Medicare Part B
Hemophilia Factor VIII
Prior Authorization

FDA APPROVED INDICATIONS AND DOSAGE[1-15,22]

Recombinant Factor VIII Concentrates		
Agent(s)	**Indication(s)**	**Dosage**
Advate® [Antihemophilic Factor (recombinant)] Lyophilized powder for reconstitution, for intravenous injection	Children and adults with hemophilia A (congenital factor VIII deficiency) for: • Control and prevention of bleeding episodes • Perioperative management Routine prophylaxis to prevent or reduce the frequency of bleeding episodes Not indicated for von Willebrand disease	• Control/prevention of bleeding episodes and perioperative management: Dose (IU) = body weight (kg) x desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg per IU/dL); frequency based on type of bleed • Routine Prophylaxis: 20-40 IU/kg every other day (3-4 times weekly); can dose every third day to maintain trough levels ≥1%
Adynovate® [Antihemophilic Factor (recombinant) PEGylated] Lyophilized powder for solution for intravenous injection	Children and adults with hemophilia A (congenital factor VIII deficiency) for: On-demand treatment and control of bleeding episodes Perioperative management Routine prophylaxis to reduce the frequency of bleeding episodes Limitation of Use: Not indicated for von Willebrand disease	One unit/kg body weight will raise the factor VIII level by 2% IU/dL • On-demand treatment and control of bleeding episodes and perioperative management: Estimated Increment of factor VIII (IU/dL or % of normal) = [Total Dose (IU)/body weight (kg)] x 2 (IU/dL per IU/kg) -Dose (IU) = Body Weight (kg) x Desired factor VIII Rise (IU/dL or % of Normal) x 0.5 (IU/kg per IU/dL) • Routine prophylaxis: Administer 40-50 IU/kg 2 times/week (starting dose of 55 IU/kg 2 times/week for patients <12 years of age with a maximum of 70 IU/kg
Afstyla® [antihemophilic Factor (recombinant), Single Chain]	Adults and children with hemophilia A (congenital Factor VIII deficiency) for:	One unit/kg body weight will raise the factor VIII level by 2 IU/dL

Lyophilized powder for solution for intravenous injection	On-demand treatment and control of bleeding episodes Routine prophylaxis to reduce the frequency of bleeding episodes Perioperative management of bleeding Limitation of Use: Not indicated for von Willebrand disease	• Calculating Required Dose: Dose (IU) = Body Weight (kg) x Desired Factor VIII Rise (IU/dL or % of normal) x 0.5 (IU/kg per IU/dL) • Routine prophylaxis: ≥12 years: The recommended starting regimen is 20 to 50 IU/kg administered 2 to 3 times weekly <12 years: The recommended starting regimen is 30 to 50 IU/kg of administered 2 to 3 times weekly. More frequent or higher doses may be required in children <12 years of age to account for the higher clearance in this age group
Eloctate® [Antihemophilic Factor (recombinant), Fc Fusion Protein] Lyophilized powder for solution for intravenous injection	Adults and children with Hemophilia A (congenital Factor VIII deficiency) for: On-demand treatment and control of bleeding episodes Perioperative management of bleeding Routine prophylaxis to reduce the frequency of bleeding episodes Limitation of Use: Not indicated for von Willebrand disease	One unit per kilogram body weight will raise the Factor VIII level by 2% • On-demand treatment and control of bleeding episodes and perioperative management: Required Dose (IU) = Body Weight (kg) x Desired Factor VIII Rise (IU/dL or % of normal) x 0.5 (IU/kg per IU/dL) • Routine prophylaxis: 50 IU/kg every 4 days. Adjust to a range of 25-65 IU/kg every 3-5 days based on clinical response Children<6 years old: 50 IU/kg twice weekly. Adjust dose to a range of 25-65 IU/kg every 3-5 days based on clinical response

		Children may require up to 80 IU/kg given more frequently
Esperoct® [antihemophilic factor (recombinant). glycopeglated-exei] Lyophilized powder for solution for intravenous injection	Adults and children with hemophilia A for: ● On-demand treatment and control of bleeding episodes ● Perioperative management of bleeding ● Routine prophylaxis to reduce the frequency of bleeding episodes	One unit per kilogram body weight will raise the Factor VIII level by 2 IU/dL ● On-demand treatment/control of bleeding episodes: Adolescents (≥ 12 years of age)/adults: 40 IU/kg for minor/moderate bleeds and 50 IU/kg for major bleeds Children (< 12 years of age):65 IU/kg for minor/moderate/major bleeds ● Perioperative management for minor/major surgery: Adolescents (≥ 12 years of age)/adults: preoperative dose of 50 IU/kg. Frequency of administration to be determined by the treating physician Children (< 12 years of age): preoperative dose of 65 IU/kg. Frequency of administration to be determined by the treating physician ● Routine prophylaxis: Adolescents (≥ 12 years of age)/adults: 50 IU/kg every 4 days. A regimen may be individually adjusted to less or more frequent dosing based on bleeding episodes Children (< 12 years of age): 65 IU/kg twice weekly. A regimen may be individually adjusted to less

		or more frequent dosing based on bleeding episodes Esperoct also may be dosed to achieve a specific target Factor VIII activity level, depending on the severity of hemophilia, for on-demand treatment/control of bleeding episodes or perioperative management. To achieve a specific target Factor VIII activity level, use the following formula: Dosage (IU) = Body Weight (kg) X Desired factor VIII increase (IU/dL or % normal) X 0.5 (IU/kg per IU/dL)
Helixate FS® [Antihemophilic Factor (recombinant), Formulated with Sucrose] Lyophilized powder for reconstitution for intravenous injection	On-demand treatment and control of bleeding episodes in adults and children with hemophilia A Perioperative management of bleeding in adults and children with hemophilia A Routine prophylaxis to reduce the frequency of bleeding episodes in children with hemophilia A and to reduce the risk of joint damage in children without pre-existing joint damage Routine prophylaxis to reduce the frequency of bleeding episodes in adults with hemophilia A Not indicated for the treatment of von Willebrand disease	• Control of bleeding episodes and perioperative management: Dose (units) = body weight (kg) x desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg per IU/dL) • Titrate doses to patient's clinical response • Determine treatment frequency based on type of bleeding episode • For routine prophylaxis in adults: 25 units per kg three times a week • For routine prophylaxis in children: 25 units per kg every other day • See prescribing information for dosing for On-Demand Treatment/Control of Bleeding Episodes and Dosing for Perioperative Management of Bleeding

Jivi® [antihemophilic factor (recombinant), PEGylated-aucl] Lyophilized powder for solution for intravenous use	Use in previously treated adults and adolescents (12 years of age and older) with hemophilia A (congenital Factor VIII deficiency) for: • On-demand treatment and control of bleeding episodes • Perioperative management of bleeding • Routine prophylaxis to reduce the frequency of bleeding episodes Limitations of use: • Jivi is not indicated for use in children < 12 years of age due to a greater risk for hypersensitivity reactions • Jivi is not indicated for use in previously untreated patients (PUPs) • Jivi is not indicated for the treatment of von Willebrand disease	• Control of bleeding episodes and perioperative management: Expected recovery: one unit per kilogram body weight of Jivi will increase the Factor VIII level by 2 international units per deciliter (IU/dL) Required dose (IU) = body weight (kg) X desired Factor VIII rise (% of normal or IU/dL) X reciprocal of expected recovery (or observed recovery, if available) • Routine prophylaxis: 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. A regimen may be further individually adjusted to less or more frequent dosing.
Kogenate FS® [Antihemophilic Factor (recombinant), Formulated with sucrose] Lyophilized powder for reconstitution with vial adapter for intravenous use	On-demand treatment and control of bleeding episodes in adults and children with hemophilia A Perioperative management of bleeding in adults and children with hemophilia A	• Control of bleeding episodes and perioperative management: Dose (units) = body weight (kg) x desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg per IU/dL) • Titrate doses to patient's clinical response

	Routine prophylaxis to reduce the frequency of bleeding episodes in children with hemophilia A and to reduce the risk of joint damage in children without pre-existing joint damage Routine prophylaxis to reduce the frequency of bleeding episodes in adults with hemophilia A Not indicated for the treatment of von Willebrand disease	• Determine treatment frequency based on type of bleeding episode • For routine prophylaxis in adults: 25 units per kg three times a week • For routine prophylaxis in children: 25 units per kg every other day *See prescribing information for dosing for On-Demand Treatment/Control of Bleeding Episodes and Dosing for Perioperative Management of Bleeding
Kovaltry® [Antihemophilic Factor (Recombinant)] Lyophilized powder for solution for intravenous injection	Indicated for use in adults and children with hemophilia A (congenital Factor VIII deficiency) for: • On-demand treatment and control of bleeding episodes • Perioperative management of bleeding • Routine prophylaxis to reduce the frequency of bleeding episodes Not indicated for the treatment of von Willebrand disease	• Control of bleeding episodes and perioperative management: 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 of 2 IU/dL per IU/kg) • Routine prophylaxis: Adults and adolescents: 20-40 IU/kg 2 or 3 times per week Children ≤12 years old: 25-50 IU/kg 2 times per week, 3 times per week or every other day
NovoEight® [Antihemophilic Factor (Recombinant)] Lyophilized powder for solution for intravenous use	Adults and children with hemophilia A for: • On-demand control and prevention of bleeding • Perioperative management • Routine prophylaxis to prevent or reduce the frequency of bleeding episodes.	Determine the dose using the following formula: Required Dose (IU) = Body Weight (kg) × Desired Factor VIII Increase (IU/dL or % normal) × 0.5 • Base the dose and frequency on the individual clinical response • See prescribing information for dosing for

	Not indicated for the treatment of von Willebrand disease	On-Demand Treatment/Control of Bleeding Episodes and Dosing for Perioperative Management of Bleeding
Nuwiq® [Antihemophilic Factor (Recombinant)] Lyophilized powder for solution for intravenous injection	Adults and children with Hemophilia A for: • On-demand treatment and control of bleeding episodes • Perioperative management of bleeding • Routine prophylaxis to reduce the frequency of bleeding episodes Not indicated for the treatment of von Willebrand disease.	Determine dose using the following formula for adolescents and adults: Required IU = body weight (kg) x desired Factor VIII rise (%) (IU/dL) x 0.5 (IU/kg per IU/dL) • Dosing for routine prophylaxis: 2-11 years old: 30-50 IU/kg every other day or three times per week 12-17 years old: 30-40 IU/kg every other day *See prescribing information for dosing for On-Demand Treatment/Control of Bleeding Episodes and Dosing for Perioperative Management of Bleeding
Recombinate™ [Antihemophilic Factor (Recombinant)] Lyophilized powder for reconstitution for intravenous injection	Indicated in hemophilia A (classical hemophilia) for the prevention and control of hemorrhagic episodes It is also indicated in the perioperative management of patients with hemophilia A (classical hemophilia) It can be of therapeutic value in patients with acquired Factor VIII inhibitors not exceeding 10 Bethesda Units per mL. Not indicated for the treatment of von Willebrand disease.	• The expected in vivo peak increase in Factor VIII level expressed as IU/dL of plasma or % (percent) of normal can be estimated by multiplying the dose administered per kg body weight (IU/kg) by two. This pharmacokinetic data demonstrated a peak recovery point above the pre-infusion baseline of approximately 2.0 IU/dL per IU/kg body weight *See prescribing information for dosing for On-Demand Treatment/Control of Bleeding Episodes and Dosing for Perioperative Management of Bleeding

Xyntha®/Xyntha® Solofuse™ [Antihemophilic factor (recombinant)] Lyophilized powder for solution for intravenous injection	Indicated for use in adults and children with hemophilia A for: ● On-demand treatment for control and prevention of bleeding episodes ● Perioperative management ● Routine prophylaxis to reduce the frequency of bleeding episodes Not indicated in patients with von Willebrand's disease	● The required dose is determined using the following formula: Dosage (International Units) = body weight (kg) × desired factor VIII rise (IU/dL or % of normal) × 0.5 (IU/kg per IU/dL) *See prescribing information for dosing for On-Demand Treatment/Control of Bleeding Episodes and Dosing for Perioperative Management of Bleeding
Human Plasma-Derived Immunoaffinity-Purified Factor VIII Concentrates		
Agent(s)	**Indication(s)**	**Dosage**
Hemofil M® [Antihemophilic Factor (Human), Method M, Monoclonal] Dried preparation for reconstitution for intravenous use	Indicated in hemophilia A (classical hemophilia) for the prevention and control of hemorrhagic episodes. Not indicated for the treatment of von Willebrand disease	● The expected in vivo peak AHF level, expressed as IU/dL of plasma or % (percent) of normal, can be calculated by multiplying the dose administered per kg body weight (IU/kg) by two *See prescribing information for dosing for On-Demand Treatment/Control of Bleeding Episodes and Dosing for Perioperative Management of Bleeding
Koāte/Koāte®-DVI [Antihemophilic Factor (Human)] Lyophilized powder for solution for intravenous injection	Treatment of classical hemophilia (hemophilia A) in which there is a demonstrated deficiency of activity of the plasma clotting factor, Factor VIII for: ● Control or prevention of bleeding episodes ● In order to perform emergency and elective surgery on individuals with hemophilia	● The dosage required (IU) can be estimated by the following formula: [Body weight (kg) X desired % Factor VIII increase (% of normal)] ÷ [2%/IU/kg] = Dosage required (IU) *See prescribing information for dosing for On-Demand Treatment/Control of Bleeding Episodes and Dosing for Perioperative Management of Bleeding

	Koāte-DVI contains naturally occurring von Willebrand factor, which is co-purified as part of the manufacturing process. Koāte-DVI has not been investigated for efficacy in the treatment of von Willebrand disease and is not approved for such usage	
Monoclate-P® [Antihemophilic Factor (Human) C Pasteurized] Lyophilized concentrate for reconstitution for intravenous use	Indicated for treatment of classical hemophilia (Hemophilia A) ● Affected individuals frequently require therapy following minor accidents ● Surgery, when required in such individuals, must be preceded by temporary corrections of the clotting abnormality. Surgical prophylaxis in severe AHF deficiency can be accomplished with an appropriately dosed pre-surgical IV bolus of Monoclate-P followed by intermittent maintenance doses Not indicated for the treatment of von Willebrand disease.	As a general rule 1 unit of AHF activity per kg will increase the circulating AHF level by 2%. ● The following formula provides a guide of dosage calculations for both adult and pediatric patients: Number of AHF = Body weight x desired Factor VIII x 0.5 I.U. Required (in kg) increase (% normal) *See prescribing information for dosing for On-Demand Treatment/Control of Bleeding Episodes and Dosing for Perioperative Management of Bleeding

CLINICAL RATIONALE

Hemophilia A, also called Factor VIII (FVIII) deficiency or classic hemophilia, is a genetic disorder caused by missing or defective Factor VIII (FVIII), a clotting protein. Although it is passed down from parents to children, about 1/3 of cases found have no previous family history.[16]

Treatment for hemophilia A is dependent on several factors and there is not a universal therapy that will work for all patients. Clinically the hallmark of bleeding in hemophilia is bleeding into the joints, muscles, and soft tissues. The severity and the risk of that bleeding can be correlated to the residual amount of factor activity that can be measured in the blood. Patients with severe disease have less than 1% residual activity, and often have zero. These are the patients who are at risk for spontaneous as well as traumatic bleeding. Having over 5% residual amount makes bleeding into the joints very unusual (although not inconceivable), and most bleeding is triggered only by trauma. Residual activity of 1-5%

appears for the most part to prevent spontaneous bleeding, but patients can still be at risk for joint bleeds with even relatively minor trauma.[22]

The main goal of any therapy is to completely prevent bleeding. The current World Hemophilia Federation Guidelines for the Management of Hemophilia state:[23]

- Both virus-inactivated plasma-derived and recombinant clotting factor concentrates (CFCs), as well as other hemostasis products when appropriate can be used for treatment of bleeding and prophylaxis in people with hemophilia
- Prophylaxis is the standard of care for people with severe hemophilia, and for some people with moderate hemophilia or for those with a severe bleeding phenotype and/or a high risk of spontaneous life-threatening bleeding
- Episodic CFC replacement should not be considered a long-term option for the management of hemophilia as it does not alter its natural history of spontaneous bleeding and related complications
- Emerging therapies in development with alternative modes of delivery (e.g., subcutaneous injection) and novel targets may overcome the limitations of standard CFC replacement therapy (i.e., need for intravenous administration, short half-life, risk of inhibitor formation).
- The development of gene therapies for hemophilia has advanced significantly, with product registration likely in the near future
- Gene therapy should make it possible for some people with hemophilia to aspire to and attain much better health outcomes and quality of life than that attainable with currently available hemophilia therapies
- Given the ongoing advances transforming the hemophilia treatment landscape, it is important to establish systems to constantly monitor developments in emerging and gene therapies for hemophilia and make them available as soon as possible following approval by regulatory authorities

The MASAC suggests the number of doses required for provision of home therapy varies greatly and is dependent upon the type of hemophilia (FVIII, FIX), the level of severity (severe, moderate, mild), the presence of an inhibitor, the prescribed regimen (on-demand, prophylaxis, immune tolerance), the number of bleeding episodes experienced regardless of the prescribed regimen, individual pharmacokinetics, the products utilized, and the level of physical activity.[15] For patients on prophylaxis, a minimum of one major dose and two minor doses should be available in addition to the prophylactic doses utilized monthly. For patients with severe or moderate hemophilia treated on-demand, the number of doses required to be available at home may be based upon historical bleeding patterns, with at least one major and two minor doses added to assure a level of safety.[17]

A major dose is defined as a correction of clotting factor that achieves a level of 60-100+% clotting factor activity that is utilized to treat a bleeding episode that is expected to require a higher hemostatic level such as when bleeds occur in a target joint, or joint/area with a risk of significant sequelae (e.g., hip, head, GI bleed). A minor dose is defined as a correction of clotting factor that achieves a level of 30-60% clotting factor activity that is utilized to treat a bleeding episode that is treated early, in a non-critical area and treatable with a lower hemostatic level (e.g., early non-major joints, small muscle bleeds, and skin/soft tissue, etc.).[17]

Recombinant FVIII (rFVIII) products are treatment of choice for hemophilia A as recommended by MASAC. First generation rFVIII products contain animal and/or human plasma-derived proteins in the cell culture medium and in the final formulation vial (Recombinate). Second generation rFVIII products contain animal or human plasma

proteins in the culture medium but not in the final formulation (Helixate, Kogenate). Third/fourth generation rFVIII products do not contain any animal or human plasma-derived proteins in the culture medium or in the final formulation vial.[19]

In view of the demonstrated benefits of prophylaxis (regular/scheduled administration of clotting factor concentrate to prevent bleeding) begun at a young age in persons with hemophilia A or B, MASAC recommends that prophylaxis be considered optimal therapy for individuals with severe hemophilia A (FVIII <1%). Prophylactic therapy should be instituted early (prior to the onset of frequent bleeding), with the aim of keeping the trough FVIII level above 1% between doses. Optimal dosing and frequency should be determined for each individual by appropriate laboratory monitoring. It is also recommended that individuals on prophylaxis have regular follow-up visits to evaluate joint status, to document any complications such as inhibitors, and to record any bleeding episodes that occur during prophylaxis.[18]
Approximately 1 in 5 people with hemophilia A will develop an antibody – called an inhibitor – to the clotting factor concentrate(s) used to treat or prevent their bleeding episodes. Developing an inhibitor is one of the most serious and costly medical complications of a bleeding disorder because it becomes more difficult to treat bleeds. Inhibitors most often appear in the first 50 exposure days of clotting factor concentrates.[23,25]

The National Hemophilia Foundation classifies inhibitors as low responding and high responding in addition to low titer (< 5 BU) and high titer (≥ 5 BU). In low responding inhibitors when the patient receives Factor VIII the inhibitor titer does not rise. These patients can be treated with higher doses of the CFC. If the inhibitor titer increases with CFC it is considered high- responding. For high responding inhibitors, the situation becomes much more complicated as even large doses of infused CFC are often rendered ineffectual by the sheer potency of the antibody response.[26]

In the cases of high-responding inhibitors treatment is based on several components including the type of hemophilia and the nature of the bleed. During a life or limb-threatening bleeding episode, physicians can remove antibodies from the body using plasmapheresis. This is only a temporary solution however as within a few days the body will produce large amounts of new antibodies. For the person with a high responding inhibitor there are therapies that can effectively treat bleeds by circumventing the need to replace FVIII. These agents are commonly referred to as bypassing agents (BPAs) and include activated prothrombin complex concentrate (aPCC) and recombinant activated Factor VII concentrates. Hemlibra, a therapy that does not function by FVIII or Factor IX replacement, is a newer therapy that can be used for these patients.[26]

If left unchecked, a persistent inhibitor will present a severe burden on patients and families, as the ongoing physical, emotional, and in many cases financial toll continue to intensify. Healthcare providers will often attempt to proactively stamp out an inhibitor through immune tolerance therapy (ITI). ITI is an approach to inhibitor eradication where the body's immune system begins to tolerate a therapy after daily doses of factor are administered over time. The majority of people who undergo ITI therapy will see an improvement within 12 months, but more difficult cases can take two years or longer.[27] There is a general consensus that failure of ITI is the inability to achieve successful tolerance within 2-3 years of initiation of an ITI regimen.[24]

ITI can take several months to several years to be effective. The Hemophilia Federation of America recommends that if success has not occurred within 33 months of beginning ITT

and there is a lack of a 20% decrease in the inhibitor titer over a 6 month period, that it is considered a failure.[20]

Emicizumab-kxwh is a recombinant, humanized, bispecific immunoglobulin G4 monoclonal antibody that substitutes for part of the cofactor function of activated factor VIII (FVIII) by bridging activated factor IX and Factor X. Emicizumab-kxwh is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults and children of all ages, newborn and older, with hemophilia A with and without Factor VIII inhibitors. There is significant reduction in annualized bleeding rates at all doses for all age groups, with or without inhibitors.[21]

There is limited data on the concomitant use of emicizumab prophylaxis during ITI. There is a case series of children with hemophilia A and inhibitors who underwent ITI in combination with emicizumab prophylaxis (Atlanta Protocol), and a larger clinical trial of this protocol is underway [MOTIVATE study (NCT04023019)].[21] The MOTIVATE study is a non-interventional, multicenter, observational, international study in male persons with hemophilia A who have developed inhibitors to any replacement coagulation Factor VIII (FVIII product). The purpose of the study is to capture different approaches in the management and to evaluate the efficacy and safety of immune tolerance induction, including the combination of FVIII and emicizumab. Patient will be assigned to 1 of 3 groups based on the treatments they receive, and may switch to another group if their treatment is changed. The 3 groups are:[28]

- ITI with Nuwiq, Octanate, or Wilate
- ITI with Nuwiq, Octanate, or Wilate with emicizumab
- Prophylaxis with emicizumab, aPCC, or recombinant FVIIIa without immune tolerance induction

People with bleeding disorders experience both acute and chronic pain associated with bleeding. Bleeding into soft tissues and joints, whether spontaneous or associated with trauma, often causes acute pain. Repeated bleeding events over time can lead to long-term changes in affected tissues, particularly joints. Chronic arthropathy causes disability and reduces quality of life due to chronic pain.[29]
Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain in patients with bleeding disorders. Non-steroidal anti-inflammatory drugs (NSAIDs) should typically be avoided in patients with bleeding disorders, particularly higher doses over extended durations, due to risks of potential short-term interference with platelet function and of GI ulcer formation. Selective COX-2 inhibitors (e.g., celecoxib) appear to be associated with decreased risk of anti-platelet effects and ulcer formation when compared to NSAIDs and may be considered.[29]

Safety[1-15,22]

- **Advate** is contraindicated in:
    - Patients who have 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)
- **Adynovate** is contraindicated in:
    - Patients who have had prior anaphylactic reaction to Adynovate, the parent molecule (Advate), mouse or hamster protein, or excipients of Adynovate
- **Afstyla** is contraindicated in:
    - Patients who have had life-threatening hypersensitivity reactions, including anaphylaxis to Afstyla or its excipients, or hamster proteins

- **Eloctate** is contraindicated in:
    - Patients who have had life-threatening hypersensitivity reactions, including anaphylaxis, to Eloctate or excipients of Eloctate (sucrose, sodium chloride, L-histidine, calcium chloride and polysorbate 20)
- **Esperoct** is contraindicated in:
    - Patients who have known hypersensitivity to Esperoct or its components, including hamster protein
- **Helixate FS** is contraindicated in:
    - Patients who have life-threatening hypersensitivity reactions, including anaphylaxis to mouse or hamster protein or other constituents of the product
- **Hemofil M** is contraindicated in:
    - Patients with a known hypersensitivity to the active substance, to excipients, or to mouse proteins
- **Jivi** is contraindicated in:
    - Patients who have a history of hypersensitivity reactions to the active substance, polyethylene glycol (PEG), mouse or hamster proteins, or other constituents of the product
- **Koāte/Koāte-DVI** is contraindicated in:
    - Patients who have had hypersensitivity reactions, including anaphylaxis, to Koāte or its components
- **Kogenate FS** is contraindicated in:
    - Patients who have life-threatening hypersensitivity reactions, including anaphylaxis to mouse or hamster protein or other constituents of the product
- **Kovaltry** is contraindicated in:
    - Patients who have history of hypersensitivity reactions to the active substance, mouse or hamster protein, or other constituents of the product
- **Monoclate P** is contraindicated in:
    - Known hypersensitivity to mouse protein is a contraindication to Monoclate-P
- **NovoEight** is contraindicated in:
    - Patients who have had life-threatening hypersensitivity reactions, including anaphylaxis, to NovoEight or its components, including hamster proteins
- **Nuwiq** is contraindicated in:
    - Patients who have manifested life-threatening hypersensitivity reactions, including anaphylaxis, to the product or its components
- **Recombinate** is contraindicated in:
    - Patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product or its components, including bovine, mouse or hamster proteins
- **Xyntha** is contraindicated in:
    - Patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product or its components, including hamster proteins

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Document History
Original Prime Standard Part B criteria, approved by P&T UM Committee 12/2021

Medicare Part B Hemophilia Factor VIII Prior Authorization

Coverage and policy application are contingent on National Coverage Determinations (NCD) and Local Coverage Determinations (LCD). An NCD or LCD that is applicable to the drug or product must be used in lieu of applicable medical necessity criteria. Also, please note that Prior Authorization criteria cannot be stricter than an NCD or LCD with specified step therapy requirements.

TARGET PREFERRED AGENT(S)	TARGET NON-PREFERRED AGENT(S)
Target preferred and non-preferred agent(s) to be determined client	Target preferred and non-preferred agent(s) to be determined client
Advate® [Antihemophilic Factor (recombinant)] **Adynovate®** [Antihemophilic Factor (recombinant) PEGylated] **Afstyla® (longer acting)** [antihemophilic Factor (recombinant), Single Chain] **Eloctate®** [Antihemophilic Factor (recombinant), Fc Fusion Protein] **Esperoct®** [antihemophilic factor (recombinant). glycopeglated-exei] **Helixate FS®** [Antihemophilic Factor (recombinant), Formulated with Sucrose] **Hemofil M®** [Antihemophilic Factor (Human), Method M, Monoclonal] **Jivi®** [antihemophilic factor (recombinant), PEGylated-aucl] **Koāte®/Koāte®-DVI** [Antihemophilic Factor (Human)] **Kogenate FS®** [Antihemophilic Factor (recombinant), Formulated with sucrose] **Kovaltry®** [Antihemophilic Factor (Recombinant)] **Monoclate-P®** [Antihemophilic Factor (Human) C Pasteurized] **NovoEight®** [Antihemophilic Factor (Recombinant)] **Nuwiq®** [Antihemophilic Factor (Recombinant)] **Recombinate™** [Antihemophilic Factor (Recombinant)] **Xyntha®/Xyntha® Solofuse™** [Antihemophilic factor (recombinant)]	

Brand (generic)	GPI	Multisource Code	HCPCS/ J Code
Advate [Antihemophilic Factor (recombinant)]			
250 Unit Single-dose vial	85100010252120	M, N, O, or Y	J7192

Brand (generic)	GPI	Multisource Code	HCPCS/ J Code
500 Unit Single-dose vial	85100010252130	M, N, O, or Y	J7192
1000 Unit Single-dose vial	85100010252140	M, N, O, or Y	J7192
1500 Unit Single-dose vial	85100010252150	M, N, O, or Y	J7192
2000 Unit Single-dose vial	85100010252170	M, N, O, or Y	J7192
3000 Unit Single-dose vial	85100010252180	M, N, O, or Y	J7192
4000 Unit Single-dose vial	85100010252185	M, N, O, or Y	J7192
Adynovate [Antihemophilic Factor (recombinant) PEGylated]			
250 Unit Single-use vial	85100010402120	M, N, O, or Y	J7207
500 Unit Single-use vial	85100010402130	M, N, O, or Y	J7207
750 Unit Single-use vial	85100010402135	M, N, O, or Y	J7207
1000 Unit Single-use vial	85100010402140	M, N, O, or Y	J7207
1500 Unit Single-use vial	85100010402145	M, N, O, or Y	J7207
2000 Unit Single-use vial	85100010402150	M, N, O, or Y	J7207
3000 Unit Single-use vial	85100010402160	M, N, O, or Y	J7207
Afstyla [antihemophilic Factor (recombinant), Single Chain]			
250 Unit Single-use vial	85100010556420	M, N, O, or Y	J7210
500 Unit Single-use vial	85100010556430	M, N, O, or Y	J7210

Brand (generic)	GPI	Multisource Code	HCPCS/ J Code
1000 Unit Single-use vial	85100010556440	M, N, O, or Y	J7210
1500 Unit Single-use vial	85100010556445	M, N, O, or Y	J7210
2000 Unit Single-use vial	85100010556450	M, N, O, or Y	J7210
2500 Unit Single-use vial	85100010556455	M, N, O, or Y	J7210
3000 Unit Single-use vial	85100010556460	M, N, O, or Y	J7210
Eloctate [Antihemophilic Factor (recombinant), Fc Fusion Protein]			
250 Unit Single-use vial	85100010302120	M, N, O, or Y	J7205, J7192
500 Unit Single-use vial	85100010302125	M, N, O, or Y	J7205, J7192
750 Unit Single-use vial	85100010302130	M, N, O, or Y	J7205, J7192
1000 Unit Single-use vial	85100010302135	M, N, O, or Y	J7205, J7192
1500 Unit Single-use vial	85100010302145	M, N, O, or Y	J7205, J7192
2000 Unit Single-use vial	85100010302155	M, N, O, or Y	J7205, J7192
3000 Unit Single-use vial	85100010302165	M, N, O, or Y	J7205, J7192
4000 Unit Single-use vial	85100010302170	M, N, O, or Y	J7205, J7192
5000 Unit Single-use vial	85100010302175	M, N, O, or Y	J7205, J7192
6000 Unit Single-use vial	85100010302180	M, N, O, or Y	J7205, J7192
Esperoct [antihemophilic factor (recombinant). glycopeglated-exei]			

Brand (generic)	GPI	Multisource Code	HCPCS/ J Code
500 Unit Single-use vial	85100010352130	M, N, O, or Y	J7204
1000 Unit Single-use vial	85100010352140	M, N, O, or Y	J7204
1500 Unit Single-use vial	85100010352145	M, N, O, or Y	J7204
2000 Unit Single-use vial	85100010352150	M, N, O, or Y	J7204
3000 Unit Single-use vial	85100010352160	M, N, O, or Y	J7204
Helixate FS [Antihemophilic Factor (recombinant), Formulated with Sucrose]			
500 Unit Single-use vial	85100010206430	M, N, O, or Y	J7192
1000 Unit Single-use vial	85100010206440	M, N, O, or Y	J7192
3000 Unit Single-use vial	85100010206460	M, N, O, or Y	J7192
Hemofil M [Antihemophilic Factor (Human), Method M, Monoclonal]			
250 Unit Single-dose bottle	85100010002110	M, N, O, or Y	J7190
500 Unit Single-dose bottle	85100010002130	M, N, O, or Y	J7190
1000 Unit Single-dose bottle	85100010002140	M, N, O, or Y	J7190
1700 Unit Single-dose bottle	85100010002146	M, N, O, or Y	J7190
Jivi [antihemophilic factor (recombinant), PEGylated-aucl]			
500 Unit Single-use vial	85100010412130	M, N, O, or Y	J7208
1000 Unit Single-use vial	85100010412140	M, N, O, or Y	J7208
2000 Unit Single-use vial	85100010412150	M, N, O, or Y	J7208

Brand (generic)	GPI	Multisource Code	HCPCS/ J Code
3000 Unit Single-use vial	85100010412160	M, N, O, or Y	J7208
Koāte/Koāte-DVI [Antihemophilic Factor (Human)]			
250 Unit Single-use vial	85100010002110	M, N, O, or Y	J7190
500 Unit Single-use vial	85100010002130	M, N, O, or Y	J7190
1000 Unit Single-use vial	85100010002140	M, N, O, or Y	J7190
Kogenate FS [Antihemophilic Factor (recombinant), Formulated with sucrose]			
250 Unit Single-use vial	85100010206420	M, N, O, or Y	J7192
500 Unit Single-use vial	85100010206430	M, N, O, or Y	J7192
1000 Unit Single-use vial	85100010206440	M, N, O, or Y	J7192
2000 Unit Single-use vial	85100010206450	M, N, O, or Y	J7192
3000 Unit Single-use vial	85100010206460	M, N, O, or Y	J7192
Kovaltry [Antihemophilic Factor (Recombinant)]			
250 Unit Single-use vial	85100010252120	M, N, O, or Y	J7211
500 Unit Single-use vial	85100010252130	M, N, O, or Y	J7211
1000 Unit Single-use vial	85100010252140	M, N, O, or Y	J7211
2000 Unit Single-use vial	85100010252170	M, N, O, or Y	J7211
3000 Unit Single-use vial	85100010252180	M, N, O, or Y	J7211
Monoclate-P [Antihemophilic Factor (Human) C Pasteurized]			
1500 Unit Single-dose vial	85100010006475	M, N, O, or Y	J7190

Brand (generic)	GPI	Multisource Code	HCPCS/ J Code
NovoEight [Antihemophilic Factor (Recombinant)]			
250 Unit Single-use vial	85100010332120	M, N, O, or Y	J7182
500 Unit Single-use vial	85100010332130	M, N, O, or Y	J7182
1000 Unit Single-use vial	85100010332140	M, N, O, or Y	J7182
1500 Unit Single-use vial	85100010332150	M, N, O, or Y	J7182
2000 Unit Single-use vial	85100010332160	M, N, O, or Y	J7182
3000 Unit Single-use vial	85100010332170	M, N, O, or Y	J7182
Nuwiq [Antihemophilic Factor (Recombinant)]			
250 Unit Injection Single-use vial	85100010222120	M, N, O, or Y	J7209
250 Unit Kit Single-use vial	85100010226420	M, N, O, or Y	J7209
500 Unit Injection Single-use vial	85100010222130	M, N, O, or Y	J7209
500 Unit Kit Single-use vial	85100010226430	M, N, O, or Y	J7209
1000 Unit Injection Single-use vial	85100010222140	M, N, O, or Y	J7209
1000 Unit Kit Single-use vial	85100010226440	M, N, O, or Y	J7209
2000 Unit Injection Single-use vial	85100010222160	M, N, O, or Y	J7209
2000 Unit Kit Single-use vial	85100010226460	M, N, O, or Y	J7209
2500 Unit Injection Single-use vial	85100010222165	M, N, O, or Y	J7209

Brand (generic)	GPI	Multisource Code	HCPCS/ J Code
2500 Unit Kit Single-use vial	85100010226465	M, N, O, or Y	J7209
3000 Unit Injection Single-use vial	85100010222170	M, N, O, or Y	J7209
3000 Unit Kit Single-use vial	85100010226470	M, N, O, or Y	J7209
4000 Unit Injection Single-use vial	85100010222180	M, N, O, or Y	J7209
4000 Unit Kit Single-use vial	85100010226480	M, N, O, or Y	J7209
Recombinate [Antihemophilic Factor (Recombinant)]			
220-400 Unit Single-use vial	85100010202115	M, N, O, or Y	J7192
401-800 Unit Single-use vial	85100010202125	M, N, O, or Y	J7192
801-1240 Unit Single-use vial	85100010202135	M, N, O, or Y	J7192
1241-1800 Unit Single-use vial	85100010202145	M, N, O, or Y	J7192
1801-2400 Unit Single-use vial	85100010202155	M, N, O, or Y	J7192
Xyntha/Xyntha Solofuse [Antihemophilic factor (recombinant)]			
250 Unit Single-use vial	85100010266420	M, N, O, or Y	J7185
500 Unit Single-use vial	85100010266430	M, N, O, or Y	J7185
1000 Unit Single-use vial	85100010266440	M, N, O, or Y	J7185
2000 Unit Single-use vial	85100010266460	M, N, O, or Y	J7185
3000 Unit Single-use vial	85100010266470	M, N, O, or Y	J7185

CRITERIA FOR APPROVAL

Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. The requested agent is being used for ONE of the following:
    a. An FDA approved indication
    OR
    b. An indication in CMS approved compendia

    AND
2. If the client has preferred agents, then ONE of the following:
    a. The requested agent is the preferred agent
    OR
    b. Information has been provided that indicates the patient has been treated with the requested agent in the past 365 days
    OR
    c. There is documentation that the patient has had an ineffective treatment response to the active ingredient(s) of ALL preferred agent(s)
    OR
    d. The patient has a documented intolerance, hypersensitivity, or FDA labeled contraindication to the active ingredient(s) of ALL preferred agent(s)
    OR
    e. The prescriber has submitted documentation indicating ALL preferred agent(s) are likely to be ineffective or are likely to cause an adverse reaction or other harm to the patient

    AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent
    AND
4. The requested quantity (dose) is within FDA labeled dosing or supported in compendia for the requested indication

Length of Approval: up to 12 months