brand new day
HEALTHCARE YOU CAN FEEL GOOD ABOUT

CENTRAL HEALTH MEDICARE PLAN

Medical Policy

Clotting Disorder Therapy	
MEDICAL POLICY NUMBER	Med_Clin_Ops_046
POLICY OWNER	Christine Gilroy, MD, MSPH Assoc Chief Medical Officer
EFFECTIVE DATE	MAY 24, 2021
APPLICABLE PRODUCT AND MARKET (For Medicare Advantage products check http://www.cms.gov before applying this policy. If there is applicable CMS NCD, LCD or guidance, CMS policy should be used in lieu of this policy.)	Individual Family Plan: ALL Small Group: ALL Medicare Advantage: ALL

IMPORTANT INFORMATION – PLEASE READ BEFORE USING THIS POLICY*: These services may or may not be covered by all Brand New Day/Central Health Medicare Plan. Please refer to Member's plan document for specific coverage information. If there is a difference between this policy and Member's plan document, Member's plan document will be used to determine coverage. Brand New Day/Central Health Medicare Plan may use tools developed by third parties, such as MCG™ Care Guidelines and InterQual® Criteria, to assist in administering health benefits. Brand New Day/Central Health Medicare Plan Medical Policies, MCG™ Care Guidelines or InterQual® Criteria are not intended to be used without the independent clinical judgment of a qualified health care provider considering the individual circumstances of each member's case. For Medicare products, CMS Policies including National Coverage Determinations and Local Coverage Determinations will take precedent over Brand New Day/Central Health Medicare Plan or third-party policies. Brand New Day/Central Health Medicare Plan Medical Policies, MCG™ Care Guidelines and InterQual® Criteria do not constitute the practice of medicine or medical advice. The treating health care providers are solely responsible for diagnosis, treatment, and medical advice.*

For Medicare Advantage members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed and applied prior to applying the criteria set forth in this medical policy. Refer to the CMS website at http://www.cms.gov for additional information.

Members may contact Brand New Day/Central Health Medicare Plan Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Brand New Day/ Central Health Medicare Plan policy may contact the Health Plan.

PURPOSE

To promote consistency between reviewers in clinical coverage decision-making by providing the criteria that generally determine the medical necessity of Clotting Disorder therapy.

POLICY/CRITERIA

Prior Authorization and Medical Review is required.

Initial
Applicable Products

Criteria A Anti-Inhibitor Antibody	Hemlibra
Criteria B Anti-Inhibitor Coagulant Complex	Feiba NF
Criteria C Factor VIIa	NovoSeven RT
Criteria D Factor VIIa	Sevenfact
Criteria E Factor VIII/vWF Complex	Alphanate, Humate-P
Criteria F Factor VIII/vWF Complex	Wilate
Criteria G Factor VIII	Advate, Adynovate, Eloctate, Helixate FS, Hemofil M, Koate/-DVI, Kogenate FS, Monoclate-P, NovoEight, Recombinate, Xyntha, Nuwiq, Afstyla, Kovaltry, Jivi, Esperoct
Criteria H Factor VIII (Recombinant)	Obizur
Criteria I Coagulation Factor XIII A-subunit	Tretten
Criteria J Factor XIII	Corifact
Criteria K Factor IX	AlphaNine SD, Mononine, Profilnine SD, Alprolix, Bebulin, BeneFIX, Idelvion, Ixinity, Rebinyn, Rixubis
Criteria L Factor X	Coagadex
Criteria M von Willebrand Factor	Vonvendi

Criteria A – Hemlibra

Initial authorization will be provided for 3 months and may be renewed every 12 months thereafter.

1. Hemophilia A (congenital Factor VIII deficiency) is confirmed by blood coagulation testing; **AND**
2. Patient has confirmed inhibitors to Factor VIII; **AND**
    a. Hemlibra is used for routine prophylaxis to prevent or reduce the frequency of episodic bleeding; **AND**
    b. Hemlibra will not be used in combination with Immune Tolerance Induction (ITI); **AND**
        i. Patient has had at least two documented episodes of spontaneous bleeding into joints; **OR**
        ii. Patient had a documented trial and failure of Immune Tolerance Induction (ITI); **OR**
        iii. Patient had a documented trial and failure of, or is currently on, routine prophylaxis with a bypassing agent (i.e., NovoSeven, Feiba); **OR**
3. Patient does not have confirmed inhibitors to Factor VIII; **AND**
    a. Hemlibra is used for routine prophylaxis to prevent or reduce the frequency of episodic bleeding; **AND**
    b. Hemlibra is being used as treatment in one of the following:
        i. Patient must have severe hemophilia A (factor VIII level of <1%); **OR**
        ii. Patient has had at least two documented episodes of spontaneous bleeding into joints; **AND**
    c. Patient is not a suitable candidate for treatment with shorter half-life Factor VIII (recombinant) products at a total weekly dose of 100 IU/kg or less (as attested by the prescribing physician with appropriate clinical rationale).

Hemlibra

Indication	Dose
Routine Prophylaxis Congenital Hemophilia A with or without inhibitors	Loading Dose: 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks **Max allowed**: 690 billable units (BU) weekly x 4 doses Maintenance Dose: • 1.5 mg/kg once weekly (360 BU weekly); **OR** • 3 mg/kg every two weeks (690 BU every 2 weeks); **OR** • 6 mg/kg every four weeks (1380 BU every 4 weeks)

Note: *Patient must be dosed at a frequency that will produce the least wastage per dose based on available vial sizes of 30 mg, 60 mg, 105 mg, and 150 mg.*

Criteria B - Feiba NF

Unless otherwise specified*, the initial authorization will be provided for 3 months and may be renewed every 12 months thereafter.

1. Diagnosis of Hemophilia A (congenital factor VIII deficiency) **OR** Hemophilia B (congenital factor IX deficiency) is confirmed by blood coagulation testing; **AND**
2. Documentation confirming patient has Factor VIII inhibitors (Hemophillia A) **OR** Factor IX inhibitors (Hemophilia B); **AND**
3. Feiba is used to treat at least one of the following:
    a. Control and prevention of acute episodic bleeding (episodic treatment of acute hemorrhage); **OR**
    b. Perioperative management (Authorization will be limited to 1 month*)
    c. Routine prophylaxis to prevent or reduce the frequency of episodic bleeding; **AND**
        i. Patient has at least two documented episodes of spontaneous bleeding into joints; **AND**
4. Patient has a documented trial and failure of Immune Tolerance Induction (ITI); **AND**
5. Patient has a documented trial and failure or contraindication to emicizumab-kxwh (Hemlibra) therapy. (**Hemophilia A ONLY**)

Feiba

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A / Hemophilia B with inhibitors	Joint hemorrhage 50—100 units/kg IV every 12 hours until pain and acute disabilities are improved Mucous Membrane Bleeding 50—100 units/kg IV every 6 hours for at least 1 day or until bleeding is resolved Soft tissue hemorrhage 100 units/kg IV every 12 hours until resolution of bleed Other severe hemorrhage 100 units/kg IV every 6—12 hours until resolution of bleed
Routine Prophylaxis Congenital Hemophilia A/ Hemophilia B with inhibitors	85 units/kg IV every other day
Perioperative management Congenital Hemophilia A / Hemophilia B with inhibitors	Preoperative 50—100 units/kg IV administered as a 1 time dose immediately prior to surgery Postoperative 50 – 100 units/kg IV administered every 6 – 12 hours postoperatively until resolution of bleed and healing is achieved

Criteria C - NovoSeven RT

Unless otherwise specified*, the initial authorization will be provided for 3 months and may be renewed for a period of 12 months thereafter.

1. Diagnosis of Hemophilia A (congenital factor VIII deficiency) **OR** Hemophilia B (congenital factor IX deficiency) is confirmed by blood coagulation testing; **AND**
   a. Documentation confirming patient has Factor VIII inhibitors (Hemophillia A) **OR** Factor IX inhibitors (Hemophilia B); **AND**
   b. NovoSeven RT is used to treat at least one of the following:
      - Control and prevention of acute episodic bleeding (episodic treatment of acute hemorrhage); **OR**
      - Perioperative management (Authorization will be limited to 1 month*); **OR**
      - Routine prophylaxis to prevent or reduce the frequency of bleeding episodes when the following criteria are also met:
        (1) Patient has at least two documented episodes of spontaneous bleeding into joints; **OR**
        (2) Patient has documented trial and failure of Immune Tolerance Induction (ITI); **AND**
        (3) Patient has documented trial and failure or contraindication to Hemlibra (Hemophilia A ONLY).

2. Diagnosis of Acquired Hemophilia Is confirmed by blood coagulation testing; AND
   a. NovoSeven RT is used to treat at least **one** of the following:
      - Control and prevention of acute episodic bleeding (episodic treatment of acute hemorrhage); **OR**
      - Perioperative management (Authorization will be limited to 1 month*)

3. Diagnosis of congenital Factor VII Deficiency is confirmed by blood coagulation testing; AND
   a. NovoSeven RT is used to treat at least one of the following:
      - Control and prevention of acute episodic bleeding (episodic treatment of acute hemorrhage); **OR**
      - Perioperative management (Authorization will be limited to 1 month*)

4. Diagnosis of Glanzmann's Thrombasthenia is confirmed by blood coagulation testing; AND
   a. NovoSeven RT is used to treat at least **one** of the following:
      - Control and prevention of acute episodic bleeding (episodic treatment of acute hemorrhage); **OR**
      - Perioperative management (Authorization will be limited to 1 month*); AND
   b. The use of platelet transfusions is known or suspected to be ineffective or contraindicated with or without antibodies to platelets.

NovoSeven RT

Indication	Dose
Control and prevention of bleeding: Congenital Hemophilia A or B with inhibitors	Hemostatic 90 mcg/kg every 2 hours, adjustable based on severity of bleeding until hemostasis is achieved, or until the treatment has been judged to be inadequate. Post-Hemostatic 90 mcg/kg every 3-6 hours after hemostasis is achieved for severe bleeds
Control and prevention of bleeding: Acquired Hemophilia	70-90 mcg/kg every 2-3 hours until hemostasis is achieved
Control and prevention of bleeding: Congenital Factor VII deficiency	15-30 mcg/kg every 4-6 hours until hemostasis is achieved
Control and prevention of bleeding: Glanzmann's Thrombasthenia	90 mcg/kg every 2-6 hours in severe bleeding episodes requiring systemic hemostatic therapy until hemostasis is achieved
Perioperative management Congenital Hemophilia A or B with inhibitors	Minor Initial: 90 mcg/kg immediately before surgery, repeat every 2 hours during surgery. Post-Op: 90 mcg/kg every 2 hours after surgery for 48 hours, then every 2-6 hours until healing has occurred. Major Initial: 90 mcg/kg immediately before surgery, repeat every 2 hours during surgery. Post-Op: 90 mcg/kg every 2 hours after surgery for 5 days, then every 4 hours or by continuous infusion, via pump, at 50 mcg/kg/hr until healing occurs.
Perioperative management Acquired Hemophilia	70-90 mcg/kg immediately before surgery and every 2-3 hours for the duration of surgery and until hemostasis is achieved
Perioperative management Congenital Factor VII deficiency	15-30 mcg/kg immediately before surgery and every 4-6 hours for the duration of surgery and until hemostasis is achieved
Perioperative management Glanzmann's Thrombasthenia	Initial: 90 mcg/kg immediately before surgery and repeat every 2 hours for the duration of the procedure. Post-Op: 90 mcg/kg every 2-6 hours to prevent post-operative bleeding

Criteria D – Sevenfact

Initial authorization will be provided for 3 months and may be renewed for 12 months thereafter.

1. Patient is 12 years of age or older; **AND**
2. Diagnosis of Hemophilia A (congenital Factor VIII Deficiency) **OR** Hemophilia B (congenital Factor IX Deficiency) has been confirmed by blood coagulation testing; **AND**
3. Confirmation patient has Hemophilia A (Factor VIII) inhibitors or Hemophilia B (Factor IX) inhibitors; **AND**
4. Sevenfact will be used for treatment and control of bleeding episodes (episodic treatment of acute hemorrhage); **AND**
5. Sevenfact will not be used for treatment of congenital factor VII deficiency.

Sevenfact

Indication	Dose
Control and treatment of bleeding: Congenital Hemophilia A or B with inhibitors	For Mild or Moderate Bleeds: – 75 mcg/kg repeated every 3 hours until hemostasis is achieved or – Initial dose of 225 mcg/kg. If hemostasis is not achieved within 9hours, additional 75 mcg/kg doses may be administered every 3 hours as needed to achieve hemostasis For Severe Bleeds: – 225 mcg/kg initially, followed if necessary 6 hours later with 75mcg/kg every 2 hours until hemostasis is achieved.

Criteria E - Alphanate, Humate-P

Unless otherwise specified*, the initial authorization will be provided for 3 months and may be renewed for 3-month intervals until PK testing is completed. Once PK testing is completed, renewal authorization will be provided for 12 months.

1. Diagnosis of Hemophilia A (congenital factor VIII deficiency) is confirmed by blood coagulation testing; **AND**
    a. Requested drug is used to treat at least **one** of the following:
        i. Control and prevention of acute bleeding episodes (episodic treatment of acute hemorrhage)
        ii. Perioperative management **(Alphanate ONLY)** (Authorization will be limited to 1 month*)
        iii. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
            1. Patient must have severe hemophilia A (factor VIII level of <1%); **OR**
            2. Patient has at least two documented episodes of spontaneous bleeding into joints
2. Diagnosis of von Willebrand disease (vWD) is confirmed by blood coagulation and von Willebrand factor testing; **AND**
    a. Requested drug is used to treat spontaneous and trauma-induced bleeding episodes **(Humate-P ONLY)**; **OR**
    b. Requested drug is used as surgical bleeding prophylaxis during major or minor procedures in patients with VWD in whom desmopressin (DDAVP) is either ineffective or contraindicated (Authorization will be limited to 1 month*).

    Note: Alphanate is **not** indicated for patients with severe vWD (Type 3) undergoing major surgery

Max Units (per dose and over time) [HCPCS Unit]:

- Alphanate: 55,200 billable units per 28 day supply
- Humate-P: 55,200 billable units per 28 day supply

Note: If the request is for routine prophylaxis, for Hemophilia A, and the requested dose exceeds the above dosing limits, a half-life study should be performed to determine the appropriate dose and dosing interval.

- For members with a BMI ≥ 30, a half-life study should be performed to determine the appropriate dose and dosing interval.
- For minimally treated patients (< 50 exposure days to factor products) previously receiving a different factor product, inhibitor testing is required at baseline, then at every comprehensive care visit (yearly for the mild and moderate patients, semi-annually for the severe patients)

Medical Policy

Alphanate

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	The expected in vivo peak increase in FVIII level expressed as IU/dL (or % normal) can be estimated using the following formulas: Dosage (units) = body weight (kg) x desired FVIII rise (IU/dL or % normal) x 0.5 (IU/kg per IU/dL) **OR** IU/dL (or %of normal) = [Total Dose (IU)/body weight (kg)] x 2 <u>Minor</u> FVIII:C levels should be brought to 30% of normal (15 IU FVIII/kg twice daily) until hemorrhage stops and healing has been achieved (1-2 days). <u>Moderate</u> FVIII:C levels should be brought to 50% (25 IU FVIII/kg twice daily) until healing has been achieved (2-7 days, on average). <u>Major</u> FVIII:C levels should be brought to 80-100% for at least 3-5 days (40-50 IU FVIII/kg twice daily). Following this treatment period, FVIII levels should be maintained at 50% (25 IU FVIII/kg twice daily) until healing has been achieved. Major hemorrhages may require treatment for up to 10 days. Intracranial hemorrhages may require prophylaxis therapy for up to 6 months.
Perioperative management Congenital Hemophilia A	Prior to surgery, the levels of FVIII:C should be brought to 80-100% of normal (40-50 IU FVIII/kg). For the next 7-10 days after surgery, or until healing has been achieved, the patient should be maintained at 60-100% FVIII levels (30-50 IU FVIII/kg twice daily).
Control and prevention of bleeding and perioperative management von Willebrand Disease (VWD)	The ratio of VWF:RCo to FVIII in Alphanate varies by lot, so with each new lot, check the IU VWF:RCo/Vial to ensure accurate dosing. <u>Minor</u> <u>*Pre-operative/pre-procedure dose (Target FVIII:C Activity – 40-50 IU/dL):*</u> Adults: 60 IU VWF:RCo/kg body weight. Pediatrics: 75 IU VWF:RCo/kg body weight. <u>*Maintenance dose (Target FVIII:C Activity – 40-50 IU/dL):*</u> Adults: 40 to 60 IU VWF:RCo/kg body weight at 8 to 12 hour intervals as clinically needed for 1-3 days. Pediatrics: 50 to 75 IU VWF:RCo/kg body weight at 8 to 12 hour intervals as clinically needed for 1-3 days. <u>Major</u> <u>*Pre-operative/pre-procedure dose (Target FVIII:C Activity – 100 IU/dL):*</u> Adults: 60 IU VWF:RCo/kg body weight. Pediatrics: 75 IU VWF:RCo/kg body weight. <u>*Maintenance dose (Target FVIII:C Activity – 100 IU/dL):*</u> Adults: 40 to 60 IU VWF:RCo/kg body weight at 8 to 12 hour intervals as clinically needed for at least 3-7 days. Pediatrics: 50 to 75 IU VWF:RCo/kg body weight at 8 to 12 hour intervals as clinically needed for at least 3-7 days.

Humate-P

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	One International Unit (IU) of Factor VIII (FVIII) activity per kg body weight will increase the circulating FVIII level by approximately 2.0 International Units (IU)/dL. Minor Loading dose 15 IU FVIII:C/kg to achieve a FVIII:C plasma level of approximately 30% of normal; one infusion may be sufficient. If needed, half of the loading dose may be given once or twice daily for 1-2 days. Moderate Loading dose 25 IU FVIII:C/kg to achieve a FVIII:C plasma level of approximately 50% of normal, followed by 15 IU FVIII:C/kg every 8-12 hours for the first 1-2 days to maintain the FVIII:C plasma level at 30% of normal. Continue the same dose once or twice daily for up to 7 days or until adequate wound healing is achieved. Major Initially 40-50 IU FVIII:C/kg, followed by 20-25 IU FVIII:C/kg every 8 hours to maintain the FVIII:C plasma level at 80-100% of normal for 7 days. Continue the same dose once or twice daily for another 7 days to maintain the FVIII:C level at 30-50% of normal.
Control and prevention of bleeding von Willebrand Disease (VWD)	Administer 40 to 80 International Units (IU) VWF:RCo (corresponding to 17 to 33 International Units (IU) FVIII in Humate-P) per kg body weight every 8 to 12 hours. Adjust the dosage based on the extent and location of bleeding. Administer repeat doses as long as needed based on monitoring of appropriate clinical and laboratory measures.
Perioperative management von Willebrand Disease (VWD)	**Loading Doses** Major *VWF:Rco Target Peak Plasma Level – 100 IU/dLTarget FVIII:C Activity – 80-100 IU/dL* ((Target peak plasma VWF:RCo level – baseline plasma VWF:RCo level) x Body wt (kg)) /IVR (in vivo recovery) If the IVR is not available, assume an IVR of 2.0 IU/dL per IU/kg and calculate the loading dose as follows: (100 – baseline plasma VWF:RCo) x BW (kg)/2.0 Minor *VWF:Rco Target Peak Plasma Level – 50-60 IU/dLTarget FVIII:C Activity – 40-50 IU/dL* ((Target peak plasma VWF:RCo level – baseline plasma VWF:RCo level) x Body wt (kg)) /IVR (in vivo recovery) Emergency *VWF:Rco Target Peak Plasma Level – 100 IU/dLTarget FVIII:C Activity – 80-100 IU/dL* Administer a dose of 50-60 IU VWF:RCo/kg body weight.**Maintenance Doses** The initial maintenance dose of Humate-P for the prevention of excessive bleeding during and after surgery should be half of the loading dose, irrespective of additional dosing required to meet FVIII:C targets. Subsequent maintenance doses should be based on the patient's VWF:RCo and FVIII levels.

Criteria F – Wilate

Unless otherwise specified*, the initial authorization will be provided for 3 months and may be renewed for 3-month intervals until PK testing is completed. Once PK testing is completed, renewal authorization will be provided for 12 months.

1. Diagnosis of Hemophilia A (congenital factor VIII deficiency) is confirmed by blood coagulation testing; **AND**
    a. Wilate is used to treat **one** of the following:
        i. Control and prevention of acute bleeding episodes (episodic treatment of acute hemorrhage)
        ii. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
            1. Patient must have severe hemophilia A (factor VIII level of <1%); **OR**
            2. Patient has at least two documented episodes of spontaneous bleeding into joints.
2. Diagnosis of von Willebrand disease (vWD) is confirmed by blood coagulation and von Willebrand factor testing; **AND**
    a. Wilate is used for perioperative management of bleeding (Authorization will be limited to 1 month*); **OR**
    b. Wilate is used to treat spontaneous and trauma-induced bleeding episodes in at least one of the following:
        i. Patients with severe vWD; **OR**
        ii. Patients with mild or moderate vWD in whom the use of desmopressin is known or suspected to be ineffective or contraindicated (Authorization will be limited to 1 month*).

Max Units (per dose and over time) [HCPCS Unit]:

- Wilate: 55,200 billable units per 28 day supply

Note: If the request is for routine prophylaxis, for Hemophilia A, and the requested dose exceeds the above dosing limits, a half-life study should be performed to determine the appropriate dose and dosing interval.

- For members with a BMI ≥ 30, a half-life study should be performed to determine the appropriate dose and dosing interval.
- For minimally treated patients (< 50 exposure days to factor products) previously receiving a different factor product, inhibitor testing is required at baseline, then at every comprehensive care visit (yearly for the mild and moderate patients, semi-annually for the severe patients)

Wilate

Indication	Dose
Control of bleeding episodes VWD	The ratio between VWF:RCo and FVIII activities in Wilate is approximately 1:1. The dosage should be adjusted according to the extent and location of the bleeding. Minor and Moderate Loading dose: 20-40 IU/kg; Maintenance dose: 20-30 IU/kg every 12-24 hours until VWF:Rco and FVIII activity trough levels > 30%, for up to 3 days. Major Loading dose: 40-60 IU/kg; Maintenance dose: 20-40 IU/kg every 12-24 hours until VWF:Rco and FVIII activity trough levels > 50%, for up to 5-7 days.
Perioperative managementof bleeding vWD	Minor Loading dose: 30-60 IU/kg; Maintenance dose: 15-30 IU/kg or half of the loading dose every 12-24 hours until wound healing achieved, up to 3 days. VWF:Rco trough levels > 30% and peak levels 50%. Major Loading dose: 40-60 IU/kg; Maintenance dose: 20-40 IU/kg or half the loading dose every 12-24 hours (at least 2 doses within the first 24 hours after the start of surgery)until wound healing achieved, up to 6 days or more. VWF:Rco trough levels > 50% and peak levels 100%.
Control and prevention of bleeding/ Routine Prophylaxis Congenital Hemophilia A	Calculation of the required dose of Factor VIII is based on the empirical finding that 1IU Factor VIII per kg body weight raises the plasma Factor VIII activity by approximately 2% of normal activity or 2 IU/dL when assessed using the one stage clotting assay. Use the following formula to determine the required dose: – *Required IU = body weight (kg) x desired Factor VIII rise (%) (IU/dL) x 0.5 (IU/kg per IU/dL)* – *Expected Factor VIII rise (% of normal) = 2 x administered IU / body weight (kg)* Dose and duration of therapy depend on the patient's weight, type and severity of hemorrhage, FVIII level, and presence of inhibitors. Titrate dose and frequency to the patient's clinical response, individual needs, severity of deficiency, severity of hemorrhage, desired FVIII level, and presence of inhibitor, and the patient's clinical condition. Patients may vary in their pharmacokinetic (e.g., half-life, in vivo recovery) and clinical responses to Wilate. **Routine Prophylaxis** A guide for dosing as routine prophylaxis to reduce the frequency of bleeding is provided below. Exact dosing should be defined by the patient's clinical status and response. **Dosing for Hemorrhages** A guide for dosing in the treatment of major and minor hemorrhages is provided below. Exact dosing should be defined by the patient's clinical status and response.

Hemorrhage Type	Recommended Dose (IU/kg)	Frequency	Frequency
Minor	30-40	Repeat every 12-24 hours	At least 1 day, until bleed stops
Moderate	30-40	Repeat every 12-24 hours	3+ days, until bleed stops
Major	35-50	Repeat every 12-24 hours	3+ days, until bleed stops
Life-Threatening	35-50	Repeat every 8-24 hours	Until threat has resolved

Criteria G – Advate, Adynovate, Eloctate, Helixate FS, Hemofil M, Koate/-DVI, Kogenate FS, Monoclate-P, NovoEight, Recombinate, Xyntha, Nuwiq, Afstyla, Kovaltry, Jivi, Esperoct

Unless otherwise specified*, the initial authorization will be provided for 3 months and may be renewed for 3-month intervals until PK testing is completed. Once PK testing is completed, renewal authorization will be provided for 12 months.

1. Diagnosis of Hemophilia A (congenital factor VIII deficiency) is confirmed by blood coagulation testing; **AND**
2. If request is for Jivi, patient must be 12 years of age and older; **AND**
3. Requested drug is used to treat at least **one** of the following:
    a. Control and prevention of acute bleeding episodes (episodic treatment of acute hemorrhage); **OR**
    b. Perioperative management (Authorization will be limited to 1 month*); **OR**
    c. Routine prophylaxis; **AND**
        i. Used to prevent or reduce the frequency of bleeding episodes; OR
        ii. Used to prevent or reduce the frequency of bleeding episodes and reduce the risk of joint damage in children with pre-existing joint damage (**Kogenate-FS ONLY); AND**
            1. Patient must have severe hemophilia A (factor III level of <1%); **OR**
            2. Patient has at least two documented episodes of spontaneous bleeding into joints

Max Units (per dose and over time) [HCPCS Unit]:

- Advate: 73,600 billable units per 28 day supply
- Adynovate: 36,800 billable units per 28 day supply
- Afstyla: 69,000 billable units per 28 day supply
- Eloctate: 40,250 billable units per 30 day supply
- Kogenate: 43,125 billable units per 30 day supply
- Kovaltry: 86,250 billable units per 30 day supply
- Novoeight: 82,800 billable units per 28 day supply
- Nuwiq: 86,250 billable units per 30 day supply
- Hemofil M: 55,200 billable units per 28 day supply
- Koate DVI: 55,200 billable units per 28 day supply
- Recombinate: 55,200 billable units per 28 day supply
- Xyntha/Xyntha Solofuse: 41,400 billable units per 28 day supply
- Jivi: 41,400 billable units per 30 day supply
- Esperoct: 40,250 units per 28 days

Note: If the request is for routine prophylaxis and the requested dose exceeds dosing limits listed above or if member BMI≥ 30, a half-life study should be performed to determine the appropriate dose and dosing interval.

- If the request is for Eloctate, Adynovate, Jivi, or Esperoct, the following criteria should be met:
    - Patient is not a suitable candidate for a standard non- extended half-life (EHL) factor VIII product.

- A half-life study must be scheduled to determine the appropriate dose and dosinginterval of the EHL product when initiated.
- Prior to switching to Eloctate, Adynovate, Jivi, or Esperoct a half-life study should also be performed on current non- EHL factor VIII product to ensure that a clinical benefit will be achieved.

- If the request exceeds any of the following dosing limits, documentation must be submitted specifying why the member is not a suitable candidate for Hemlibra and alternative EHL factor VIII products.
  - 50 IU/kg every 4 days (total weekly dose of 87.5 IU/kg) for Eloctate
  - 40 IU/kg twice weekly (total weekly dose of 80 IU/kg) for Adynovate
  - 60 IU/kg every 5 days (total weekly dose of 84 IU/kg) for Jivi
  - 50 IU/kg every 4 days (total weekly dose of 87.5 IU/kg) for Esperoct
- For minimally treated patients (< 50 exposure days to factor products) previously receiving a different factor product, inhibitor testing is required at baseline, then at every comprehensive care visit (yearly for the mild and moderate patients, semi-annually for the severe patients)

Advate

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	Dose (IU/kg) = desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg per IU/dL) Minor Circulating Factor VIII required (% of normal) (20-40%) = 10-20 IU/ kg -Repeat every 12-24 hours as needed (every 8 to 24 hours for patients under age of 6). Continue until the bleeding episode is resolved (as indicated by relief of pain) or healing is achieved (approximately 1 to 3 days). Moderate Circulating Factor VIII required (% of normal) (30-60%) = 15-30 IU/ kg - Repeat every 12-24 hours as needed (every 8 to 24 hours for patients under age of 6). Continue until the bleeding episode is resolved (as indicated by relief of pain) or healing is achieved (approximately 3 days or more). Major Circulating Factor VIII required (% of normal) (60-100%) = 30-50 IU/ kg - Repeat every 8-24 hours as needed (every 6 to 12 hours for patients under age of 6). Continue until the bleeding episode is resolved.
Routine Prophylaxis Congenital Hemophilia A	For prophylaxis regimen to prevent or reduce frequency of bleeding episodes, dose between 20 to 40 IU per kg every other day (3 to 4 times weekly). Alternatively, anevery third day dosing regimen targeted to maintain FVIII trough levels ≥ 1% maybe employed. Adjust dose based on the patient's clinical response.

Perioperative management Congenital Hemophilia A	Minor Circulating Factor VIII required (% of normal) (60-100%) = 30-50 IU/ kg –Single dose within one hour of the operation. Repeat after 12- 24 hours for optional additional dosing as needed to control bleeding. Major Circulating Factor VIII required (% of normal) (80-120%) = Preoperative: 40-60 IU/kg to achieve 100% activity. Followed by a repeat dose every 8-24 hours (every 6 to24 hours for patients under age of 6) postoperatively until healing is complete.

Adynovate

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	Dose (IU) = Body Weight (kg) x Desired factor VIII rise (IU/dL or % of normal) x 0.5(IU/kg per IU/dL) Minor Target Factor VIII level (IU/dL or % of normal) (20-40%) = 10-20 IU/kg -Repeat every 12-24 hours until the bleeding episode is resolved Moderate Target Factor VIII level (IU/dL or % of normal) (30-60%) = 15-30 IU/kg - Repeat every 12-24 hours until the bleeding episode is resolved Major Target Factor VIII level (IU/dL or % of normal) (60-100%) = 30-50 IU/kg - Repeat every 8-24 hours until the bleeding episode is resolved.
Perioperative management Congenital Hemophilia A	Minor Target Factor VIII required (% of normal) (60-100%) = 30-50 IU/ kg –Single dose within one hour of the operation. Repeat after 24 hours, if necessary, single dose or repeat as needed until bleeding is resolved. Major Target Factor VIII required (% of normal) (80-120%) (pre- and post- operative) = 40- 60 IU/ kg within 1 hour of the operation to achieve 100% activity. Repeat dose every 8-24 hours (every 6 to 24 hours for patients under age of 12) to maintain FVIII activity within the target range and continue until adequate wound healing.
Routine Prophylaxis Congenital Hemophilia A	Administer 40-50 IU per kg body weight 2 times per week in children and adults (12 years and older). Administer 55 IU per kg body weight 2 times per week in children (<12 years) with a maximum of 70 IU per kg. Adjust the dose based on the patient's clinical response.

Medical Policy

Afstyla

Indication	Dose
Treatment and control of bleeding Congenital Hemophilia A	Dose (IU) = Body Weight (kg) x Desired factor VIII rise (IU/dL or % of normal) x 0.5(IU/kg per IU/dL) Minor Target Factor VIII level (IU/dL or % of normal) 20-40% -Repeat every 12-24 hours until the bleeding episode is resolved. Moderate Target Factor VIII level (IU/dL or % of normal) 30-60%- Repeat every 12-24 hours until the bleeding episode is resolved. Major Target Factor VIII level (IU/dL or % of normal) 60-100%- Repeat every 8-24 hours until the bleeding episode is resolved.
Perioperative management Congenital Hemophilia A	Minor Target Factor VIII level (IU/dL or % of normal) 30-60%- Repeat every 24 hours, for at least one day, until the bleeding episode is resolved Major Target Factor VIII level (IU/dL or % of normal) 80-100%- Repeat every 8-24 hours until adequate wound healing, then continue for at least another 7 days to maintain a Factor VIII activity of 30-60% (IU/dL).
Routine Prophylaxis Congenital Hemophilia A	Adults and adolescents *(≥12yrs old)*: Administer 20-50 IU per kg body weight 2 to 3times per week. Adjust the dose based on the patient's clinical response. Children *(<12 yrs old):* Administer 30-50 IU per kg body weight 2 to 3 times per week. Adjust the dose based on the patient's clinical response.

Medical Policy

Eloctate

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	Dose (IU/kg) = Desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg perIU/dL) Minor and Moderate Circulating Factor VIII required (% of normal) (40-60%) = 20-30 IU/ kg -Repeat every 24-48 hours as needed (every 12 to 24 hours for patients under age of 6). Continue until the bleeding episode is resolved. Major Circulating Factor VIII required (% of normal) (80-100%) = 40-50 IU/ kg - Repeat every 12-24 hours as needed (every 8 to 24 hours for patients under age of 6). Continue until the bleeding episode is resolved (approximately 7-10 days).
Routine Prophylaxis Congenital Hemophilia A	Adults: The recommended starting regimen is 50 IU/kg administered every 4 days. The regimen may be adjusted based on patient response with dosing in the range of 25-65 IU/kg at 3-5 day intervals. Children < 6 years of age: The recommended starting regimen is 50 IU/kg administered twice weekly. The regimen may be adjusted based on patient response with dosing in the range of 25-65 IU/kg at 3-5 day intervals. More frequent or higher doses up to 80 IU/kg may be required.
Perioperative management Congenital Hemophilia A	Minor Circulating Factor VIII required (% of normal) (50-80%) = 25-40 IU/ kg -Repeat every 24 hours as needed (every 12 to 24 hours for patients under age of 6). Continue at least 1 day until healing is achieved. Major Circulating Factor VIII required (% of normal) (80-120%) = Preoperative: 40-60 IU/kg – Followed by a repeat dose of 40-50 IU/kg after 8-24 hours (6 to 24 hours for patients under age of 6). Continue every 24 hours until adequate wound healing; then continue therapy for at least 7 days to maintain FVII activity within the target range.

Medical Policy

Esperoct

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td>Control and prevention of bleeding Congenital Hemophilia A</td><td>One IU of Factor VIII activity corresponds to the quantity of Factor VIII in one milliliter of normal human plasma. The calculation of the required dosage of Factor VIII is based on the empirical finding that one IU of Factor VIII per kg body weight raises the plasma Factor VIII activity by two IU/dL.
To achieve a specific target Factor VIII activity level, use the following formula: Dosage (IU) = Body Weight (kg) × Desired Factor VIII Increase (IU/dL or % normal) × 0.5 ; OR
<table>
<tr><th>Type of bleeding</th><th>Adolescents/Adults ≥12 years Dose (IU/kg)</th><th>Children <12 years Dose (IU/kg)</th><th>Additional doses</th></tr>
<tr><td>Minor
Early hemarthrosis, mild muscle bleeding, or oral bleeding</td><td>40</td><td>65</td><td>One dose should be sufficient</td></tr>
<tr><td>Moderate
More extensive hemarthrosis, musclebleeding, or hematoma</td><td>40</td><td>65</td><td>An additional dose may be administered after 24 hours</td></tr>
<tr><td>Major
Life- or limb-threatening hemorrhages, gastro- intestinal bleeding, intracranial,intra-abdominal or intrathoracic bleeding, fractures</td><td>50</td><td>65</td><td>Additional dose(s) may be administered approximately every 24 hours</td></tr>
</table></td></tr>
<tr><td>Routine Prophylaxis Congenital Hemophilia A</td><td>– Adults and adolescents (≥ 12 years): The recommended starting dose is 50 IU per kg body weight every 4 days. This regimen may be individually adjusted to less or more frequent dosing based on bleeding episodes.
– Children (< 12 years): A dose of 65 IU per kg body weight twice weekly. This regimen may be individually adjusted to less or more frequent dosing based on bleeding episodes.</td></tr>
<tr><td>Perioperative management Congenital Hemophilia A</td><td>To achieve a specific target Factor VIII activity level, use the following formula: Dosage (IU) = BodyWeight (kg) × Desired Factor VIII Increase (IU/dL or % normal) × 0.5 ; OR
<table>
<tr><th>Type of surgery</th><th>Adolescents/Adults ≥12 years Dose (IU/kg)</th><th>Children <12 years Dose (IU/kg)</th><th>Additional doses</th></tr>
<tr><td>Minor
Including tooth extraction</td><td>50</td><td>65</td><td>Additional dose(s) can be given after 24 hours if necessary</td></tr>
<tr><td>Major Intracranial, intra-abdominal, intrathoracic, or joint replacement surgery</td><td>50</td><td>65</td><td>Additional doses can be given every 24 hours for the first week and then approximately every 48 hours until wound healing has occurred</td></tr>
</table></td></tr>
</table>

Medical Policy

Hemofil M

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	Dose (IU/kg) = Desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg perIU/dL) Early hemarthrosis or muscle bleed or oral bleed Circulating Factor VIII required (% of normal) (20-40%) = - Begin infusion every 12 to 24 hours for one-three days until the bleeding episode as indicated by pain is resolved or healing is achieved. More extensive hemarthrosis, muscle bleed, or hematoma Circulating Factor VIII required (% of normal) (30-60%) = Repeat every 12-24hours for usually three days or more until pain and disability are resolved. Life threatening bleeds such as head injury, throat bleed, severe abdominal pain Circulating Factor VIII Required (% of normal) (60-100%) = Repeat every 8-24hours until the bleeding threat is resolved.
Perioperative management Congenital Hemophilia A	Minor Circulating Factor VIII required (% of normal) (60-80%) A single infusion plus oral antifibrinolytic therapy within one hour is sufficient in approximately 70% of cases. Major Circulating Factor VIII required (% of normal) (80-100% pre- and post-operative):Repeat dose every 8-24 hours depending on state of healing.

Jivi

Indication	Dose
Control of bleeding episodes Congenital Hemophilia A	Dose (IU/kg) = Desired factor VIII rise (IU/dL or % of normal) x reciprocal of expected recovery (or observed recovery, if available) (e.g., 0.5 for a recovery of 2IU/dL per IU/kg) Minor Circulating Factor VIII required (% of normal) (20-40%) – 10-20IU/kg repeat dose every 24-48 hours until bleed resolves Moderate Circulating Factor VIII required (% of normal) (30-60%) – 15-30IU/kg repeat dose every 24-48 hours until bleed resolves Major Circulating Factor VIII Required (% of normal) (60-100%) – 30-50IU/kg repeat dose every 8-24 hours until bleed resolves

Perioperative management Congenital Hemophilia A	Minor Circulating Factor VIII required (% of normal) (30-60%) – 15-30IU/kg repeat dose every 24 hours for at least 1 day until healing is achieved Major Circulating Factor VIII required (% of normal) (80-100%) – 40-50IU/kg repeat dose every 12-24 hours until adequate wound healing is complete, then continue therapy for at least another 7 days to maintain Factor VIII activity of 30–60% (IU/dL)
Routine Prophylaxis Congenital Hemophilia A	The recommended initial regimen is 30–40 IU/kg twice weekly. Based on the bleeding episodes, the regimen may be adjusted to 45–60 IU/kg every 5 days or may be further individually adjusted to less or more frequent dosing.

Koate DVI

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	Dose (IU/kg) = Desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg perIU/dL) Mild Circulating Factor VIII required (% of normal) (20%) = 10 IU/kg- Therapy need not be repeated unless there is evidence of further bleeding. Moderate Circulating Factor VIII required (% of normal) (30-50%) = 15-25 IU/kg - If further therapy is required, repeated doses of 10-15 IU per kg every 8-12 hours may be given. Severe Circulating Factor VIII Required (% of normal) (80-100%) =40-50 IU/kg – followed by a maintenance dose of 20-25 IU per kg every 8-12 hours.
Routine prophylaxis Hemophilia A **§**	25-40 IU/kg three times weekly or 15-30 IU/kg three times weekly. Adjust dosing regimen based on individual response.
Perioperative management Congenital Hemophilia A	For major surgical procedures, the Factor VIII level should be raised to approximately 100% by giving a preoperative dose of 50 IU/kg. The Factor VIIIlevel should be checked to assure that the expected level is achieved before the patient goes to surgery. In order to maintain hemostatic levels, repeat infusions may be necessary every 6 to 12 hours initially, and for a total of 10 to 14 days until healing is complete. The intensity of Factor VIII replacement therapy required depends on the type of surgery and postoperative regimen employed. For minor surgical procedures, less intensive treatment schedules may provide adequate hemostasis.

Medical Policy

Kogenate FS

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	Dose (IU/kg) = Desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg perIU/dL) Minor Circulating Factor VIII required (% of normal) (20-40%) = 10-20 IU/ kg -Repeat dose if there is evidence of further bleeding and continue until the bleeding episode is resolved. Moderate Circulating Factor VIII required (% of normal) (30-60%) = 15-30 IU/ kg - Repeat every 12-24 hours as needed. Continue until the bleeding episode is resolved. Major Circulating Factor VIII Required (% of normal) (80-100%) = Initial: 40-50 IU/ kg; Repeat 20-25 IU/kg every 8-12 hours until the bleeding episode is resolved.
Routine Prophylaxis Congenital Hemophilia A	Routine Prophylaxis in Adults 25 units per kg of body weight three times per week. Routine Prophylaxis in Children 25 IU/kg of body weight every other day.
Perioperative management Congenital Hemophilia A	Minor Circulating Factor VIII required (% of normal) (30-60%) = 15-30 IU/ kg – Repeat every 12- 24 hours until bleeding is resolved. Major Circulating Factor VIII required (% of normal) (100%) = Preoperative: 50 IU/ kg to achieve 100% activity. Followed by a repeat dose every 6-12 hours to keep FVIII activity in desired range. Continue until healing is complete.

Medical Policy

Kovaltry

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	• Required dose (IU) = body weight (kg) x desired Factor VIII rise (% of normal or IU/dL) x reciprocal of expected/observed recovery (e.g., 0.5 for a recovery of2 IU/dL per IU/kg) • Estimated Increment of Factor VIII (IU/dL or % of normal) = [Total Dose(IU)/body weight (kg)] x 2 (IU/dL per IU/kg) <u>Minor</u> (Early hemarthrosis, minor muscle, oral bleeds) Factor VIII level required (IU/dL or % of normal): 20-40 – repeat every 12-24 hours at least 1 day, until bleeding episode as indicated by pain is resolved orhealing is achieved. <u>Moderate</u> (More extensive hemarthrosis, muscle bleeding, or hematoma) Factor VIII level required (IU/dL or % of normal): 30-60 – repeat every 12-24hours for 3 to 4 days or more until pain and acute disability are resolved. <u>Major</u> (Intracranial, intra-abdominal or intrathoracic hemorrhages, gastrointestinal bleeding, central nervous system bleeding, bleeding in the retropharyngeal or retroperitoneal spaces, or iliopsoas sheath, life or limb threatening hemorrhage) Factor VIII level required (IU/dL or % of normal): 60-100 – repeat every 8-24hours until bleeding is resolved.
Routine Prophylaxis Congenital Hemophilia A	Individualize the patient's dose based on clinical response: • Adults and adolescents: 20 to 40 IU of KOVALTRY per kg of body weight two or three times per week. • Children ≤12 years old: 25 to 50 IU of KOVALTRY per kg body weight twice weekly, three times weekly, or every other day according to individual requirements
Perioperative management Congenital Hemophilia A	<u>Minor</u> (Such as tooth extraction) Factor VIII level required (IU/dL or % of normal): 30-60 (pre- and post-operative) – repeat every 24 hours at least 1 day until healing is achieved. <u>Major</u> (Such as intracranial, intraabdominal, intrathoracic, or joint replacement surgery) Factor VIII level required (IU/dL or % of normal): 80-100 – repeat every 8-24 hours until adequate wound healing is complete, then continue therapy for at least another 7 days to maintain Factor VIII activity of 30-60% (IU/dL).

Novoeight

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	Dose (IU/kg) = Desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg perIU/dL) Minor Circulating Factor VIII required (% of normal) (20-40%), every 12 – 24 hours for at least 1 day until the bleeding episode is resolved Moderate Circulating Factor VIII required (% of normal) (30-60%), every 12 – 24 hours until pain and acute disability are resolved, approximately 3-4 days Major Circulating Factor VIII Required (% of normal) (60-100%), every 8 – 24 hours until resolution of bleed, approximately 7-10 days.
Perioperative management Hemophilia A	Dose (IU/kg) = Desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg perIU/dL) Minor Circulating Factor VIII required (% of normal) (30-60%) every 24 hours for at least 1 day until healing is achieved. Major Circulating Factor VIII required (% of normal) (80-100%) every 8 – 24 hours until adequate wound healing, then continue therapy for at least 7 days to maintain a factor VIII activity of 30 – 60% (IU/dL)
Prophylaxis to prevent or reduce the frequency of bleeding episodes Hemophilia A	Adults and adolescents (≥12 yrs): 20-50 IU/kg three times weekly **OR** 20-40 IU/kg every other day Children (<12 yrs): 25-60 IU/kg three times weekly **OR** 25-50 IU/kg every other day

Medical Policy

Nuwiq

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	Dose Required IU = body weight (kg) x desired Factor VIII rise (%) (IU/dL) x 0.5 (IU/kgper IU/dL) Expected Factor VIII rise (% of normal) = 2 x administered IU/body weight (kg) Minor Required peak post-infusion Factor VIII activity (% of normal or IU/dL): 20-40every 12 – 24 hours for at least 1 day until the bleeding episode is resolved Moderate to Major Required peak post-infusion Factor VIII activity (% of normal or IU/dL): 30-60every 12 – 24 hours for 3-4 days or more until the bleeding episode is resolved Life-threatening Required peak post-infusion Factor VIII activity (% of normal or IU/dL): 60-100every 8 – 24 hours bleeding risk is resolved
Routine Prophylaxis Congenital Hemophilia A	Dose Required IU = body weight (kg) x desired Factor VIII rise (%) (IU/dL) x 0.5 (IU/kgper IU/dL) Expected Factor VIII rise (% of normal) = 2 x administered IU/body weight (kg)Adolescents (12-17 years) and adults 30 – 40 IU/kg every other day Children (2-11 years) 30 – 50 IU/kg every other day or three times per week
Perioperative management Congenital Hemophilia A	Dose Required IU = body weight (kg) x desired Factor VIII rise (%) (IU/dL) x 0.5 (IU/kgper IU/dL) Expected Factor VIII rise (% of normal) = 2 x administered IU/body weight (kg)Minor Required peak post-infusion Factor VIII activity (% of normal or IU/dL): 30-60 (pre- and post-operative) every 24 hours for at least 1 day until healing is achieved Major Required peak post-infusion Factor VIII activity (% of normal or IU/dL): 80-100(pre- and post-operative) every 8 - 24 hours until adequate wound healing, then continue therapy for at least another 7 days to maintain Factor VIII activity of 30% to 60% (IU/dL)

Recombinate

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	Dose (IU/kg) = Desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg perIU/dL) Early hemarthrosis or muscle bleed or oral bleed Circulating Factor VIII required (% of normal) (20-40%) - Begin infusion every 12 to 24 hours for one-three days until the bleeding episode as indicated by pain is resolved or healing is achieved. More extensive hemarthrosis, muscle bleed, or hematoma Circulating Factor VIII required (% of normal) (30-60%) - Repeat every 12-24hours for usually three days or more until pain and disability are resolved. Life threatening bleeds such as head injury, throat bleed, severe abdominal pain Circulating Factor VIII Required (% of normal) (60-100%) - Repeat every 8-24 hours until the bleeding threat is resolved.
Routine prophylaxis Hemophilia A **§**	25-40 IU/kg three times weekly or 15-30 IU/kg three times weekly. Adjust dosing regimen based on individual response.
Perioperative management Congenital Hemophilia A	Minor Circulating Factor VIII required (% of normal) (60-80%) - A single infusion plus oral antifibrinolytic therapy within one hour is sufficient in approximately 70%of cases. Major Circulating Factor VIII required (% of normal) (80-100% pre- and post- operative) - Repeat dose every 8-24 hours depending on state of healing.

Xyntha/Xyntha Solofuse

Indication	Dose
Control and prevention of bleeding Congenital Hemophilia A	Dose (IU/kg) = Desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg perIU/dL) Minor Circulating Factor VIII required (% of normal) (20-40%) - Repeat dose every 12-24 hours for least 1 day, depending upon the severity of the bleeding episode. Moderate Circulating Factor VIII required (% of normal) (30-60%) - Repeat every 12-24hours as needed. Continue for 3-4 days or until adequate local hemostasis is achieved. Major Circulating Factor VIII Required (% of normal) (60-100%) - Repeat every 8-24hours until bleeding is resolved.

Perioperative management Congenital Hemophilia A	Minor Circulating Factor VIII required (% of normal) (30-60%) - Repeat every 12- 24 hours. Continue for 3-4 days or until adequate local hemostasis is achieved. For tooth extraction, a single infusion plus oral antifibrinolytic therapy within 1 hour may be sufficient. Major Circulating Factor VIII required (% of normal) (60-100%) - Repeat every 8-24 hours. Continue until threat is resolved, or in the case of surgery, until adequate local hemostasis and wound healing are achieved.
Routine prophylaxis Hemophilia A	Adults and adolescents (≥12 years): The recommended starting regimen is 30IU/kg of Xyntha administered 3 times weekly. Children (<12 years): The recommended starting regimen is 25 IU/kg of Xyntha administered every other day. More frequent or higher doses may be required in children <12 years of age to account for the higher clearance in this age group. Note: Adjust the dosing regimen (dose or frequency) based on the patient's clinical response.

§ Utrecht and/or Malmö protocols used as basis for dosing

Criteria H – Obizur

Initial authorization will be provided for 3 months and may be renewed for 3-month intervals until PK testing is completed. Once PK testing is completed, renewal authorization will be provided for 12 months.

1. Diagnosis of acquired Hemophilia A (Factor VIII deficiency) is confirmed by blood coagulation testing; **AND**
2. Obizur is used to treat acute episodic bleeding (episodic treatment of acute hemorrhage); **AND**
3. Obizur will NOT to be used for congenital hemophilia A or vWD.

Max Units (per dose and over time) [HCPCS Unit]:

- Obizur: 115,000 billable units per 90 day supply

Note: For members with a BMI ≥ 30, a half-life study should be performed to determine the appropriate dose and dosing interval.

- For minimally treated patients (< 50 exposure days to factor products) previously receiving a different factor product, inhibitor testing is required at baseline, then at every comprehensivecare visit (yearly for the mild and moderate patients, semi-annually for the severe patients)

Obizur

Indication	Dose
Bleeding episodes Acquired HemophiliaA	Minor and Moderate Loading dose: 200IU/kg; Maintenance dose: Titrate to maintain recommended FVIII trough levels at 50-100 IU/dL every 4 to 12 hours Major Loading dose: 200 IU/kg; Maintenance dose: Titrate to maintain recommended FVIII trough levels at 100-200 (to treat an acute bleed), then 50-100 IU/dL (after acute bleed is controlled) every 4 to 12 hours

Criteria I – Tretten

Initial authorization will be provided for 3 months and may be renewed every 12 months thereafter.

1. Diagnosis of congenital Factor XIII **A-subunit** deficiency is confirmed by blood coagulation testing; **AND**
2. Tretten is used for routine prophylaxis of bleeding.

Tretten

Indication	Dose
Routine prophylaxis for bleeding Congenital factorXIII A-subunit deficiency	35 international units (IU) per kilogram body weight once monthly to achieve a target trough level of FXIII activity at or above 10% using a validated assay.

Criteria J – Corifact

Unless otherwise specified*, the initial authorization will be provided for 3 months and may be renewed for a period of 12 month thereafter.

- Diagnosis of Congenital Factor XIII deficiency is confirmed by blood coagulation testing; **AND**
- Corifact is used for one of the following:
    a. Routine prophylactic treatment; **OR**
    b. Perioperative management of surgical bleeding (Authorization will be limited to 1 month*)

Corifact

Indication	Dose
Routine prophylaxisfor bleeding Congenital factor XIII deficiency	40 International Units (IU) per kg body weight at a rate not to exceed 4 mL per minute, given every 28 days. Adjust dose ±5 IU per kg to maintain 5% to 20% trough level of FXIII activity.
Perioperative management Congenital factorXIII deficiency	40 International Units (IU) per kg body weight at a rate not to exceed 4 mL per minute. Dosing should be individualized based on the patient's FXIII activity level, type of surgery, and clinical response. Monitor patient's FXIII activity levels during and after surgery. Dose adjustment will need to be made depending on when last prophylactic dose was given. ▪ Within 7 days – Additional dose may not be needed ▪ 8-21 days - Additional partial or full dose may be needed based on FXIII activity level ▪ 21-28 days - Full prophylactic dose

Criteria K – AlphaNine SD, Mononine, Profilnine SD, Alprolix, Bebulin, BeneFIX, Idelvion, Ixinity, Rebinyn, Rixubis

Unless otherwise specified*, the initial authorization will be provided for 3 months and may be renewed for 3-month intervals until PK testing is completed. Once PK testing is completed, renewal authorization will be provided for 12 months.

1. Diagnosis of Hemophilia B (congenital factor IX deficiency) is confirmed by blood coagulation testing; **AND**
2. Requested drug is used to treat at least **one** of the following:
    a. On demand treatment and control of bleeding episodes
        i. For Ixinity, patient is 12 years of age or older
    b. Perioperative management (**EXCLUDING AlphaNine SD, Mononine, Profilnine SD)** (Authorization will be limited to 1 month*)
        i. For Ixinity, patient is 12 years of age or older
    c. Routine prophylaxis to prevent or reduce frequency of bleeding episodes (**EXCLUDING AlphaNine SD, Rebinyn**); **AND**
        i. Patient must have severe hemophilia B (factor IX level of <1%); **OR**
        ii. Patient has at least two documented episodes of spontaneous bleeding into joints
3. Requested drug is not used for induction of immune tolerance in members with Hemophilia B (applicable to **Alprolix, BeneFIX, Idelvion, Ixinity, Rebinyn, Rixubis ONLY**)

Max Units (per dose and over time) [HCPCS Unit]:

- Alprolix, Rebinyn: 23,000 billable units per 28-day supply
- Idelvion: 25,300 billable units per 28-day supply
- AlphaNine SD, Ixinity, Profilnine, Mononine: 36,800 billable units per 28-day supply
- BeneFIX: 46,000 billable units per 28-day supply
- Rixubis: 73,600 billable units per 28-day supply

Note: If the request is for prophylaxis and the requested dose exceeds dosing limits listed above, a half-life study should be performed to determine the appropriate dose and dosing interval.

- If the request is for Alprolix, Idelvion, or Rebinyn, a half-life study should be performed to determine the appropriate dose and dosing interval.
    - For Alprolix, 50 IU/kg every 7 days is the preferred dosing regimen. To obtain 100 IU every 10 days, a half-life study must be submitted showing a significant clinical benefit over 50 IU/kg every 7 days.
    - Prior to switching to Alprolix, Idelvion, or Rebinyn, a half-life study should also be performed on current non- EHL factor IX product to ensure that a clinical benefit will be achieved.
- For members with a BMI ≥ 30, a half-life study should be performed to determine the appropriate dose and dosing interval.
- For minimally treated patients (< 50 exposure days to factor products) previously receiving a different factor product, inhibitor testing is required at baseline, then at every comprehensive care visit (yearly for the mild and moderate patients, semi-annually for the severe patients)

Medical Policy

Alprolix

Indication	Dose
Control and prevention of bleeding episodes Hemophilia B	One unit per kilogram body weight increases the circulating Factor IX level by 1%(IU/dL). Estimate the required dose or the expected in vivo peak increase in Factor IX level expressed as IU/dL (or % of normal) using the following: IU/dL (or % of normal) = [Total Dose (IU)/Body Weight (kg)] x Recovery (IU/dL per IU/kg)Minor and Moderate Circulating Factor IX required (% of normal) = 30-60 IU/dL - Repeat every 48hours prn Major Circulating Factor IX required (% of normal) = 80-100 IU/dL - Consider repeat dose after 6-10 hours, then every 24 hours for 3 days, then every 48 hours until healing achieved.
Perioperative management Hemophilia B	Minor Circulating Factor IX required (% of normal) = 50-80 IU/dL - Repeat every 24-48hours as needed, until bleeding stops and healing is achieved. Major Circulating Factor IX required (% of normal) = 60-100 IU/dL (initial level) - Consider repeat dose after 6-10 hours, then every 24 hours for 3 days, then every48 hours until bleeding stops and healing achieved.
Routine prophylaxis Hemophilia B	Adults and adolescents ≥12 years of age: 50 IU/kg once weekly or 100 IU/kg once every 10 days. Adjust dosing regimen based on individual response. Children <12 years of age Start with 60 IU/kg once weekly. Adjust dosing regimen based on individual response. More frequent or higher doses may be needed in children <12 years of age, especially in children <6 years of age.

AlphaNine SD

Indication	Dose
Control and prevention of bleeding episodes Hemophilia B	One unit per kilogram body weight increases the circulating Factor IX level by 1%(IU/dL). Number of Factor IX IU required = body wt (kg) x Desired increase in Plasma Factor IX(percent) x 1.0 IU/kg Minor: Circulating Factor IX required (20 – 30 % of normal) = 20-30 IU/kg - Repeat every12 hours as needed for 1-2 days Moderate: Circulating Factor IX required (25 - 50% of normal) = 25-50 IU/kg - Repeat every12 hours as needed for 2-7 days Major Circulating Factor IX required (50% of normal) = 30-50 IU/kg - Repeat dose every 12 hours as needed for 3-5 days. Following this treatment period, FIX levels should be maintained at 20% (20 IU FIX/kg/twice daily) until healing has been achieved. Major hemorrhages may require treatment for up to 10 days
Routine prophylaxis Hemophilia B §	25-40 IU/kg two times weekly or 15-30 IU/kg two times weekly. Adjust dosing regimen based on individual response.

Perioperative management Hemophilia B	Prior to surgery, FIX should be brought to 50-100% of normal (50-100 IU/kg repeat every 12 hours). For the next 7 to 10 days, or until healing has been achieved, the patient should be maintained at 50-100%FIX levels (50-100 IU/kg every 12 hours).

Mononine

Indication	Dose
Control and prevention of bleeding episodes and perioperative management Hemophilia B	One unit per kilogram body weight increases the circulating Factor IX level by 1%(IU/dL). Estimate the required dose with the following formula: Number of Factor IX IU required (IU) = Body Weight (in kg) x desired Factor IX increase (% or IU/dL normal) x 1.0 IU/kg [per IU/dL] Minor Spontaneous Hemorrhage Prophylaxis Circulating Factor IX required (% of normal)(15-25%) = up to 20-30 IU/kg for one dose. Repeat in 24 hours if necessary. Major Trauma or Surgery Circulating Factor IX required (% of normal)(25-50%) = up to 75 IU/kg dosed every 18-30 hours depending on T1/2 and measured Factor IX levels. Continue forup to 10 days depending upon nature of insult.

BeneFIX

Indication	Dose
Control and prevention of bleeding episodes and perioperative management of Hemophilia B	One IU per kilogram body weight increases the circulating Factor IX level by 0.8 ± 0.2 IU/dL in adolescents/adults (≥12 years) and 0.7 ± 0.3 IU/dL in children (< 12years). Initial dose: Number of Factor IX IU required (IU) = body weight (kg) x desired factor IX increase (% of normal or IU/dL) x reciprocal of observed recovery (IU/kgper IU/dL) • Minor hemorrhage: Circulating Factor IX activity required [% of normal or(IU/dL)]: 20-30, dosed every 12 to 24 hours for 1 to 2 days. • Moderate hemorrhage: Circulating Factor IX activity required [% of normal or(IU/dL)]: 25-50, dosed every 12 to 24 hours for 2 to 7 days until bleeding stops and healing begins. • Major hemorrhage: Circulating Factor IX activity required [% of normal or(IU/dL)]: 50-100, dosed every 12 to 24 hours for 7 to 10 days. *Dosage and duration of treatment with BeneFIX depend on the severity of the factor IX deficiency, the location and extent of bleeding, and the patient's clinical condition, age and recovery of factor IX.*
Routine prophylaxisto reduce the frequency of bleeding episodes	Patients ≥ 16 years of age: • 100 IU/kg once weekly • Adjust the dosing regimen (dose or frequency) based on the patient's clinical response.

Medical Policy

Rebinyn

Indication	Dose
On-demand treatment and controlof bleeding episodes Congenital Hemophilia B	Minor and Moderate 40 IU/kg of actual body weight. A single dose should be sufficient for minor and moderate bleeds. Additional doses of 40 IU/kg can be given. Major 80 IU/kg of actual body weight. Additional doses of 40 IU/kg can be given.
Perioperative management of bleeding Congenital Hemophilia B	Minor Pre-op: 40 IU/kg of actual body weight (single pre-op dose should be sufficient)Post-op: Additional doses can be given if required Major Pre-op: 80 IU/kg of actual body weight Peri/Post-op: 40 IU/kg of actual body weight. As clinically needed for the perioperative management of bleeding, repeated doses of 40 IU/kg (in 1-3 day intervals) within the first week after major surgery may be administered. Due to the long half-life, the frequency of dosing in the post-surgical setting may be

Profilnine

Indication	Dose
Control and prevention of bleeding episodes Hemophilia B	Patients ≥ 18 years of age: One unit per kilogram body weight increases the circulating Factor IX level by 1% (IU/dL). Number of Factor IX IU required = body wt (kg) x Desired increase in Plasma Factor IX(percent) x 1.0 IU/kg Minor to Moderate Single dose of product sufficient to raise plasma Factor IX levels to 20-30% of normal. 20-30 IU/kg every 16-24 hours until hemorrhage stops and healing is achieved. For minor, may repeat for 1-2 days, for moderate, may repeat for 2-7days. Major Single dose of product sufficient to raise plasma Factor IX levels to 30-50% of normal. 30-50 IU/kg every 16-24 hours for up to 3-10 days. Following this treatment period, maintain Factor IX levels at 20% of normal until healing has been achieved.
Routine prophylaxis Hemophilia B **§**	Patients ≥ 18 years of age: 25-40 IU/kg two times weekly or 15-30 IU/kg two times weekly. Adjust dosing regimen based on individual response.

Perioperative management Hemophilia B	Patients ≥ 18 years of age: Surgery associated with bleeding in Factor IX deficient patients require Factor IX levels of 30-50% of normal. For dental extractions, the Factor IX level should be raised to 50% of normal immediately prior to procedure. 30-50 IU/kg every 16-24 hours for 7-10 days until healing is achieved. Maintain Factor IX levels at 30- 50% of normal until healing has been achieved.

Idelvion

Indication	Indication
Control and prevention of bleeding episodes	• One IU of IDELVION per kg body weight is expected to increase the circulating activity of Factor IX as follows: ○ Adolescents and adults: 1.3 IU/dL per IU/kg ○ Pediatrics (<12 years): 1 IU/dL per IU/kg • Dosage and duration of treatment with IDELVION depends on the severity of the Factor IX deficiency, the location and extent of bleeding, and the patient's clinical condition, age and recovery of Factor IX. • Determine the initial dose using the following formula: ○ Required Dose (IU) = Body Weight (kg) x Desired Factor IX rise (% of normal or IU/dL) x (reciprocal of recovery (IU/kg per IU/dL)) • Adjust dose based on the patient's clinical condition and response. Minor/Moderate Desired peak Factor IX Level (% of normal or IU/dL): 30-60, dosed every 48-72hours for at least 1 day until healing is achieved Major Desired peak Factor IX Level (% of normal or IU/dL): 60-100, dosed every 48-72hours for 7-14 days until healing is achieved. Maintenance dose is weekly.
Perioperative management Hemophilia B	Minor Desired peak Factor IX Level (% of normal or IU/dL): 50-80, dosed every 48-72hours for at least 1 day until healing is achieved Major Desired peak Factor IX Level (% of normal or IU/dL): 60-100, dosed every 48-72hours for 7-14 days until healing is achieved. Repeat dose every 48-72 hours for the first week or until healing is achieved. Maintenance dose is once or twice weekly.
Routine prophylaxis Hemophilia B	Patients ≥12 years of age: 25-40 IU/kg body weight every 7 days. Patients who are well-controlled on this regimen may be switched to a 14-day interval at 50-75 IU/kg body weight. Patients <12 years of age: 40-55 IU/kg body weight every 7 days.

Medical Policy

Ixinity

Indication	Dose
Control and prevention of bleeding episodesCongenital Hemophilia B	One IU per kg body weight increases the circulating activity of factor IX by 0.98IU/dL. Patients ≥ 12 years of age: • Initial dose: Required factor IX units (IU) = body weight (kg) x desired factor IX increase (% of normal of IU/dL) x reciprocal of observed recovery (IU/kg perIU/dL) • Maintenance dose: Depends upon the type of bleed or surgery, clinical response, and the severity of the underlying factor IX deficiency • Minor bleeding episode: Desired peak Factor IX Level (% of normal or IU/dL):30-60, dosed every 24 hours on days 1-3 until healing is achieved
	• Moderate bleeding episode: Desired peak Factor IX Level (% of normal or IU/dL): 40-60, dosed every 24 hours on days 2-7 until healing is achieved • Major or life threatening bleeding episode: Desired peak Factor IX Level (% of normal or IU/dL): 60-100, dosed every 12-24 hours on days 2-14 until healing is achieved
Perioperative management Congenital Hemophilia B	Patients ≥ 12 years of age: Minor surgery: • Pre-op: Desired peak Factor IX Level (% of normal or IU/dL) 50-80 • Post-op: Desired peak Factor IX Level (% of normal or IU/dL) 30-80, dosed every 24 hours on days 1-5, depending on type of procedure Major surgery: • Pre-op: Desired peak Factor IX Level (% of normal or IU/dL) 60-80 • Post-op: Desired peak Factor IX Level (% of normal or IU/dL) 40-60, dosed every 8-24 hours on days 1-3, then 30-50 dosed every 8-24 hours on days 4-6,and then 20-40 dosed every 8 - 24 hours on days 7-14
Routine prophylaxis to reduce the frequency of bleeding episodes	Patients ≥ 18 years of age: • 40 to 70 IU/kg twice weekly • Adjust the dose based on the individual patient's bleeding pattern and physical activity.

Medical Policy

Rixubis

Indication	Dose
Control and prevention of bleeding episodes Hemophilia B	One IU per kilogram body weight increases the circulating activity of Factor IX by 0.7 IU/dL for patients <12 years of age and 0.9 IU/dL for patients ≥ 12 years of age. Initial dose = body wt (kg) x desired factor IX increase (percent of normal or IU/dL)x reciprocal of observed recovery (IU/kg per IU/dL) Minor Circulating Factor IX level required (% or IU/dL) = 20-30 every 12 - 24 hours for at least 1 day, until healing is achieved Moderate Circulating Factor IX level required (% or IU/dL) = 25-50 every 12 - 24 hours for 2-7 days, until bleeding stops and healing is achieved Major Circulating Factor IX level required (% or IU/dL) = 50-100 every 12 - 24 hours for7-10 days, until bleeding stops and healing is achieved
Routine prophylaxis Hemophilia B	Dosing for previously treated patients (PTPs): Patients <12 years of age 60 – 80 IU/kg twice weekly Patients ≥ 12 years of age 40 – 60 IU/kg twice weekly Adjust the dose based on the individual patient's age, bleeding pattern, and physical activity.
Perioperative management Hemophilia B	Minor Circulating Factor IX level required (% or IU/dL) = 30-60 every 24 hours for at least 1 day, until healing is achieved Major Circulating Factor IX level required (% or IU/dL) = 80-100 every 8 - 24 hours for 7-10 days, until bleeding stops and healing is achieved

§ Utrecht and/or Malmö protocols used as basis for dosing

Criteria L – Coagadex

Unless otherwise specified*, the initial authorization will be provided for 3 months and may be renewed for a period of 6 months thereafter.

1. Diagnosis of Hereditary Factor X deficiency is confirmed by blood coagulation testing; **AND**
2. Coagadex is used for **one** of the following:
    a. On-demand treatment and control of bleeding episodes
    b. Perioperative management of surgical bleeding in patients with mild deficiency (Authorization will be limited to 1 month*)
    c. Routine prophylaxis to reduce the frequency of bleeding episodes: **AND**
        i. Patient has severe factor X deficiency (factor X level of <1%); **OR**
        ii. Patient has at least two documented episodes of spontaneous bleeding into joints.

Coagadex

Indication	Dose
On-demand treatment and control of bleeding episodes due to Factor X deficiency	– Children (<12 years of age): 30 IU/kg at first sign of bleeding, repeat every 24hours until bleeding stops. – Adults and adolescents (≥12 years of age): 25 IU/kg at first sign of bleeding, repeat every 24 hours until bleeding stops. *Do not administer more than 60 IU/kg daily.
Perioperative management of bleeding in patients with mild and moderate Factor X deficiency	Pre-surgery: Calculate the dose to raise plasma Factor X levels to 70-90 IU/dL using the formula: • Children (<12 years of age): Dose (IU) = Body Weight (kg) x Desired Factor XRise (IU/dL) x 0.6 (The dosing formula is based on observed recovery of 1.7 IU/dL per IU/kg). • Adults & adolescents (≥12 years of age): Dose (IU) = Body Weight (kg) x Desired Factor X Rise (IU/dL) x 0.5 (The dosing formula is based on observed recovery of 2 IU/dL per IU/kg). Post-surgery: Repeat dose as necessary to maintain plasma Factor X levels at a minimum of 50IU/dL until the patient is no longer at risk of bleeding due to surgery * Do not administer more than 60 IU/kg daily.
Prophylaxis of bleeding episodes	– Children (<12 years of age): 40 IU/kg twice weekly – Adults and adolescents (≥12 years of age): 25 IU/kg twice weekly Monitor trough blood levels of Factor X targeting ≥5 IU/dL and adjust dosage to clinical response and trough levels. Do not exceed a peak level of 120 IU/dL. * Do not administer more than 60 IU/kg daily.

Criteria M – Vonvendi

Unless otherwise specified*, the initial authorization will be provided for 3 months and may be renewed for a period of 12 months thereafter.

1. Patient is 18 years of age or older; **AND**
2. Diagnosis of von Willebrand disease (vWD) is confirmed by blood coagulation and von Willebrand factor testing; AND
3. Vonvendi is used for perioperative management (Authorization will be limited to 1 month*); **OR**
4. Vonvendi is used as on-demand treatment and control of bleeding episodes in **one** of the following:
    a. Patient has severe vWD; OR
    b. Patient has mild or moderate vWD and the use of desmopressin is known or suspected to be ineffective or contraindicated.

Vonvendi

Indication	Dose
Control of bleeding episodes VWD	• For each bleeding episode, administer the first dose of Vonvendi with an approved recombinant (non-von Willebrand factor containing) factor VIII if factor VIII baseline levels are below 40% or are unknown. • If recombinant factor VIII is required, give recombinant factor VIII within10 minutes of completing Vonvendi infusion at a ratio of 1.3:1 (i.e., 30% more Vonvendi than recombinant factor VIII, based on the approximate mean recoveries of 1.5 and 2 IU/dL for Vonvendi and recombinant factor VIII, respectively). <u>Minor:</u> Loading dose: 40-50 IU/kg; Maintenance dose: 40-50 IU/kg every 8-24 hoursas clinically required <u>Major:</u> Loading dose: 50-80 IU/kg; Maintenance dose: 40-60 IU/kg every 8-24 hoursfor approximately 2 to 3 days as clinically required
Perioperative management of bleeding VWD	<u>Elective Surgical Procedure</u> A preoperative dose may be administered 12-24 hours prior to surgery to allow the endogenous factor VIII levels to increase to at least 30 IU/dL (minor surgery) or 60 IU/dL (major surgery) before the loading dose (1 hour preoperative dose) of rVWF, with or without recombinant factor VIII, is administered. • Ensure baseline FVIII:C level is available prior to determining the need for12-24 hr preoperative dose. FVIII:C level should also be assessed within 3 hours prior to initiating the surgical procedure. If the level is at the recommended minimum target levels (30 IU/dL for minor surgery and 60 IU/dL for major surgery), administer a dose of Vonvendi alone (without factor VIII treatment) within 1 hour prior to the procedure. If the FVIII:C level is below the recommended minimum target level, administer complete dose of

	Vonvendi followed by recombinant factor VIII within 10 minutes to raise VWF:RCo and FVIII:C. • Assess baseline VWF:RCo levels within 3 hours of administration of the 12-24 hr preoperative dose. If the 12-24 hour preoperative dose is not administered, then assess baseline level VWF:RCo prior to surgery. When possible, measure incremental recovery (IR) for Vonvendi before surgery. For calculation of IR, measure baseline plasma VWF:RCo. Then infuse a dose of 50 IU/kg of Vonvendi. Measure VWF:RCo, 30 minutes after infusion of Vonvendi. • Use the following formula to calculate IR: IR= [Plasma VWF:RCo at30 minutes (IU/dL) – Plasma VWF:RCo at baseline (IU/dL)]/Dose(IU/kg). <u>Emergency Surgical Procedure</u> • A 12-24 hr preoperative dose may not be feasible in subjects requiring emergency surgery. Baseline VWF:RCo and FVIII:C levels should be assessed within 3 hours prior to initiating the surgical procedure if it is feasible. The loading dose (1 hour preoperative dose) can be calculated as the difference in the target peak and baseline plasma VWF:RCo levels divided by the IR. If the IR is not available, assume an IR of 2.0 IU/dL per IU/kg. If baseline VWF:RCo and FVIII:C is not available, as a general guidance a loading dose (1 hour preoperative dose), 40 to 60 IU/kg VWF:RCo, should be administered. Additionally, recombinant factor VIII at a dose of 30 to 45 IU/kg may be infused sequentially, preferably within 10 minutes after the Vonvendi infusion in patients whose factor VIII plasma levels already are (or are highly likely to be) less than 40 to 50 IU/dL for minor surgery or 80 to 100 IU/dL for major surgery. ***Note: refer to the package insert for recommended VWF:RCo and FVIII:Ctarget peak plasma levels and dosing guidelines for perioperative management of bleeding.***

Dispensing Requirements for Rendering Providers (Hemophilia Management Program)

- Prescriptions cannot be filled without an expressed need from the patient, caregiver or prescribing practitioner. Auto-filling is not allowed.
- Monthly, rendering provider must submit for authorization of dispensing quantity before delivering factor product. Information submitted must include:
    - Original prescription information, requested amount to be dispensed, vial sizes available to be ordered from the manufacturer, and patient clinical history (including patient product inventory and bleed history)
    - Factor dose should not exceed +1% of the prescribed dose and a maximum of three vials may be dispensed per dose. If unable to provide factor dosing within the required threshold, below the required threshold, the lowest possible dose able to be achieved above +1% should be dispensed. Prescribed dose should not be increased to meet assay management requirements.
- The cumulative amount of medication(s) the patient has on-hand should be taken into account when dispensing factor product. Patients should not have more than 5 extra doses on-hand for the treatment of acute bleeding episodes.
- Dispensing requirements for renderings providers are a part of the hemophilia management program. This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide.

Renewal

Coverage can be renewed based upon the following criteria:

A. Patient continues to meet indication-specific relevant criteria identified in section III; **AND**
B. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: symptoms of allergic-anaphylactic reactions (anaphylaxis, dyspnea, rash, etc.), thromboembolic events (venous thrombosis, pulmonary embolism, myocardial infarction, stroke, etc.), development of neutralizing antibodies (inhibitors), etc.; **AND**
C. Any increases in dose must be supported by an acceptable clinical rationale (i.e. weight gain, half-life study results, increase in breakthrough bleeding when patient is fully adherent to therapy, etc.); **AND**
D. The cumulative amount of medication(s) the patient has on-hand will be taken into account when authorizing. The authorization will allow up to 5 doses on-hand for the treatment of acute bleeding episodes as needed for the duration of the authorization; **AND**
E. Treatment of acute bleeding episodes/Treatment of Spontaneous and trauma-induced bleeding episodes/On-demand treatment of bleeding episodes
    a. Renewals will be approved for a 6 month authorization period
F. Prevention of acute bleeding episodes/Routine prophylaxis to prevent or reduce the frequency of bleeding episodes
    a. Renewals will be approved for a 12 month authorization period; **AND**
G. Patient has demonstrated a beneficial response to therapy (i.e., the frequency of bleeding episodes has decreased from pre-treatment baseline)

LIMITATIONS/EXCLUSIONS

1. Any indication other than those listed above due to insufficient evidence of therapeutic value
2. **OBIZUR ONLY:**
    a. Use in patients with baseline anti- porcine factor VIII inhibitor titer greater than 20 BU
3. **RIXUBIS ONLY:**
    a. Known hypersensitivity to the product or its excipients including hamster protein
    b. Disseminated Intravascular Coagulation (DIC)
    c. Signs of fibrinolysis
4. **JIVI ONLY:**
    a. Use in previously untreated patients (PUPs)
    b. Known history of hypersensitivity reactions to the active substance, polyethylene glycol (PEG), mouse or hamster proteins, or other constituents of the product
5. **FEIBA NF ONLY:**
    a. Known anaphylactic or severe hypersensitivity reactions to the product or any of its components, including factors of the kinin generating system
    b. Disseminated intravascular coagulation (DIC)
    c. Acute thrombosis or embolism (including myocardial infarction)
6. **CORIFACT ONLY**:
    a. Known anaphylactic or severe systemic reactions to human plasma-derived products
7. **HUMATE-P ONLY:**
    a. Known anaphylactic or severe systemic reaction to antihemophilic factor or von Willebrand factor preparations
8. **MONONINE & HEMOFIL M ONLY:**
    a. Known hypersensitivity to mouse protein
9. **BENEFIX/IDELVION/IXINITY/REBINYN/NOVOEIGHT/XYNTHA/ESPEROCT ONLY:**
    a. Known life-threatening, immediate hypersensitivity reactions, including anaphylaxis, to the product or its components, including hamster protein
10. **ALPROLIX ONLY:**
    a. Known history of hypersensitivity reactions, including anaphylaxis, to the product or its excipients (sucrose, mannitol, sodium chloride, L-histidine and polysorbate 20)
11. **ELOCTATE ONLY:**
    a. Known life-threatening hypersensitivity reactions to the product or its excipients (sucrose, sodium chloride, L-histidine, calcium chloride and polysorbate 20)
12. **ADVATE ONLY:**
    a. Known life-threatening hypersensitivity reactions, including anaphylaxis, to mouse or hamster protein or other constituents of the product (mannitol, trehalose, sodium chloride, histidine, Tris, calcium chloride, polysorbate 80, and/or glutathione)
13. **ADYNOVATE ONLY:**
    a. Known prior anaphylactic reaction to ADYNOVATE, to the parent molecule (ADVATE), mouse or hamster protein, or excipients of ADYNOVATE (e.g. Tris, mannitol, trehalose, glutathione, and/or polysorbate 80)
14. **KOGENATE FS ONLY:**
    a. Known life-threatening hypersensitivity reactions, including anaphylaxis to mouse or hamster protein or other constituents of the product (sucrose, glycine, histidine, sodium, calcium chloride, polysorbate 80, imidazole, tri-n-butyl phosphate, and copper)

15. **RECOMBINATE ONLY:**
    a. Known life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product or its components, including bovine, mouse or hamster proteins
16. **AFSTYLA ONLY:**
    a. Known life-threatening hypersensitivity reactions, including anaphylaxis to the product or its excipients (e.g., polysorbate 80) or hamster proteins
17. **KOVALTRY ONLY:**
    a. Known history of hypersensitivity reactions to the active substance, to any of the excipients, or to mouse or hamster proteins
18. **VONVENDI ONLY:**
    a. Known life-threatening hypersensitivity reactions to the product or constituents of the product (tri-sodium citrate-dihydrate, glycine, mannitol, trehalose-dihydrate, polysorbate 80, and hamster or mouse proteins)

DEFINITIONS

Hemophilia A Factor VIII (FVIII) deficiency or classic hemophilia	Genetic disorder caused by missing or defective factor VIII, a clotting protein
Hemophilia B Factor IX (FIX) deficiency or Christmas disease	Genetic disorder caused by missing or defective factor IX, a clotting protein.
Congenital factor VII deficiency Hageman Factor	XII deficiency is inherited in an autosomal recessive fashion, meaning both parents must carry the gene to pass it on to their children
Glanzmann Thrombasthenia	Genetic disorder in which the platelets have qualitative or quantitative deficiencies of the fibrinogen receptor αIIbβ3
von Willebrand disease (vWD)	Genetic disorder caused by missing or defective von Willebrand factor (VWF), a clotting protein. VWF binds factor VIII, a key clotting protein, and platelets in blood vessel walls, which help form a platelet plug during the clotting process.

CODING

Applicable Procedure Code	
J7170	Injection, emicizumab-kxwh, (Hemlibra) 0.5 mg
J7175	Injection, factor x, (human), 1 i.u. (Coagadex)
J7179	Injection, von willebrand factor (recombinant), (Vonvendi), 1 i.u. vwf:rco
J7180	Injection, factor XIII (antihemophilic factor, human) (Corifact), 1 IU
J7181	Injection, factor XIII A-subunit, (recombinant), (Tretten) per IU
J7182	Injection, factor VIII, (antihemophilic factor, recombinant), (NovoEight), per IU
J7183	Injection, von Willebrand factor complex (human), (Wilate), 1 IU vWF:RCo
J7185	Injection, factor VIII (antihemophilic factor, recombinant) (Xyntha), per IU
J7186	Injection, antihemophilic factor VIII/von Willebrand factor complex (human), per factor VIII i.u. (Alphanate)
J7187	Injection, von Willebrand factor complex (Humate-P), per IU VWF:RCO
J7188	Injection, factor VIII (antihemophilic factor, recombinant), (Obizur) per IU
J7189	Factor VIIa (antihemophilic factor, recombinant), (NovoSeven RT) per 1 mcg
J7190	Factor VIII (antihemophilic factor, human) per IU (Hemofil M, Koate, Monoclate-P)
J7192	Factor VIII (antihemophilic factor, recombinant) per IU, (Advate, Helixate FS, Kogenate-FS, Recombinate)
J7193	Factor IX (antihemophilic factor, purified, nonrecombinant) per IU (AlphaNine SD, Mononine)
J7194	Factor IX complex, (Profilnine SD) per IU
J7195	Injection, factor IX (antihemophilic factor, recombinant) per IU (BeneFIX, Ixinity)
J7198	Antiinhibitor, per IU (Feiba NF)
J7199	Hemophilia clotting factor, not otherwise classified
J7200	Injection, factor IX, (antihemophilic factor, recombinant), (Rixubis), per IU
J7201	Injection, factor ix, fc fusion protein, (recombinant), (Alprolix), 1 i.u.
J7202	Injection, factor ix, albumin fusion protein, (recombinant), (Idelvion), 1 i.u.
J7203	Injection, factor ix (antihemophilic factor, recombinant), glycopegylated, (Rebinyn), 1 i.u.
J7204	Injection, factor viii, antihemophilic factor (recombinant), glycopegylated-exei, per iu (Esperoct)
J7205	Injection, factor VIII Fc fusion protein (recombinant), per IU (Eloctate)
J7207	Injection, factor viii, (antihemophilic factor, recombinant), pegylated, 1 i.u. (Adynovate)
J7208	Injection, factor viii (antihemophilic factor, recombinant) pegylated-aucl, (Jivi), 1 i.u.
J7209	Injection, factor viii, (antihemophilic factor, recombinant), (Nuwiq), 1 i.u.
J7210	Injection, factor viii, (antihemophilic factor, recombinant), (Afstyla), 1 i.u
J7211	Injection, factor viii, (antihemophilic factor, recombinant), (Kovaltry), 1 i.u
J7212	Intravenous Powder for Solution, Factor viia, (antihemophilic factor, recombinant)-jncw (Sevenfact), 1 microgram
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)

96367	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); additional sequential infusion of a new drug/substance, up to 1 hour (List separately in addition to code for primary procedure)
96368	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); concurrent infusion (List separately in addition to code for primary procedure)
96369	Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); initial, up to 1 hour, including pump set-up and establishment of subcutaneous infusion site(s)
96370	Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
96371	Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); additional pump set-up with establishment of new subcutaneous infusion site(s) (List separately in addition to code for primary procedure)
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
96373	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); intra-arterial
96374	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); intravenous push, single or initial substance/drug
96375	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); each additional sequential intravenous push of a new substance/drug (List separately in addition to code for primary procedure)
96376	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); each additional sequential intravenous push of the same substance/drug provided in a facility (List separately in addition to code for primary procedure)
96377	Application of on-body injector (includes cannula insertion) for timed subcutaneous injection
96379	Unlisted therapeutic, prophylactic, or diagnostic intravenous or intra-arterial injection or infusion
99601	Home infusion/specialty drug administration, per visit (up to 2 hours);
99602	Home infusion/specialty drug administration, per visit (up to 2 hours); each additional hour (List separately in addition to code for primary procedure)

Applicable ICD-10 Codes	
D66	Hereditary factor VIII deficiency
D67	Hereditary factor IX deficiency
D68.0	Von Willebrand's disease
D68.1	Hereditary factor XI deficiency
D68.2	Hereditary deficiency of other clotting factors
D68.311	Acquired hemophilia
D68.9	Coagulation defect, unspecified
D69.1	Qualitative platelet defects
R58	Hemorrhage, not elsewhere classified

EVIDENCE BASED REFERENCES

1. Advate [package insert]. Westlake Village, CA; Baxter Healthcare. November 2016. Accessed October 20, 2017.
2. Product Information: ADYNOVATE intravenous injection, antihemophilic factor (recombinant) pegylated intravenous injection. Baxalta US Inc. (per manufacturer), Westlake Village, CA, 2017. Accessed July 10, 2019.
3. Alphanate [package insert]. Los Angeles, CA; Grifols Biologicals Inc.; March 2015. Accessed October 20, 2017.
4. AlphaNine SD [package insert]. Los Angeles, CA; Grifols Biologicals Inc.; January 2013. Accessed October 20, 2017.
5. Alprolix [package insert]. Cambridge, MA; Biogen Idec, Inc.; April 2017. Accessed October 20, 2017.
6. BeneFIX [package insert]. Philadelphia, PA; Wyeth Biopharma; August 2015. Accessed October 20, 2017.
7. Product Information: COAGADEX(R) intravenous injection, coagulation factor X (human) intravenous injection. BPLUSA Inc (per FDA), Durham, NC, 2018. Accessed July 10, 2019.
8. Corifact [package insert]. Kankakee, IL; CSL Behring LLC; March 2015. Accessed October 20, 2017.
9. Eloctate [package insert]. Cambridge, MA; Biogen Idec Inc.; January 2017. Accessed October 20, 2017.
10. Fieba NF [package insert]. Westlake Village, CA; Baxter Healthcare. April 2016. Accessed October 20, 2017.
11. Helixate FS [package insert]. Kankakee, IL; CSL Behring LLC; May 2016. Accessed October 20, 2017.
12. Hemofil M [package insert]. Westlake Village, CA; Baxter Healthcare. February 2016. Accessed October 20, 2017.
13. Humate-P [package insert]. Kankakee, IL; CSL Behring LLC; June 2014.
14. Product Information: IDELVION(R) powder for intravenous injection solution, coagulation factor IX (recombinant) albumin fusion protein (rIX-FP) powder for intravenous injection solution. CSL Behring LLC, Kankakee, IL, 2016.
15. Ixinity [package insert]. Winnipeg, Manitoba, Canada. Cangene Corporation; August 2016. Accessed October 20, 2017.
16. Koate DVI [package insert]. Research Triangle Park, NC; Grifols Therapeutics Inc.; August 2012. Accessed October 20, 2017.
17. Kogenate FS [package insert]. Whippany, NJ. Bayer HealthCare LLC; August 2015. Accessed October 20, 2017.
18. Monoclate P [package insert]. Kankakee, IL; CSL Behring LLC; February 2014. Accessed October 20, 2017.
19. Mononine [package insert]. Kankakee, IL; CSL Behring LLC; April 2016. Accessed October 20, 2017.
20. Novoeight [package insert]. Bagsvaerd, Denmark; Novo Nordisk; November 2016. Accessed July October 20, 2017.
21. NovoSeven RT [package insert]. Bagsvaerd, Denmark; Novo Nordisk; March 2016. Accessed October 20, 2017.

22. NUWIQ [package insert]. Elersvagen, Sweden; Octapharma AB; September 2015. Accessed October 20, 2017.
23. Obizur [package insert]. Westlake Village, CA; Baxter Healthcare. October 2015. Accessed October 20, 2017. 27. Profilnine [package insert]. Los Angeles, CA; Grifols Biologicals Inc.; November 2013. Accessed October 20, 2017.
24. Recombinate [package insert]. Westlake Village, CA; Baxter Healthcare. August 2016.
25. Tretten [package insert]. Bagsvaerd, Denmark; Novo Nordisk; April 2014.
26. Product Information: VONVENDI(R) lyophilized powder for intravenous injection, von Willebrand factor (recombinant) lyophilized powder for intravenous injection. Baxalta US Inc (per manufacturer), Lexington, MA, 2018.
27. Wilate [package insert]. Hoboken, NJ; Octapharma USA; August 2015. Accessed October 20, 2017.
28. Xyntha [package insert]. Philadelphia, PA; Wyeth Biopharma; December 2014. Accessed October 20, 2017.
29. KOVALTRY [package insert]. Whippany, NJ, Bayer Healthcare; March 2016. Accessed July 16, 2018.
30. AFSTYLA [package insert]. Kankakee, IL, CSL Behring LLC; September 2017.
31. REBINYN [package insert]. Plainsboro, NJ, Novo Nordisk Inc; June 2017.
32. Hemlibra [package insert]. South San Francisco, CA; Genentech; November 2017.
33. Jivi [package insert]. Whippany, NJ; Bayer; August 2018.
34. Esperoct [package insert]. Plainsboro, NJ: Novo Nordisk Inc; October 2019 40.
35. Sevenfact [package insert]. Louisville, KY: HEMA Biologics, April 2020.

POLICY HISTORY

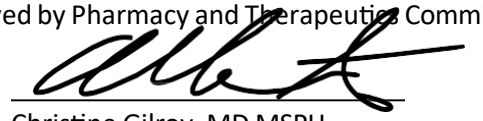
Revision History	Month Day, Year	Updates
Original Effective Date	MAY 24, 2021	
Revision	January 1, 2024	Updated to Brand New Day/Central Health Medicare Plan (no policy revisions made)
P&T Committee Endorsement	MAY 24, 2021	

Medical Policy

DISCLAIMER

Brand New Day/Central Health Medicare Plan medical policies address technology assessment of new and emerging treatments, devices, drugs, etc. They are developed to assist in administering plan benefits and do not constitute an offer of coverage nor medical advice. Brand New Day/Central Health Medicare Plan medical policies contain only a partial, general description of plan or program benefits and do not constitute a contract. Brand New Day/Central Health Medicare Plan does not provide health care services and, therefore, cannot guarantee any results or outcomes. Treating providers are solely responsible for medical advice and treatment of members. Our medical policies may be updated and therefore are subject to change without notice. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). MCG™ and Care Guidelines® are trademarks of MCG Health, LLC (MCG). InterQual® Criteria is copyrighted by McKesson Corporation.

Approved by Pharmacy and Therapeutics Committee

By: 
Christine Gilroy, MD MSPH

Date: 9/1/2021