Class IV
Patients with pulmonary hypertension with inability to carry out any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity.

LIV. REFERENCES

1. Tracleer [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; October 2018.
2. Bosentan [package insert]. Parsippany, NJ: Actavis Pharma Inc.; October 2018.
3. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
4. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
5. Badesch DB, Champion HC, Gomez-Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S55-S66.
6. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol.* 2013;62:D34-S41.
7. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
8. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S78-S84.
9. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
10. Abman, SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.
11. Klinger, JR., Elliott, CG, Levine, DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019:155(3): 565-586.
12. IBM Micromedex® DRUGDEX® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com (cited: April 29, 2019).
13. Galie, N., McLaughlin, VV, Rubin, LJ, Simonneau, G. An overview of the 6th World Symposium on Pulmonary Hypertension. Eur Respir J 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.

Reference number
2156-A

SPECIALTY GUIDELINE MANAGEMENT

TREMFYA (guselkumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Treatment of adult patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Moderate to severe plaque psoriasis

A. Authorization of 24 months may be granted for members who are 18 years of age or older who have previously received Tremfya, Otezla, or any other biologic DMARD indicated for the treatment of moderate to severe plaque psoriasis.

B. Authorization of 24 months may be granted for treatment of moderate to severe plaque psoriasis for members who are 18 years of age or older when all of the following criteria are met:
   1. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
   2. Member meets any of the following criteria:
      a. Member has had an inadequate response or intolerance to either phototherapy (e.g.,UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
      b. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine or acitretin (see Appendix).
      c. Member has severe psoriasis that warrants a biologic DMARD as first-linetherapy.

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Tremfya as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Tremfya or any other biologic DMARD or targeted synthetic DMARD (e. g., Xeljanz) are exempt from requirements related to TB screening in this Policy.

V. APPENDIX

Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Cannot be used due to risk of treatment-related toxicity
4. Drug interaction
5. Pregnancy or planning pregnancy (male or female)
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

VI. REFERENCES

1. Tremfya [package insert]. Horsham, PA: Janssen Biotech, Inc.; October 2017.
2. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis andpsoriatic arthritis. Section 4: Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol.* 2009;61:451-485.
3. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
4. Reich K, Armstrong, AW, Foley P, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the treatment of patients with moderate to severe psoriasis with randomized withdrawal and retreatment: Results from the phase III, double-blind, placebo- and active comparator–controlled VOYAGE 2 trial. *Am J Clin Dermatol*. 2017;76(3):418-431.
5. Blauvelt A, Papp KA, Griffiths, CEM, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: Results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. *Am J Clin Dermatol*. 2017;76(3):405-417.

Reference number(s)
1644-A

SPECIALTY GUIDELINE MANAGEMENT

Remodulin injection (treprostinil injection)
treprostinil injection (generic)

POLICY

LV. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. **Pulmonary Arterial Hypertension**
   Remodulin is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to diminish symptoms associated with exercise.
2. **Pulmonary Arterial Hypertension in Patients Requiring Transition from Epoprostenol**

In patients with PAH requiring transition from epoprostenol, Remodulin is indicated to diminish the rate of clinical deterioration. Consider the risks and benefits of each drug prior to transition.

All other indications are considered experimental/investigational and are not a covered benefit.

LVI. CRITERIA FOR INITIAL APPROVAL

Indefinite authorization may be granted for treatment of PAH when ALL of the following criteria are met:

A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).

B. PAH was confirmed by either criterion (1) or criterion (2) below:

12. Pretreatment right heart catheterization with all of the following results:
    i. mPAP ≥ 25 mmHg
    ii. PCWP ≤ 15 mmHg
    iii. PVR > 3 Wood units
13. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
    xvii. Post cardiac surgery
    xviii. Chronic heart disease
    xix. Chronic lung disease associated with prematurity
    xx. Congenital diaphragmatic hernia

LVII. CONTINUATION OF THERAPY

Indefinite authorization may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

LVIII. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases
- 1.4.5 Schistosomiasis

1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.11 Chronic thromboembolic PH
4.12 Other pulmonary artery obstructions
- 4.12.1 Sarcoma (high or intermediate grade) or angiosarcoma
- 4.12.2 Other malignant tumors
  - Renal carcinoma
  - Uterine carcinoma
  - Germ cell tumours of the testis
  - Other tumours
- 4.12.3 Non-malignant tumours
  - Uterine leiomyoma
- 4.12.4 Arteritis without connective tissue disease
- 4.12.5 Congenital pulmonary artery stenosis
- 4.12.6 Parasites
  - Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.9 Complex congenital heart disease

LIX. REFERENCES

1. Remodulin [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; July 2018.
2. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
3. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus

Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
4. Badesch DB, Champion HC, Gomez-Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S55-S66.
5. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol.* 2013;62:D34-S41.
6. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
7. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S78-S84.
8. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
9. Abman, SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.
10. Klinger, JR., Elliott, CG, Levine, DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019:155(3): 565-586.
11. Galie, N., McLaughlin, VV, Rubin, LJ, Simonneau, G. An overview of the 6th World Symposium on Pulmonary Hypertension. Eur Respir J 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.

Reference number(s)
1902-A

SPECIALTY GUIDELINE MANAGEMENT

TYKERB (lapatinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Tykerb is indicated in combination with:
1. Capecitabine for the treatment of patients with advanced or metastatic breast cancer whose tumors overexpress human epidermal growth factor receptor 2 (HER2) and who have received prior therapy including an anthracycline, a taxane, and trastuzumab
2. Letrozole for the treatment of postmenopausal women with hormone receptor (HR)-positive metastatic breast cancer that overexpresses the HER2 receptor for whom hormonal therapy is indicated

B. Compendial Uses
1. Recurrent or metastatic HER2-positive breast cancer in combination with trastuzumab
2. Recurrent or stage IV hormone receptor-positive, HER2-positive breast cancer in combination with aromatase inhibition in postmenopausal women
3. Metastatic central nervous system (CNS) lesions if active against primary tumor (breast)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Breast cancer
Authorization of 12 months may be granted for the treatment of HER2-positive breast cancer when Tykerb is used in combination with an aromatase inhibitor (eg, letrozole, anastrozole, exemestane), trastuzumab, or capecitabine.

B. Metastatic CNS lesions
Authorization of 12 months may be granted for the treatment of metastatic CNS lesions from HER2- positive breast cancer.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Tykerb [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; April 2017.

2. The NCCN Drugs & Biologics Compendium™ © 2017 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed January 16, 2018.
3. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology: breast cancer. Version 2.2016. http://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed January 16, 2018.

Reference number(s)
1846-A

SPECIALTY GUIDELINE MANAGEMENT

TYSABRI (natalizumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Tysabri is indicated for inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn's disease with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of TNF-α.

2. Tysabri is indicated as monotherapy for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active Crohn's disease (CD)
Authorization of 12 months may be granted to members who have received any other biologic indicated for the treatment of moderately to severely active Crohn's disease.

B. Relapsing forms of multiple sclerosis (MS)
Authorization of 12 months may be granted to members who have been diagnosed with a relapsing forms of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse) and those who have been tested for anti-JCV antibodies.

C. Clinically isolated syndrome (CIS)
Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome and those who have been tested for anti-JCV antibodies.

III. CONTINUATION OF THERAPY

A. Crohn's disease (CD)
Authorization of 12 months may be granted for all members (including new members) who achieve or maintain a positive clinical response with Tysabri as evidenced by low disease activity or improvement in signs and symptoms of the condition.

B. Relapsing forms of multiple sclerosis (MS) or clinically isolated syndrome (CIS)
Authorization of 12 months may be granted for all members (including new members) who achieve or maintain a positive clinical response with Tysabri as evidenced by experiencing disease stability or improvement.

IV. OTHER

For all indications: Members cannot use Tysabri concomitantly with any other MS agent (except Ampyra),

immunosuppressants, or TNF inhibitors (e.g., adalimumab, infliximab).

V. REFERENCES

1. Tysabri [package insert]. Cambridge, MA: Biogen Idec, Inc; August 2019.
2. Talley NJ, Abreu MT, Achkar J, et al. An evidence-based systematic review on medical therapies for inflammatory bowel disease. *Am J Gastroenterol*. 2011;106(Suppl 1):S2-S25.
3. Lichtenstein GR, Loftus Jr EV, Isaacs KI, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018;113:481-517.

Reference number(s)
1648-A

SPECIALTY GUIDELINE MANAGEMENT

Ventavis (iloprost inhalation solution)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Ventavis is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (NYHA Class), and lack of deterioration.

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
   1. Pretreatment right heart catheterization with all of the following results:
      i. mPAP ≥ 25 mmHg
      ii. PCWP ≤ 15 mmHg
      iii. PVR > 3 Wood units
   2. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
      i. Post cardiac surgery
      ii. Chronic heart disease
      iii. Chronic lung disease associated with prematurity
      iv. Congenital diaphragmatic hernia

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with an indication listed in Section II who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

IV. APPENDIX

WHO Classification of Pulmonary Hypertension

1 PAH
1.1 Idiopathic (PAH)
1.2 Heritable PAH
1.3 Drug- and toxin-induced PAH
1.4. PAH associated with:
1.4.1 Connective tissue diseases

1.4.2 HIV infection
1.4.3 Portal hypertension
1.4.4 Congenital heart diseases
1.4.5 Schistosomiasis
1.5 PAH long-term responders to calcium channel blockers
1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement
1.7 Persistent PH of the newborn syndrome

2 PH due to left heart disease
2.1 PH due to heart failure with preserved LVEF
2.2 PH due to heart failure with reduced LVEF
2.3 Valvular heart disease
2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH

3 PH due to lung diseases and/or hypoxia
3.1 Obstructive lung disease
3.2 Restrictive lung disease
3.3 Other lung disease with mixed restrictive/obstructive pattern
3.4 Hypoxia without lung disease
3.5 Developmental lung disorders

4 PH due to pulmonary artery obstruction
4.1 Chronic thromboembolic PH
4.2 Other pulmonary artery obstructions
4.2.1 Sarcoma (high or intermediate grade) or angiosarcoma
4.2.2 Other malignant tumors
Renal carcinoma
Uterine carcinoma
Germ cell tumours of the testis
Other tumours
4.2.3 Non-malignant tumours
Uterine leiomyoma
4.2.4 Arteritis without connective tissue disease
4.2.5 Congenital pulmonary artery stenosis
4.2.6 Parasites
Hydatidosis

5 PH with unclear and/or multifactorial mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders
5.2 Systemic and metabolic disorders: Pulmonary Langerhans cell histiocytosis, Gaucher disease, glycogen storage disease, neurofibromatosis, sarcoidosis
5.3 Others: chronic renal failure with or without hemodialysis, fibrosing mediastinitis
5.4 Complex congenital heart disease

V. REFERENCES

1. Ventavis [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; October 2017.
2. Chin KM, Rubin LJ. Pulmonary arterial hypertension. *J Am Coll Cardiol*. 2008;51(16):1527-1538.
3. McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009;53(17):1573-1619.
4. Badesch DB, Champion HC, Gomez-Sanchez MA, et al. Diagnosis and assessment of pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S55-S66.

5. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol.* 2013;62:D34-S41.
6. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
7. Barst RJ, Gibbs SR, Ghofrani HA, et al. Updated evidence-based treatment algorithm in pulmonary arterial hypertension. *J Am Coll Cardiol.* 2009;54:S78-S84.
8. Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults. CHEST guideline and expert panel report. *Chest*. 2014;46(2):449-475.
9. Abman, SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132(21):2037-99.
10. Klinger, JR., Elliott, CG, Levine, DJ, et al. Therapy for Pulmonary Arterial Hypertension in Adults: Update of the CHEST Guidelines and Expert Panel Report. *Chest*. 2019:155(3): 565-586.
11. Galie, N., McLaughlin, VV, Rubin, LJ, Simonneau, G. An overview of the 6th World Symposium on Pulmonary Hypertension. Eur Respir J 2019; 53: 1802148; DOI: 10.1183/13993003.02148-2018. Published 24 January 2019.

Reference number(s)
1666-A

SPECIALTY GUIDELINE MANAGEMENT

XALKORI (crizotinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Xalkori is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK) or ROS1-positive as detected by an FDA-approved test.

B. Compendial Uses
1. NSCLC, recurrent, advanced or metastatic ALK rearrangement-positive or ROS1 rearrangement-positive tumors
2. NSCLC with high-level MET amplification or MET exon 14 skipping mutation
3. Inflammatory myofibroblastic tumor (IMT) with ALK translocation
4. Anaplastic large cell lymphoma, relapsed or refractory ALK-positive
5. Recurrent brain metastases from ALK rearrangement-positive NSCLC or ROS1 rearrangement-positive NSCLC

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation or translocation status, ROS-1 mutation status, MET exon 14 skipping mutation status, or high-level MET amplification status (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Non-small cell lung cancer (NSCLC)
Authorization of 12 months may be granted for treatment of NSCLC when the member meets any of the following criteria:
1. Member has recurrent, advanced or metastatic ALK-positive NSCLC (including brain metastases from NSCLC).
2. Member has recurrent, advanced or metastatic ROS1-positive NSCLC (including brain metastases from NSCLC).
3. Member has NSCLC with high-level MET amplification or MET exon 14 skipping mutation.

B. Inflammatory myofibroblastic tumor (IMT)
Authorization of 12 months may be granted for treatment of ALK-positive IMT.

C. Anaplastic large cell lymphoma (ALCL)
Authorization of 12 months may be granted for treatment of relapsed or refractory ALK-positive ALCL.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Xalkori [package insert]. New York, NY: Pfizer Inc.; January 2019.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Non-Small Cell Lung Cancer (Version 3.2019). 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology Soft Tissue Sarcoma (Version 2.2019). 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.
5. The NCCN Clinical Practice Guidelines in Oncology T-Cell Lymphomas (Version 2.2019). 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.
6. The NCCN Clinical Practice Guidelines in Oncology Central Nervous System Cancers (Version 1.2019). 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.

Reference number(s)
2011-A

SPECIALTY GUIDELINE MANAGEMENT

XELJANZ (tofacitinib)
XELJANZ XR (tofacitinib extended release tablets)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
A. Moderately to severely active rheumatoid arthritis
B. Active psoriatic arthritis
C. Moderately to severely active ulcerative colitis

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 24 months may be granted to members who have previously received Xeljanz, Xeljanz XR or any biologic DMARD indicated for the treatment of moderately to severely active rheumatoid arthritis.

2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
   i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
   ii. Member has an intolerance or contraindication to methotrexate (see Appendix).

B. Active psoriatic arthritis (PsA)

1. Authorization of 24 months may be granted to members who have previously received Xeljanz, Xeljanz XR or any biologic DMARD indicated for the treatment of active psoriatic arthritis. Xeljanz/XeljanzXR must be used in combination with a nonbiologic DMARD (e.g., methotrexate, leflunomide, sulfasalazine, etc.)

2. Authorization of 24 months may be granted for treatment of active PsA when all of the following criteria are met:
   i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate (MTX) or other nonbiologic disease-modifying antirheumatic drugs (DMARDs) (e.g., leflunomide, sulfasalazine, etc.)
   ii. Xeljanz/Xeljanz XR is used in combination with a nonbiologic DMARD (e.g., methotrexate, leflunomide, sulfasalazine, etc.)

C. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 24 months may be granted for members who have previously received Xeljanz, Xeljanz XR or any biologic indicated for the treatment of moderately to severely active ulcerative colitis.

2. Authorization of 24 months may be granted for treatment of moderately to severely active UC if the member has had an inadequate response, intolerance or contraindication to EITHER of the following:
   i. At least ONE conventional therapy option (see Appendix B)
   ii. At least ONE biologic indicated for UC

III. CONTINUATION OF THERAPY

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Xeljanz/Xeljanz XR as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB).

Note: Members who have received Xeljanz, Xeljanz XR or any other biologic DMARD are exempt from requirements related to TB screening in this Policy.

V. APPENDICES

Appendix A: Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
   a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
   b. Rectal mesalamine (e.g., Canasa, Rowasa)
   c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
   d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
   a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
   b. Alternatives: azathioprine, mercaptopurine, sulfasalazine

3. Severe disease – induction of remission:
   a. Prednisone, hydrocortisone IV, methylprednisolone IV
   b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
   a. Azathioprine, mercaptopurine
   b. Alternative: sulfasalazine
5. Pouchitis: Metronidazole, ciprofloxacin
   a. Alternative: rectal mesalamine

VI. REFERENCES

1. Xeljanz/Xeljanz XR [package insert]. New York, NY: Pfizer, Inc.; May 2018.
2. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guidelinefor the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
3. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017*;0*:1-18.
4. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol*. 2011;65(1):137-174.
5. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis*. 2016;75(3):499-510.
6. Talley NJ, Abreu MT, Achkar J, et al. An evidence-based systematic review on medical therapies for inflammatory bowel disease. *Am J Gastroenterol.* 2011;106(Suppl 1):S2-S25.

Reference number(s)
1993-A

SPECIALTY GUIDELINE MANAGEMENT

XELODA (capecitabine)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Colorectal Cancer
   a. Xeloda is indicated as a single agent for adjuvant treatment in patients with Dukes' C colon cancer who have undergone complete resection of the primary tumor when treatment with fluoropyrimidine therapy alone is preferred.
   b. Xeloda is indicated as first-line treatment in patients with metastatic colorectal carcinoma when treatment with fluoropyrimidine therapy alone is preferred.
2. Breast Cancer
   a. Xeloda in combination with docetaxel is indicated for the treatment of patients with metastatic breast cancer after failure of prior anthracycline-containing chemotherapy.
   b. Xeloda monotherapy is also indicated for the treatment of patients with metastatic breast cancer resistant to both paclitaxel and an anthracycline-containing chemotherapy regimen or resistant to paclitaxel and for whom further anthracycline therapy is not indicated, for example, patients who have received cumulative doses of 400 mg/m^2 of doxorubicin or doxorubicin equivalents.

B. Compendial Uses
1. Anal cancer
2. Breast cancer
3. Central nervous system (CNS) metastases from breast cancer
4. Colorectal Cancer
5. Esophageal and esophagogastric junction cancer
6. Gastric cancer
7. Head and neck cancer
8. Hepatobiliary cancers (extra-/intra-hepatic cholangiocarcinoma and gallbladder cancer)
9. Occult primary tumors (cancer of unknown primary)
10. Ovarian cancer (Epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer/mucinous cancer)
11. Pancreatic adenocarcinoma
12. Penile cancer
13. Neuroendocrine and adrenal tumors

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer (CRC)
Authorization of 12 months may be granted for the treatment of colorectal cancer.

B. Breast Cancer
Authorization of 12 months may be granted for the treatment of recurrent or metastatic breast cancer.

C. Neuroendocrine and Adrenal Tumors
Authorization of 12 months may be granted for the treatment of neuroendocrine and adrenal tumors.

D. Pancreatic Adenocarcinoma
Authorization of 12 months may be granted for the treatment of pancreatic adenocarcinoma.

E. Esophageal and Esophagogastric Junction Cancers
Authorization of 12 months may be granted for the treatment of esophageal and esophagogastric junction cancers.

F. Gastric Cancer
Authorization of 12 months may be granted for the treatment of gastric cancer.

G. Extrahepatic and Intrahepatic Cholangiocarcinoma and Gallbladder Cancer
Authorization of 12 months may be granted for the treatment of extrahepatic and intrahepatic cholangiocarcinoma and gallbladder cancer.

H. Ovarian Cancer
Authorization of 12 months may be granted for the treatment of ANY of the following:
1. Epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer
2. Mucinous carcinoma

I. Head and Neck Cancer
Authorization of 12 months may be granted for the treatment of head and neck cancer.

J. CNS Metastases from Breast Cancer
Authorization of 12 months may be granted for the treatment of CNS metastases from breast cancer.

K. Occult Primary Tumors (cancer of unknown primary)
Authorization of 12 months may be granted for the treatment of occult primary tumors.

L. Penile Cancer
Authorization of 12 months may be granted for the treatment of penile cancer.

M. Anal Cancer
Authorization of 12 months may be granted for the treatment of anal cancer.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

IV. REFERENCES

1. Xeloda [package insert]. South San Francisco, CA: Genentech, Inc.; March 2015.
2. The NCCN Drugs & Biologics Compendium™ © 2018 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed July 25, 2018.

Reference number(s)
1685-A

SPECIALTY GUIDELINE MANAGEMENT

ZELBORAF (vemurafenib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Zelboraf is indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test.

   Limitation of use: Zelboraf is not indicated for treatment of patients with wild-type BRAF melanoma.

2. Zelboraf is indicated for the treatment of patients with Erdheim-Chester Disease with BRAF V600 mutation.

B. Compendial Uses

1. Melanoma (including brain metastases), BRAF V600 activating mutation-positive
2. Non-small cell lung cancer, BRAF V600E mutation-positive
3. Hairy cell leukemia
4. Thyroid carcinoma – papillary carcinoma, follicular carcinoma, Hurthle cell carcinoma, BRAF mutation-positive
5. Glioma, BRAF V600 activating mutation-positive
6. Meningioma, BRAF V600 activatingmutation-positive
7. Astrocytoma, BRAF V600 activatingmutation-positive

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Melanoma
Authorization of 12 months may be granted for treatment of melanoma (including brain metastases from melanoma) with a BRAF V600 activating mutation (e.g., BRAF V600E or BRAF V600K mutation).

B. Erdheim-Chester disease (ECD)
Authorization of 12 months may be granted for treatment of ECD with BRAF V600 mutation.

C. Non-small cell lung cancer (NSCLC)
Authorization of 12 months may be granted for treatment of BRAF V600E mutation-positive NSCLC.

D. Hairy cell leukemia
Authorization of 12 months may be granted for treatment of hairy cell leukemia.

E. Thyroid carcinoma

Authorization of 12 months may be granted for treatment of BRAF mutation-positive papillary carcinoma, follicular carcinoma, or Hurthle carcinoma.

F. Central Nervous System Cancer
Authorization of 12 months may be granted for treatment of BRAF V600 mutation-positive gliomas, meningiomas, or astrocytomas

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. REFERENCES

1. Zelboraf [package insert]. South San Francisco, CA: Genentech USA, Inc.; November 2017.
2. The NCCN Drugs & Biologics Compendium® © 2017 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed December 4, 2017.
3. Diamond EL, Dagna L, Hyman DM, et al. Consensus guidelines for the diagnosis and clinical management of Erdheim-Chester disease. Blood. 2014;124(4):483-492.
4. Haroche J, Cohen-Aubart F, Emile JF, et al. Reproducible and sustained efficacy of targeted therapy with vemurafenib in patients with BRAF V600E-mutated Erdheim-Chester disease. J Clin Oncol. 2015;33:411-418.
5. Hyman DM, Puzanov I, Subbiah V, et al. Vemurafenib in multiple nonmelanoma cancers with BRAF V600 mutations. *N Engl J Med*. 2015;373(8):726-736.
6. Clinical Consult. CVS Caremark Clinical Programs Review. Focus on Oncology Agents Clinical Programs. June 10, 2016.
7. Usubalieva A, Pierson CR, Kavran CA, et al. Primary Meningeal Pleomorphic Xanthoastrocytoma With Anaplastic Features: A Report of 2 Cases, One With *BRAFV600E* Mutation and Clinical Responseto the *BRAF* Inhibitor Dabrafenib. *Journal of neuropathology and experimental neurology*. 2015;74(10):960-969. doi:10.1097/NEN.0000000000000240.
8. Mordechai O, Postovsky S, Vlodavsky E, et al. Metastatic Rhabdoid Meningioma with *BRAF* V600E Mutation and Good Response to Personalized Therapy: Case Report and Review of the Literature. *Pediatric Hematology and Oncology*. 2015; 32:3, 207-211, DOI: 10.3109/08880018.2014.936058
9. Lassaletta, A, Guerreiro Stucklin, A, Ramaswamy, V, et al. Profound clinical and radiological response to BRAF inhibition in a 2-month-old diencephalic child with hypothalamic/chiasmatic glioma. *Pediatric Blood and Cancer*. 2016; 63: 2038-2041. doi:10.1002/pbc.26086.
10. Meletah SK, Pavlick D, Brennan T, et al. Personalized Treatment for a Patient with a BRAF V600E Mutation using Dabrafenib and a Tumor Treatment Fields Device in a High-Grade Glioma Arising from Ganglioglioma. *Journal of the National Comprehensive Cancer Network.* 2016; 14(11):1345-1350.

Reference number(s)
1668-A

SPECIALTY GUIDELINE MANAGEMENT

ZYKADIA (ceritinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Zykadia is indicated for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors are anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

B. Compendial Uses
1. NSCLC, recurrent, advanced or metastatic ALK rearrangement-positive or ROS1 rearrangement-positive tumors
2. Inflammatory myofibroblastic tumor (IMT) with ALK translocation
3. Recurrent brain metastases from ALK-positive NSCLC

All other indications are considered experimental/investigational and are not a covered benefit.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review: ALK mutation or translocation status or ROS-1 mutation status (where applicable).

III. CRITERIA FOR INITIAL APPROVAL

A. Non-small cell lung cancer (NSCLC)
Authorization of 12 months may be granted for treatment of NSCLC when the member meets either of the following criteria:
1. Member has recurrent, advanced or metastatic ALK-positive NSCLC (including brain metastases from NSCLC).
2. Member has recurrent, advanced or metastatic ROS1-positive NSCLC.

B. Inflammatory myofibroblastic tumor (IMT)
Authorization of 12 months may be granted for treatment of ALK-positive IMT.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Zykadia [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp; March 2019.
2. The NCCN Drugs & Biologics Compendium 2018 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 15, 2019.
3. The NCCN Clinical Practice Guidelines in Oncology Non-Small Cell Lung Cancer (Version 3.2019). 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.
4. The NCCN Clinical Practice Guidelines in Oncology Soft Tissue Sarcoma (Version 2.2019). 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.
5. The NCCN Clinical Practice Guidelines in Oncology Central Nervous System Cancers (Version 1.2019). 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 14, 2019.

Reference number(s)
1934-A

SPECIALTY GUIDELINE MANAGEMENT

ZYTIGA (abiraterone)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
1. Indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer.
2. Indicated in combination with prednisone for the treatment of patients with metastatic high-risk castration-sensitive prostate cancer.

B. Compendial Uses
Node-positive (N_1), non-metastatic (M_0) prostate cancer

All other indications are considered experimental/investigational and not medically necessary.

II. EXCLUSIONS

Coverage will not be provided if the requested medication is used in combination with a second-generation oral anti-androgen (e.g., apalutamide [Erleada]) or an oral androgen metabolism inhibitor (e.g., abiraterone acetate [Yonsa]).

III. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for the treatment of node positive or metastatic prostate cancer when the member has had a bilateral orchiectomy or will be using the requested medication in combination with a GnRH analog.

IV. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Zytiga [package insert]. Horsham, PA: Janssen Biotech, Inc.; June 2019.
2. Abiraterone [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; September 2018.
3. IBM Micromedex®DRUGDEX® (electronic version). IBM Watson Heath, Greenwood Village, Colorado. Available at https://www.micromedexsolutions.com. Accessed July 22, 2019.
4. The NCCN Drugs & Biologics Compendium™ © 2019 National Comprehensive Cancer Network, Inc. https://www.nccn.org Accessed July 9, 2019.

5. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology™ Prostate Cancer (Version 2.2019). https://www.nccn.org. Accessed July 9, 2019.

Reference number(s)
2171-A

SPECIALTY GUIDELINE MANAGEMENT

BOSULIF (bosutinib)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
Adult patients with:
1. Newly-diagnosed chronic phase (CP) Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML)
2. Chronic phase, accelerated phase (AP), or blast phase (BP) Ph+ CML with resistance or intolerance to prior therapy

B. Compendial Uses
1. Primary treatment of patients with advanced phase CML (accelerated phase or blast phase)
2. Follow-up therapy for CML patients after hematopoietic stem cell transplant (HSCT)
3. Therapy for relapsed or refractory Ph+ acute lymphoblastic leukemia (ALL)

All other indications are considered experimental/investigational and are not a covered benefit.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the prior authorization review:
A. Prior to initiation of therapy: results of cytogenetic and/or molecular testing for detection of the Ph chromosome or the BCR-ABL gene
B. For members requesting initiation of Bosulif therapy for treatment of CML or ALL after experiencing resistance to prior tyrosine kinase inhibitor (TKI) therapy: results of T315I mutation testing

III. CRITERIA FOR INITIAL APPROVAL

A. Chronic Myeloid Leukemia (CML)
Authorization of 6 months may be granted for treatment of CML that has been confirmed by detection of the Ph chromosome or BCR-ABL gene by cytogenetic and/or molecular testing when any of the following criteria are met:
1. Member has not received prior therapy with a TKI (e.g., dasatinib, imatinib, nilotinib, ponatinib)
2. Member experienced toxicity or intolerance to prior therapy with a TKI
3. Member experienced resistance to prior therapy with a TKI and results of mutational testing are negative for T315I mutation
4. Member has received HSCT for CML

B. Ph+ Acute Lymphoblastic Leukemia (ALL)/Lymphoblastic Lymphoma (LL)

Authorization of 12 months may be granted for treatment of relapsed or refractory Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when results of mutational testing are negative for T315I mutation.

IV. CONTINUATION OF THERAPY

A. CML

Authorization of 12 months may be granted for continued treatment of CML that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing when either of the following criteria are met:

1. BCR-ABL1 ≤ 10% for members who have been receiving Bosulif for ≤ 12 months
2. No evidence of disease progression for members who have been receiving Bosulif for > 12 months
3. Member has received HSCT

B. Ph+ ALL/LL

Authorization of 12 months may be granted for continued treatment of Ph+ ALL or LL that has been confirmed by detection of Ph chromosome or BCR-ABL gene by cytogenetic and/ or molecular testing in members who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Bosulif [package insert]. New York, NJ: Pfizer Inc.; October 2018.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 16, 2019.
3. NCCN Clinical Practice Guidelines in Oncology® Chronic Myeloid Leukemia (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 16, 2019.
4. NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2019). © 2019 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 17, 2019.

This policy applies to the following:

	Standard Opt-in		ACSF		VF	✓	Marketplace
	Standard Opt-in NTMB		PDPD		MMT		Medical Benefit
	Standard Opt-out		Generics First				Medical Benefit: Managed Medicaid

Reference #
2719-D

EXCEPTIONS CRITERIA

DISEASE-MODIFYING ANTIRHEUMATIC DRUGS FOR AUTOIMMUNE CONDITIONS

PREFERRED PRODUCTS FOR ANKYLOSING SPONDYLITIS: COSENTYX, ENBREL AND HUMIRA

PREFERRED PRODUCTS FOR CROHN'S DISEASE: PRIMARY: HUMIRA SECONDARY: STELARA

PREFERRED PRODUCTS FOR PSORIASIS: HUMIRA, OTEZLA, SKYRIZI, STELARA AND TALTZ

PREFERRED PRODUCTS FOR PSORIATIC ARTHRITIS: COSENTYX, ENBREL, HUMIRA AND OTEZLA

PREFERRED PRODUCTS FOR RHEUMATOID ARTHRITIS: ENBREL, HUMIRA, KEVZARA, AND XELJANZ/XELJANZ XR

PREFERRED PRODUCTS FOR ULCERATIVE COLITIS: HUMIRA, SIMPONI

POLICY

This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the disease-modifying antirheumatic drug (DMARD) products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to adult members requesting treatment with a targeted product. For inflammatory joint or bowel disease indications, coverage for the targeted product will continue in situations where the member is currently receiving treatment.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Disease-modifying antirheumatic drugs for autoimmune conditions

Indication	Primary Preferred Product	Secondary Preferred Product	Targeted Product(s)
Plaque psoriasis	• **Humira** (adalimumab) • **Otezla** (apremilast) • **Skyrizi** (risankizumab-rzaa) • **Stelara** (ustekinumab) • **Taltz** (ixekizumab)	• **None**	• **Cimzia** (certolizumab pegol) • **Cosentyx** (secukinumab) • **Enbrel** (etanercept) • **Ilumya** (tildrakizumab-asmn) • **Inflectra** (infliximab-dyyb) • **Renflexis** (infliximab-abda) • **Siliq** (brodalumab) • **Tremfya** (guselkumab)

This policy applies to the following:

	Standard Opt-in		ACSF		VF	✓	Marketplace
	Standard Opt-in NTMB		PDPD		MMT		Medical Benefit
	Standard Opt-out		Generics First				Medical Benefit: Managed Medicaid

Reference #
2719-D

Ankylosing spondylitis	• **Cosentyx** (secukinumab) • **Enbrel** (etancercept) • **Humira** (adalimumab)	• **None**	• **Cimzia** (certolizumab pegol) • **Inflectra** (infliximab-dyyb) • **Renflexis** (infliximab-abda) • **Simponi** (golimumab)
Psoriatic arthritis	• **Cosentyx** (secukinumab) • **Enbrel** (etanercept) • **Humira** (adalimumab) • **Otezla** (apremilast)	• **None**	• **Cimzia** (certolizumab pegol) • **Inflectra** (infliximab-dyyb) • **Orencia/Orencia Clickject** (abatacept) • **Renflexis** (infliximab-abda) • **Simponi** (golimumab) • **Stelara** (ustekinumab) • **Taltz** (ixekizumab) • **Xeljanz/Xeljanz XR** (tofacitinib)
Rheumatoid arthritis	• **Enbrel** (etanercept) • **Humira** (adalimumab) • **Kevzara** (sarilumab) • **Xeljanz/Xeljanz XR** (tofacitinib)	• **None**	• **Actemra** (tocilizumab) • **Cimzia** (certolizumab pegol) • **Inflectra** (infliximab-dyyb) • **Kineret** (anakinra) • **Olumiant** (baricitinib) • **Orencia/Orencia Clickject** (abatacept) • **Renflexis** (infliximab-abda) • **Simponi** (golimumab)
Crohn's disease	• **Humira** (adalimumab)	• **Stelara** (ustekinumab)	• **Cimzia** (certolizumab pegol) • **Entyvio** (vedolizumab) • **Inflectra** (infliximab-dyyb) • **Renflexis** (infliximab-abda)
Ulcerative colitis	• **Humira** (adalimumab) • **Simponi** (golimumab)	• **None**	• **Entyvio** (vedolizumab) • **Inflectra** (infliximab-dyyb) • **Renflexis** (infliximab-abda) • **Xeljanz/Xeljanz XR** (tofacitinib)

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

Coverage for a targeted product is provided when any of the following criteria is met:

A. Ankylosing spondylitis
   1. Member has a documented inadequate response or intolerable adverse event with all of the preferred products (Cosentyx, Enbrel, and Humira)
   2. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs
   3. The requested product is Cimzia and member is currently pregnant or breastfeeding

B. Crohn's disease

This policy applies to the following:

	Standard Opt-in		**ACSF**		**VF**	✓	**Marketplace**
	Standard Opt-in NTMB		**PDPD**		**MMT**		**Medical Benefit**
	Standard Opt-out		**Generics First**				**Medical Benefit: Managed Medicaid**

Reference #
2719-D

1. Member has a documented inadequate response or intolerable adverse event with the primary preferred product (Humira) and with the secondary preferred product (Stelara), unless there is a documented clinical reason to avoid Humira (see Appendix)
2. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs
3. The requested product is Cimzia and member is currently pregnant or breastfeeding

C. Psoriatic arthritis
1. Member has a documented inadequate response or intolerable adverse event with at least three of the preferred products (Cosentyx, Enbrel, Humira, and Otezla); unless there is a documented clinical reason to avoid Enbrel and Humira (see Appendix)
2. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs
3. The requested product is Cimzia and member is currently pregnant or breastfeeding

D. Plaque psoriasis
1. Member has a documented inadequate response or intolerable adverse event with all of the preferred products (Humira, Otezla, Skyrizi, Stelara, Taltz); unless there is a documented clinical reason to avoid Humira (see Appendix)
2. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs
3. The requested product is Cimzia and member is currently pregnant or breastfeeding

E. Rheumatoid arthritis
1. Member has a documented inadequate response or intolerable adverse event with all of the preferred products (Enbrel, Humira, Kevzara, and Xeljanz/Xeljanz XR); unless there is a documented clinical reason to avoid Enbrel and Humira (see Appendix)
2. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs
3. The requested product is Cimzia and member is currently pregnant or breastfeeding

F. Ulcerative colitis
1. Member has had a documented inadequate response or intolerable adverse event with at least one of the preferred products (Humira, Simponi), unless there is a documented clinical reason to avoid Humira and Simponi (see Appendix)
2. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs

III. Appendix: Clinical reasons to avoid a preferred TNF inhibitor(s)

- History of demyelinating disorder
- History of congestive heart failure
- History of hepatitis B virus infection
- Autoantibody formation/lupus-like syndrome
- Risk of lymphoma

REFERENCES

This policy applies to the following:

	Standard Opt-in		**ACSF**		**VF**	✓	**Marketplace**
	Standard Opt-in NTMB		**PDPD**		**MMT**		**Medical Benefit**
	Standard Opt-out		**Generics First**				**Medical Benefit: Managed Medicaid**

Reference #
2719-D

1. Actemra [package insert]. South San Francisco, CA: Genentech, Inc.; August 2017.
2. Cimzia [package insert]. Smyrna, GA: UCB, Inc.; May 2018.
3. Cosentyx [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; January 2016.
4. Enbrel [package insert]. Thousand Oaks, CA: Immunex Corporation; July 2017.
5. Entyvio [package insert]. Deerfield, IL: Takeda Pharmaceutical America, Inc.; May 2014.
6. Humira [package insert]. North Chicago, IL: AbbVie Inc.; May 2017.
7. Ilumya [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2018.
8. Inflectra [package insert]. Lake Forest, IL: Hospira, a Pfizer Company; August 2016.
9. Kevzara [package insert]. Bridgewater, NJ: Sanofi-aventis, U.S. LLC /Regeneron Pharmaceuticals, Inc.; May 2017.
10. Kineret [package insert]. Stockholm, Sweden: Swedish Orphan Biovitrum AB (publ); May 2016.
11. Olumiant [package insert]. Indianapolis, IN: Lilly USA, LLC; May 2018.
12. Orencia [package insert]. Princeton, NJ: Bristol-Meyers Squibb Company; June 2017.
13. Otezla [package insert]. Summit, NJ: Celgene Corporation; June 2017.
14. Siliq [package insert]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; February 2017.
15. Simponi [package insert]. Horsham, PA: Janssen Biotech, Inc.; June 2017.
16. Skyrizi [package insert]. North Chicago, IL: AbbVie Inc.; April 2019.
17. Stelara [package insert]. Horsham, PA: Janssen Biotech, Inc.; September 2016.
18. Taltz [package insert]. Indianapolis, IN: Eli Lilly and Company; December 2017.
19. Tremfya [package insert]. Horsham, PA: Janssen Biotech, Inc.; July 2017.
20. Xeljanz/Xeljanz XR [package insert. New York, NY: Pfizer, Inc.; May 2018.

Reference number(s)
1892-A

SPECIALTY GUIDELINE MANAGEMENT

ERBITUX® (cetuximab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
   1. Squamous Cell Carcinoma of the Head and Neck (SCCHN)
      Erbitux is indicated:
      a. In combination with radiation therapy for the initial treatment of locally or regionally advanced squamous cell carcinoma of the head and neck (SCCHN).
      b. In combination with platinum-based therapy with fluorouracil for the first-line treatment of patients with recurrent locoregional disease or metastatic SCCHN.
      c. As a single agent for the treatment of patients with recurrent or metastatic SCCHN for whom prior platinum-based therapy has failed.
   2. K-Ras Wild-type, EGFR-expressing Colorectal Cancer (CRC)
      Erbitux is indicated for the treatment of K-Ras wild-type, epidermal growth factor receptor (EGFR)-expressing, metastatic colorectal cancer (mCRC) as determined by an FDA-approved test:
      a. In combination with FOLFIRI (irinotecan, fluorouracil, leucovorin) for first-line treatment,
      b. In combination with irinotecan in patients who are refractory to irinotecan-based chemotherapy,
      c. As a single agent in patients who have failed oxaliplatin- and irinotecan-based chemotherapy or who are intolerant to irinotecan.

   Limitations of Use:
   Erbitux is not indicated for treatment of Ras-mutant colorectal cancer or when the results of the Ras mutation tests are unknown.

B. Compendial Uses
   1. Colorectal cancer
   2. Squamous cell carcinoma of the head and neck
   3. Occult primary head and neck cancer
   4. Penile cancer
   5. Squamous cell skin cancer
   6. Non-small cell lung cancer

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
A. Documentation of Ras wild-type status, where applicable.
B. Documentation of EGFR expression, where applicable.

III. CRITERIA FOR INITIAL APPROVAL

A. Colorectal Cancer

Authorization of 6 months may be granted for treatment of colorectal cancer, including small bowel adenocarcinoma, appendiceal carcinoma, and anal adenocarcinoma, for unresectable/inoperable, advanced, or metastatic disease when all of the following criteria are met:

1. The *RAS (KRAS* and *NRAS)* mutation status is negative (wild-type).
2. Member has not previously experienced clinical failure on panitumumab.

B. Squamous Cell Carcinoma of the Head and Neck

Authorization of 6 months may be granted for treatment of squamous cell carcinoma of the head and neck when any of the following criteria is met:

1. Disease is locally or regionally advanced, unresectable, recurrent, or metastatic.
2. Member is unfit for surgery.
3. Erbitux will be used in combination with radiation.

C. Occult Primary Head and Neck Cancer

Authorization of 6 months may be granted as a single agent for treatment of occult primary head and neck cancer for sequential chemoradiation.

D. Penile Cancer

Authorization of 6 months may be granted as a single agent for subsequent treatment of metastatic penile cancer.

E. Squamous Cell Skin Cancer

Authorization of 6 months may be granted for treatment of squamous cell skin cancer for inoperable positive regional lymph nodes, regional recurrence or distant metastases.

F. Non-Small Cell Lung Cancer (NSCLC)

Authorization of 6 months may be granted for subsequent treatment of recurrent, advanced or metastatic NSCLC when the following criteria are met:

1. Erbitux will be used in combination with afatinib.
2. Erbitux will be used in members with a known sensitizing EGFR mutation following disease progression on EGFR tyrosine kinase inhibitor therapy.

IV. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section III who have not experienced disease progression or an unacceptable toxicity.

V. REFERENCES

1. Erbitux [package insert]. Princeton, NJ: Bristol-Meyers Squibb Company; April 2019.
2. The NCCN Drugs & Biologics Compendium® © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed July 11, 2019.

Reference number(s)
2231-A

SPECIALTY GUIDELINE MANAGEMENT

FARYDAK (panobinostat)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indication
Farydak, in combination with bortezomib and dexamethasone, is indicated for the treatment of patients with multiple myeloma who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent. This indication is approved under accelerated approval based on progression free survival. Continued approval of this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

B. Compendial Uses
In combination with carfilzomib or in combination with dexamethasone and lenalidomide or in combination with dexamethasone and bortezomib for previously treated multiple myeloma for relapsed or progressive disease in patients who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Multiple Myeloma
Authorization of 12 months may be granted for the treatment of relapsed or progressive multiple myeloma when the all of the following criteria are met:
A. The member has received at least two prior regimens, including bortezomib and an immunomodulatory agent
B. The requested medication will be used in any of the following regimens:
   1. In combination with bortezomib and dexamethasone
   2. In combination with lenalidomide and dexamethasone
   3. In combination with carfilzomib

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who have not experienced intolerable adverse effects or disease progression while on the current regimen.

IV. REFERENCES

1. Farydak [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2016.
2. The NCCN Drugs & Biologics Compendium 2019 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed March 29, 2019.

3. The NCCN Clinical Practice Guidelines in Oncology Multiple Myeloma (Version 1.2019) 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed March 29, 2019.

PRIOR AUTHORIZATION CRITERIA

CLASS NAME **HIV DUPLICATIVE USE**

BRAND NAME (generic)*

COMBINATION DRUGS:

- **ATRIPLA (efavirenz-emtricitabine-tenofovir disoproxil fumarate)**
- **BIKTARVY (bictegravir-emtricitabine-tenofovir alafenamide)**
- **CIMDUO (lamivudine-tenofovir disoproxil fumarate)**
- **COMBIVIR (lamivudine-zidovudine)**
- **COMPLERA (rilpivirine-emtricitabine-tenofovir disoproxil fumarate)**
- **DELSTRIGO (doravirine-lamivudine-tenofovir disoproxil fumarate)**
- **DOVATO (dolutegravir-lamivudine)**
- **EPZICOM (lamivudine-abacavir)**
- **EVOTAZ (atazanavir-cobicistat)**
- **GENVOYA (elvitegravir-cobicistat-emtricitabine-tenofovir alafenamide)**
- **JULUCA (dolutegravir-rilpivirine)**
- **KALETRA (lopinavir-ritonavir)**
- **ODEFSEY (emtricitabine-rilpivirine-tenofovir alafenamide)**
- **PREZCOBIX (darunavir-cobicistat)**
- **STRIBILD (cobicistat-elvitegravir-emtricitabine-tenofovir disoproxil fumarate)**
- **SYMFI / SYMFI LO (efavirenz-lamivudine-tenofovir disoproxil fumarate)**
- **SYMTUZA (darunavir-cobicistat-emtricitabine-tenofovir alafenamide)**
- **TEMIXYS (lamivudine-tenofovir disoproxil fumarate)**
- **TRIUMEQ (abacavir-dolutegravir-lamivudine)**
- **TRIZIVIR (abacavir-lamivudine-zidovudine)**

SINGLE INGREDIENT DRUGS:

- **EDURANT (rilpivirine)**
- **EMTRIVA (emtricitabine)**
- **EPIVIR (lamivudine)**
- **NORVIR (ritonavir)**
- **PIFELTRO (doravirine)**
- **PREZISTA (darunavir)**
- **RETROVIR (zidovudine)**
- **REYATAZ (atazanavir)**
- **SUSTIVA (efavirenz)**
- **TIVICAY (dolutegravir)**
- **TYBOST (cobicistat)**
- **VIREAD (tenofovir disoproxil fumarate)**
- **VITEKTA (elvitegravir)**
- **ZIAGEN (abacavir)**

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 790-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

CVS caremark™

PROGRAM DESCRIPTION

Plans implementing the HIV Duplicative Use hard stop DUR edit will ensure patients do not take more than one antiretroviral that contains the same active ingredient. The adjudication system will look back for the duplicative agents within the past 15 days. If the patient has not filled a duplicative agent within the past 15 days, then the requested drug will be paid under the prescription benefit. If the patient does not meet the initial look back, then the system will reject with a message ('Two HIV drugs w/ same ingred; PA required') indicating that a prior authorization (PA) is required. The post DUR criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The prescriber will evaluate the patient's regimen and discontinue the duplicative drug/drug combination(s)

RATIONALE

The HIV Medication Duplication Chart below lists the affected products. Antiretroviral therapy includes various drug regimens and combination products which pose a risk for duplicative use.

This program identifies and informs prescribers of patients who may be taking two products with the same ingredients at the same time based on claim information.

HIV Medication Duplication (Drug A + B) Chart

Drug A	Drug B
Atripla (efavirenz-emtricitabine-tenofovir)	Biktarvy (bictegravir-emtricitabine-tenofovir) Cimduo (lamivudine-tenofovir) Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Emtriva (emtricitabine) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Odefsey (emtricitabine-rilpivirine-tenofovir) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Sustiva (efavirenz) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Temixys (lamivudine-tenofovir) Viread (tenofovir)
Biktarvy (bictegravir-emtricitabine-tenofovir)	Atripla (efavirenz-emtricitabine-tenofovir) Cimduo (lamivudine-tenofovir) Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Emtriva (emtricitabine) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Odefsey (emtricitabine-rilpivirine-tenofovir) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Temixys (lamivudine-tenofovir) Viread (tenofovir)
Cimduo (lamivudine-tenofovir)	Atripla (efavirenz-emtricitabine-tenofovir) Biktarvy (bictegravir-emtricitabine-tenofovir) Combivir (lamivudine-zidovudine)

	Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Dovato (dolutegravir-lamivudine) Epivir (lamivudine) Epzicom (lamivudine-abacavir) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Odefsey (emtricitabine-rilpivirine-tenofovir) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Temixys (lamivudine-tenofovir) Triumeq (abacavir-dolutegravir-lamivudine) Trizivir (abacavir-lamivudine-zidovudine) Viread (tenofovir)
Combivir (lamivudine-zidovudine)	Cimduo (lamivudine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Dovato (dolutegravir-lamivudine) Epivir (lamivudine) Epzicom (lamivudine-abacavir) Retrovir (zidovudine) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Temixys (lamivudine-tenofovir) Triumeq (abacavir-dolutegravir-lamivudine) Trizivir (abacavir-lamivudine-zidovudine)
Complera (rilpivirine-emtricitabine-tenofovir)	Atripla (efavirenz-emtricitabine-tenofovir) Biktarvy (bictegravir-emtricitabine-tenofovir) Cimduo (lamivudine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Edurant (rilpivirine) Emtriva (emtricitabine) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Juluca (dolutegravir-rilpivirine) Odefsey (emtricitabine-rilpivirine-tenofovir) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Temixys (lamivudine-tenofovir) Viread (tenofovir)
Delstrigo (doravirine-lamivudine-tenofovir disoproxil fumarate)	Atripla (efavirenz-emtricitabine-tenofovir) Biktarvy (bictegravir-emtricitabine-tenofovir) Cimduo (lamivudine-tenofovir) Combivir (lamivudine-zidovudine) Complera (rilpivirine-emtricitabine-tenofovir) Dovato (dolutegravir-lamivudine) Epivir (lamivudine) Epzicom (lamivudine-abacavir) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Odefsey (emtricitabine-rilpivirine-tenofovir) Pifeltro (doravirine) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Temixys (lamivudine-tenofovir) Triumeq (abacavir-dolutegravir-lamivudine) Trizivir (abacavir-lamivudine-zidovudine) Viread (tenofovir)

Dovato (dolutegravir-lamivudine)	Cimduo (lamivudine-tenofovir) Combivir (lamivudine-zidovudine) Delstrigo (doravirine-lamivudine-tenofovir) Epivir (lamivudine) Epzicom (lamivudine-abacavir) Juluca (dolutegravir-rilpivirine) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Temixys (lamivudine-tenofovir) Tivicay (dolutegravir) Triumeq (abacavir-dolutegravir-lamivudine) Trizivir (abacavir-lamivudine-zidovudine)
Edurant (rilpivirine)	Complera (rilpivirine-emtricitabine-tenofovir) Juluca (dolutegravir-rilpivirine) Odefsey (emtricitabine-rilpivirine-tenofovir)
Emtriva (emtricitabine)	Atripla (efavirenz-emtricitabine-tenofovir) Biktarvy (bictegravir-emtricitabine-tenofovir) Complera (rilpivirine-emtricitabine-tenofovir) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Odefsey (emtricitabine-rilpivirine-tenofovir) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir)
Epivir (lamivudine)	Cimduo (lamivudine-tenofovir) Combivir (lamivudine-zidovudine) Delstrigo (doravirine-lamivudine-tenofovir) Dovato (dolutegravir-lamivudine) Epzicom (lamivudine-abacavir) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Temixys (lamivudine-tenofovir) Triumeq (abacavir-dolutegravir-lamivudine) Trizivir (abacavir-lamivudine-zidovudine)
Epzicom (lamivudine-abacavir)	Cimduo (lamivudine-tenofovir) Combivir (lamivudine-zidovudine) Delstrigo (doravirine-lamivudine-tenofovir) Dovato (dolutegravir-lamivudine) Epivir (lamivudine) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Temixys (lamivudine-tenofovir) Triumeq (abacavir-dolutegravir-lamivudine) Trizivir (abacavir-lamivudine-zidovudine) Ziagen (abacavir)
Evotaz (atazanavir-cobicistat)	Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Prezcobix (darunavir-cobicistat) Reyataz (atazanavir) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Tybost (cobicistat)
Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir)	Atripla (efavirenz-emtricitabine-tenofovir) Biktarvy (bictegravir-emtricitabine-tenofovir) Cimduo (lamivudine-tenofovir) Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Emtriva (emtricitabine) Evotaz (atazanavir-cobicistat) Odefsey (emtricitabine-rilpivirine-tenofovir) Prezcobix (darunavir-cobicistat) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir)

	Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Temixys (lamivudine-tenofovir) Tybost (cobicistat) Viread (tenofovir) Vitekta (elvitegravir)
Juluca (dolutegravir-rilpivirine)	Complera (rilpivirine-emtricitabine-tenofovir) Dovato (dolutegravir-lamivudine) Edurant (rilpivirine) Odefsey (emtricitabine-rilpivirine-tenofovir) Tivicay (dolutegravir) Triumeq (abacavir-dolutegravir-lamivudine)
Kaletra (lopinavir-ritonavir)	Norvir (ritonavir)
Norvir (ritonavir)	Kaletra (lopinavir-ritonavir)
Odefsey (emtricitabine-rilpivirine-tenofovir)	Atripla (efavirenz-emtricitabine-tenofovir) Biktarvy (bictegravir-emtricitabine-tenofovir) Cimduo (lamivudine-tenofovir) Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Edurant (rilpivirine) Emtriva (emtricitabine) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Juluca (dolutegravir-rilpivirine) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Temixys (lamivudine-tenofovir) Viread (tenofovir)
Pifeltro (doravirine)	Delstrigo (doravirine-lamivudine-tenofovir)
Prezcobix (darunavir-cobicistat)	Evotaz (atazanavir-cobicistat) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Prezista (darunavir) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Tybost (cobicistat)
Prezista (darunavir)	Prezcobix (darunavir-cobicistat) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir)
Retrovir (zidovudine)	Combivir (lamivudine-zidovudine) Trizivir (abacavir-lamivudine-zidovudine)
Reyataz (atazanavir)	Evotaz (atazanavir-cobicistat)
Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir)	Atripla (efavirenz-emtricitabine-tenofovir) Biktarvy (bictegravir-emtricitabine-tenofovir) Cimduo (lamivudine-tenofovir) Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Emtriva (emtricitabine) Evotaz (atazanavir-cobicistat) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Odefsey (emtricitabine-rilpivirine-tenofovir) Prezcobix (darunavir-cobicistat) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Temixys (lamivudine-tenofovir) Tybost (cobicistat) Viread (tenofovir) Vitekta (elvitegravir)

Sustiva (efavirenz)	Atripla (efavirenz-emtricitabine-tenofovir) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir)
Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir)	Atripla (efavirenz-emtricitabine-tenofovir) Biktarvy (bictegravir-emtricitabine-tenofovir) Cimduo (lamivudine-tenofovir) Combivir (lamivudine-zidovudine) Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Dovato (dolutegravir-lamivudine) Epivir (lamivudine) Epzicom (lamivudine-abacavir) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Odefsey (emtricitabine-rilpivirine-tenofovir) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Sustiva (efavirenz) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Temixys (lamivudine-tenofovir) Triumeq (abacavir-dolutegravir-lamivudine) Trizivir (abacavir-lamivudine-zidovudine) Viread (tenofovir)
Symtuza (darunavir-cobicistat-emtricitabine-tenofovir)	Atripla (efavirenz-emtricitabine-tenofovir) Biktarvy (bictegravir-emtricitabine-tenofovir) Cimduo (lamivudine-tenofovir) Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Emtriva (emtricitabine) Evotaz (atazanavir-cobicistat) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Odefsey (emtricitabine-rilpivirine-tenofovir) Prezcobix (darunavir-cobicistat) Prezista (darunavir) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Temixys (lamivudine-tenofovir) Tybost (cobicistat) Viread (tenofovir)
Temixys (lamivudine-tenofovir)	Atripla (efavirenz-emtricitabine-tenofovir) Biktarvy (bictegravir-emtricitabine-tenofovir) Cimduo (lamivudine-tenofovir) Combivir (lamivudine-zidovudine) Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Dovato (dolutegravir-lamivudine) Epivir (lamivudine) Epzicom (lamivudine-abacavir) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Odefsey (emtricitabine-rilpivirine-tenofovir) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Triumeq (abacavir-dolutegravir-lamivudine) Trizivir (abacavir-lamivudine-zidovudine) Viread (tenofovir)
Tivicay (dolutegravir)	Dovato (dolutegravir-lamivudine) Juluca (dolutegravir-rilpivirine) Triumeq (abacavir-dolutegravir-lamivudine)

Triumeq (abacavir-dolutegravir-lamivudine)	Cimduo (lamivudine-tenofovir) Combivir (lamivudine-zidovudine) Delstrigo (doravirine-lamivudine-tenofovir) Dovato (dolutegravir-lamivudine) Epivir (lamivudine) Epzicom (lamivudine-abacavir) Juluca (dolutegravir-rilpivirine) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Temixys (lamivudine-tenofovir) Tivicay (dolutegravir) Trizivir (abacavir-lamivudine-zidovudine) Ziagen (abacavir)
Trizivir (abacavir-lamivudine-zidovudine)	Cimduo (lamivudine-tenofovir) Combivir (lamivudine-zidovudine) Delstrigo (doravirine-lamivudine-tenofovir) Dovato (dolutegravir-lamivudine) Epivir (lamivudine) Epzicom (lamivudine-abacavir) Retrovir (zidovudine) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Temixys (lamivudine-tenofovir) Triumeq (abacavir-dolutegravir-lamivudine) Ziagen (abacavir)
Tybost (cobicistat)	Evotaz (atazanavir-cobicistat) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Prezcobix (darunavir-cobicistat) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir)
Viread (tenofovir)	Atripla (efavirenz-emtricitabine-tenofovir) Biktarvy (bictegravir-emtricitabine-tenofovir) Cimduo (lamivudine-tenofovir) Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Odefsey (emtricitabine-rilpivirine-tenofovir) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Temixys (lamivudine-tenofovir)
Vitekta (elvitegravir)	Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir)
Ziagen (abacavir)	Epzicom (lamivudine-abacavir) Triumeq (abacavir-dolutegravir-lamivudine) Trizivir (abacavir-lamivudine-zidovudine)

REFERENCES

1. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf. Last Updated: October 25, 2018. Accessed 12/2018.

Written by: UM Development (NB)
Date Written: 06/2012
Revised: 08/2012 (added column B drugs to target drug list), 05/2013, 02/2014, 12/2014 (added Tivicay, Triumeq, Tybost and Vitekta), 01/2015 (added Evotaz & Prezcobix), (LN) 05/2015 (added denial reasons), (NB) 12/2015 (added Genvoya) 03/2016 (added

Odefsey), 04/2016 (added Descovy), 12/2016 (added “Coverage Criteria”, removed questions #1 & #2 and adjusted question #3, added “program description”); (RP/LN) 08/2017 (removed Truvada; extended duration), 12/2017-02/2018 (Added Juluca, Biktarvy), 04/2018 (Added Symfi / Symfi Lo), 07/2018 (Added Cimduo & Symtuza), 09/2018 (Added Delstrigo & Pifeltro), 12/2018 (no clinical changes), 04/2019 (Added Dovato), 10/2019 (removed Descovy; Added Temixys)

Reviewed: Medical Affairs (LB) 07/2012, 08/2012, 05/2013, 02/2014, 12/2014, 01/2015, 02/2015, (LB) 12/2015, (DC) 03/2016; (AN) 08/2017, 02/2018, 04/2018, 07/2018, 10/2018, 12/2018, 04/2019; (CHART) 10/17/2019 & 11/07/2019
External Review: 07/2012, 06/2013, 04/2014, 01/2015, 02/2015, 02/2016, 04/2016, 04/2017, 04/2018, 08/2018, 12/2018, 04/2019, 06/2019, 12/2019 (FYI)

CRITERIA FOR APPROVAL

1	According to pharmacy claims records, the requested medication represents a therapeutic duplication with an existing antiretroviral drug the patient may be taking. Will the prescriber evaluate the patient’s regimen and discontinue duplicative drug(s)?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are not taking two drugs that have the same ingredients. Your request has been denied based on the information we have. [Short Description: No discontinuation of duplicative drug(s)]

PRIOR AUTHORIZATION CRITERIA

CLASS NAME **HIV INAPPROPRIATE COMBINATIONS/INTERACTIONS**

BRAND NAME (generic)*

COMBINATION DRUGS:

- **ATRIPLA (efavirenz-emtricitabine-tenofovir disoproxil fumarate)**
- **BIKTARVY (bictegravir-emtricitabine-tenofovir alafenamide)**
- **CIMDUO (lamivudine-tenofovir disoproxil fumarate)**
- **COMBIVIR (lamivudine-zidovudine)**
- **COMPLERA (rilpivirine-emtricitabine-tenofovir disoproxil fumarate)**
- **DELSTRIGO (doravirine-lamivudine-tenofovir disoproxil fumarate)**
- **DOVATO (dolutegravir-lamivudine)**
- **EPZICOM (lamivudine-abacavir)**
- **EVOTAZ (atazanavir-cobicistat)**
- **GENVOYA (elvitegravir-cobicistat-emtricitabine-tenofovir alafenamide)**
- **JULUCA (dolutegravir-rilpivirine)**
- **KALETRA (lopinavir-ritonavir)**
- **ODEFSEY (emtricitabine-rilpivirine-tenofovir alafenamide)**
- **PREZCOBIX (darunavir-cobicistat)**
- **STRIBILD (cobicistat-elvitegravir-emtricitabine-tenofovir disoproxil fumarate)**
- **SYMFI / SYMFI LO (efavirenz-lamivudine-tenofovir disoproxil fumarate)**
- **SYMTUZA (darunavir-cobicistat-emtricitabine-tenofovir alafenamide)**
- **TEMIXYS (lamivudine-tenofovir disoproxil fumarate)**
- **TRIUMEQ (abacavir-dolutegravir-lamivudine)**
- **TRIZIVIR (abacavir-lamivudine-zidovudine)**

SINGLE INGREDIENT DRUGS:

- **APTIVUS (tipranavir)**
- **CRIXIVAN (indinavir)**
- **PIFELTRO (doravirine)**
- **EDURANT (rilpivirine)**
- **EPIVIR (lamivudine)**
- **EMTRIVA (emtricitabine)**
- **INTELENCE (etravirine)**
- **ISENTRESS (raltegravir)**
- **NORVIR (ritonavir)**
- **RESCRIPTOR (delavirdine)**
- **RETROVIR (zidovudine)**
- **REYATAZ (atazanavir)**
- **SUSTIVA (efavirenz)**
- **TYBOST (cobicistat)**
- **VIDEX (didanosine)**
- **VIRAMUNE (nevirapine)**
- **VIREAD (tenofovir disoproxil fumarate)**
- **ZERIT (stavudine)**

Status: CVS Caremark Criteria

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

PROGRAM DESCRIPTION

Plans implementing the HIV Inappropriate-Interaction hard stop DUR edit will ensure patients do not take antiretrovirals that interact with each other or are inappropriate to take together. The adjudication system will look back for the inappropriate or interacting agents within the past 15 days. If the patient has not filled an antiretroviral that interacts or is inappropriate to take with the requested drug within the past 15 days, then the requested drug will be paid under the prescription benefit. If the patient does not meet the initial look back, then the system will reject with a message ('Two inapprop.,interacting HIV drugs; PA required') indicating that a prior authorization (PA) is required. The post DUR criteria would then be applied to requests submitted for evaluation to the PA unit.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The prescriber will evaluate the patient's regimen and discontinue interacting or inappropriate drug combination(s)

RATIONALE

The Inappropriate HIV Combination Therapy Chart below lists the affected products. Per guidelines, some antiretroviral (ARV) regimens or components are not generally recommended because of suboptimal antiviral potency, unacceptable toxicities, or pharmacologic concerns. Drug-drug interactions between ARV drugs and concomitant medications are common, and may lead to increased or decreased drug exposure. In some instances, changes in drug exposure may increase toxicities or affect therapeutic responses.

This program identifies those products which are not recommended to be used in combinations which interact or are inappropriate. Recommendations for managing a particular drug interaction may differ depending on whether a new ARV is being initiated in a patient on a stable concomitant medication, or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly; therefore, the prescriber should evaluate the patient's regimen and discontinue interacting or inappropriate drug combination(s).

Inappropriate HIV Combination Therapy/Interactions Drug A + B (or Drug B + A) Chart		
Drug A	**Drug B**	**Rationale**
Atazanavir + Indinavir		*Atazanavir and indinavir can cause Grade 3 to 4 hyperbilirubinemia and jaundice.*
Evotaz (atazanavir-cobicistat) Reyataz (atazanavir)	Crixivan (indinavir)	
Emtricitabine + Lamivudine		*Emtricitabine and lamivudine have similar resistance profiles and have minimal additive antiviral activity.*
Atripla (efavirenz-emtricitabine-tenofovir) Biktarvy (bictegravir-emtricitabine-tenofovir) Complera (rilpivirine-emtricitabine-	Epivir (lamivudine) Cimduo (lamivudine-tenofovir) Combivir (lamivudine-zidovudine) Delstrigo (doravirine-lamivudine-	

tenofovir) Emtriva (emtricitabine) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Odefsey (emtricitabine-rilpivirine-tenofovir) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir)	tenofovir) Dovato (dolutegravir-lamivudine) Epzicom (lamivudine-abacavir) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Temixys (lamivudine-tenofovir) Triumeq (abacavir-dolutegravir-lamivudine) Trizivir (abacavir-lamivudine-zidovudine)	
Didanosine + Stavudine		*Didanosine and stavudine as a dual-NRTI backbone can result in a high incidence of toxicities, particularly peripheral neuropathy, pancreatitis, and lactic acidosis.*
Videx (didanosine)	Zerit (stavudine)	
Didanosine + Tenofovir Disoproxil Fumarate		*Tenofovir disoproxil fumarate (TDF) increases ddI (didanosine) concentrations, serious ddI-associated toxicities, immunologic nonresponse, early virologic failure, and resistance*
Videx (didanosine)	Viread (tenofovir disoproxil fumarate) Atripla (efavirenz-emtricitabine-tenofovir disoproxil fumarate) Cimduo (lamivudine-tenofovir disoproxil fumarate) Complera (rilpivirine-emtricitabine-tenofovir disoproxil fumarate) Delstrigo (doravirine-lamivudine-tenofovir disoproxil fumarate) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir disoproxil fumarate) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir disoproxil fumarate) Temixys (lamivudine-tenofovir disoproxil fumarate)	
Stavudine + Zidovudine		*Stavudine and zidovudine should not be used in combination because of antagonism demonstrated in vitro and in vivo.*
Zerit (stavudine)	Combivir (lamivudine-zidovudine) Retrovir (zidovudine) Trizivir (abacavir-lamivudine-zidovudine)	
Etravirine + Tipranavir *(ritonavir-boosted)*		*Tipranavir (ritonavir-boosted as a standard) significantly reduces etravirine concentrations.*
Intelence (etravirine)	Aptivus (tipranavir) (ritonavir boosted)	
Etravirine + Raltegravir (HD only)		*Concurrent use of etravirine and raltegravir may result in decreased plasma concentrations of raltegravir (HD only) and risk of diminished therapeutic effect of raltegravir (HD*

		only).
Intelence (etravirine)	Isentress (raltegravir) (HD only)	
Tipranavir*(ritonavir-boosted)* **+ Raltegravir (HD only)**		*Tipranavir (ritonavir-boosted as a standard) and raltegravir (HD only) coadministration is not recommended*
Aptivus (tipranavir) (ritonavir boosted)	Isentress (raltegravir) (HD only)	
Two NNRTIs		*Two-non-nucleoside reverse transcriptase inhibitor (2-NNRTI) combinations can cause a higher frequency of clinical adverse events that leads to treatment discontinuation.*
Rilpivirine + another NNRTI		
Complera (rilpivirine-emtricitabine-tenofovir) Edurant (rilpivirine) Odefsey (emtricitabine-rilpivirine-tenofovir) Juluca (dolutegravir-rilpivirine)	Atripla (efavirenz-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Intelence (etravirine) Pifeltro (doravirine) Rescriptor (delavirdine) Sustiva (efavirenz) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Viramune (nevirapine)	
Efavirenz + another NNRTI		
Atripla (efavirenz-emtricitabine-tenofovir) Sustiva (efavirenz) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir)	Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Edurant (rilpivirine) Intelence (etravirine) Juluca (dolutegravir-rilpivirine) Odefsey (emtricitabine-rilpivirine-tenofovir) Pifeltro (doravirine) Rescriptor (delavirdine) Viramune (nevirapine)	
Etravirine + another NNRTI		
Intelence (etravirine)	Atripla (efavirenz-emtricitabine-tenofovir) Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Edurant (rilpivirine) Juluca (dolutegravir-rilpivirine) Odefsey (emtricitabine-rilpivirine-tenofovir) Pifeltro (doravirine) Rescriptor (delavirdine) Sustiva (efavirenz) Symfi / Symfi Lo (efavirenz-	

	lamivudine-tenofovir) Viramune (nevirapine)	
Delavirdine + other NNRTI		
Rescriptor (delavirdine)	Atripla (efavirenz-emtricitabine-tenofovir) Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Edurant (rilpivirine) Intelence (etravirine) Juluca (dolutegravir-rilpivirine) Odefsey (emtricitabine-rilpivirine-tenofovir) Pifeltro (doravirine) Sustiva (efavirenz) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Viramune (nevirapine)	
Nevirapine + another NNRTI		
Viramune (nevirapine)	Atripla (efavirenz-emtricitabine-tenofovir) Complera (rilpivirine-emtricitabine-tenofovir) Delstrigo (doravirine-lamivudine-tenofovir) Edurant (rilpivirine) Intelence (etravirine) Juluca (dolutegravir-rilpivirine) Odefsey (emtricitabine-rilpivirine-tenofovir) Pifeltro (doravirine) Rescriptor (delavirdine) Sustiva (efavirenz) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir)	
Doravirine + another NNRTI		
Delstrigo (doravirine-lamivudine-tenofovir) Pifeltro (doravirine)	Atripla (efavirenz-emtricitabine-tenofovir) Complera (rilpivirine-emtricitabine-tenofovir) Edurant (rilpivirine) Intelence (etravirine) Juluca (dolutegravir-rilpivirine) Odefsey (emtricitabine-rilpivirine-tenofovir) Rescriptor (delavirdine) Sustiva (efavirenz) Symfi / Symfi Lo (efavirenz-lamivudine-tenofovir) Viramune (nevirapine)	

Two Boosters		*Two booster agents can cause a higher frequency of clinical adverse events that leads to treatment discontinuation.*
Ritonavir + Cobicistat		
Kaletra (lopinavir-ritonavir) Norvir (ritonavir)	Evotaz (atazanavir-cobicistat) Genvoya (elvitegravir-cobicistat-emtricitabine-tenofovir) Prezcobix (darunavir-cobicistat) Stribild (cobicistat-elvitegravir-emtricitabine-tenofovir) Symtuza (darunavir-cobicistat-emtricitabine-tenofovir) Tybost (cobicistat)	

REFERENCES

1. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf. Last Updated: October 25, 2018. Accessed 12/2018.

Written by:	UM Development (NB)
Date Written:	06/2012
Revised:	08/2012 (added column B drugs to target drug list), 05/2013, 02/2014 (added Isentress and Tivicay to target drug list, added greater than 2 PIs, and 2 integrase inhibitors to table), 12/2014 (added Norvir, Triumeq and Tybost to target drug list, added 2 boosters section to the table), 01/2015 (added Evotaz), (LN) 05/2015 (added denial reasons), (NB) 12/2015 (added Genvoya) 03/2016 (added Odefsey), 04/2016 (added Descovy), 11/2016 (updated drugs interacting with Descovy), 12/2016 (added "Coverage Criteria", removed questions #1 & #2 and adjusted question #3, added "program description); (RP) 06/2017 (added Isentress HD new strength) ; (RP/LN) 08/2017 (removed Truvada; extended duration), 12/2017-02/2018 (Added Juluca, Biktarvy), 04/2018 (Added Symfi / Symfi Lo), 07/2018 (Added Cimduo & Symtuza), 09/2018 (Added Delstrigo & Pifeltro), 12/2018 (no clinical changes), 04/2019 (Added Dovato), 10/2019 (Removed Descovy; Added Temixys)
Reviewed:	Medical Affairs (LB) 07/2012, 08/2012, 05/2013, 02/2014, 04/2014, 12/2014, 02/2015, (LB) 12/2015, (DC) 03/2016, (TP) 11/2016; (LCB) 06/2017: (AN) 08/2017, 02/2018, 04/2018, 07/2018, 10/2018, 12/2018, 04/2019; (CHART) 10/17/2019 & 11/07/2019 External Review: 07/2012, 06/2013, 04/2014, 01/2015, 02/2015, 02/2016, 04/2016, 12/2016, 04/2017, 08/2017, 04/2018, 08/2018, 12/2018, 04/2019, 06/2019, 12/2019 (FYI)

CRITERIA FOR APPROVAL

1	According to pharmacy claims records, the requested medication interacts with or is inappropriate with existing antiretroviral drug(s) the patient may be taking. Will the prescriber evaluate the patient's regimen and discontinue interacting or inappropriate drug combination(s)?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS**
1.	Approve, 12 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are not taking two drugs that could interact or are inappropriate to use with each other. Your request has been denied based on the information we have. [Short Description: No discontinuation of inappropriate/interacting drug(s)]