Factor VIII and Von Willebrand Factor Medical Drug Criteria Program Summary

POLICY REVIEW CYCLE

Effective Date 02-24-2025

Date of Origin

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Advate® (antihemophilic Factor [recombinant]) Lyophilized powder for reconstitution, for intravenous injection	• Children and adults with hemophilia A (congenital factor VIII deficiency) for: o Control and prevention of bleeding episodes o Perioperative management • Routine prophylaxis to prevent or reduce the frequency of bleeding episodes Advate is not indicated for the treatment of von Willebrand disease	Recombinant Factor VIII concentrate	1
Adynovate® (antihemophilic Factor [recombinant] PEGylated) Lyophilized powder for solution for intravenous injection	• Children and adults with hemophilia A (congenital factor VIII deficiency) for: o On-demand treatment and control of bleeding episodes o Perioperative management o Routine prophylaxis to reduce the frequency of bleeding episodes Limitation of Use: Adynovate is not indicated for treatment of von Willebrand disease	Recombinant Factor VIII concentrate	2
Afstyla® (antihemophilic Factor [recombinant], Single Chain) Lyophilized powder for solution for intravenous injection	• Adults and children with hemophilia A (congenital Factor VIII deficiency) for: o On-demand treatment and control of bleeding episodes o Routine prophylaxis to reduce the frequency of bleeding episodes o Perioperative management of bleeding Limitation of Use: Afstyla is not indicated for the treatment of von Willebrand disease	Recombinant Factor VIII concentrate	3
Alphanate® (antihemophilic Factor/von	• Control and prevention of bleeding in adult and pediatric patients with hemophilia A • Surgical and/or invasive procedures in adult and pediatric patients with von Willebrand disease (VWD) in whom	Pooled human antihemophilic Factor/von	4

Agent(s)	FDA Indication(s)	Notes	Ref#
Willebrand Factor Complex [human]) Lyophilized powder for solution for intravenous use	desmopressin (DDAVP) is either ineffective or contraindicated. Alphanate is not indicated for patients with severe VWD (Type 3) undergoing major surgery	Willebrand Factor complex	
Altuviiio® (antihemophilic Factor [recombinant], Fc-VWF-XTEN fusion protein-ehtl) Lyophilized powder for solution for intravenous use	• Use in adults and children with hemophilia A (congenital Factor VIII deficiency) for: o Routine prophylaxis to reduce the frequency of bleeding episodes o On-demand treatment & control of bleeding episodes o Perioperative management of bleeding Limitation of Use: Altuviiio is not indicated for the treatment of von Willebrand disease	Recombinant antihemophilic Factor	34
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: o On-demand treatment and control of bleeding episodes o Perioperative management of bleeding o Routine prophylaxis to reduce the frequency of bleeding episodes Limitation of Use: Eloctate is not indicated for treatment of von Willebrand disease.	Recombinant Factor VIII concentrate	5
Esperoct® (antihemophilic Factor [recombinant]. glycopegloyated-exei) Lyophilized powder for solution for intravenous injection	• Adults and children with hemophilia A for: o On-demand treatment and control of bleeding episodes o Perioperative management of bleeding o Routine prophylaxis to reduce the frequency of bleeding episodes Esperoct is not indicated for the treatment of von Willebrand disease	Recombinant Factor VIII concentrate	6
Hemofil M® (antihemophilic Factor [human],	• Indicated in hemophilia A (classical hemophilia) for the prevention and control of hemorrhagic episodes Hemofil M is not indicated in von Willebrand disease	Human Plasma-Derived Immunoaffinity-Purified Factor VIII concentrate	7

Agent(s)	FDA Indication(s)	Notes	Ref#
method M, monoclonal) Dried preparation for reconstitution for intravenous use			
Humate-P® (antihemophilic Factor/von Willebrand Factor Complex [human]) Lyophilized powder for reconstitution for intravenous use	• Treatment and prevention of bleeding in adults with hemophilia A • Treatment of spontaneous and trauma-induced bleeding episodes in adult and pediatric patients with von Willebrand disease (VWD) • Prevention of excessive bleeding during and after surgery in adult and pediatric patients with VWD • Use in VWD applies to patients with severe VWD as well as patients with mild to moderate VWD where the use of desmopressin is known or suspected to be inadequate Humate-P is not indicated for the prophylaxis of spontaneous bleeding episodes in VWD	Pooled human plasma derived antihemophilic Factor/von Willebrand Factor complex	8
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: o On-demand treatment and control of bleeding episodes o Perioperative management of bleeding o Routine prophylaxis to reduce the frequency of bleeding episodes Limitations of Use: • Jivi is not indicated for use in children less than 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	Recombinant Factor VIII concentrate	9
Koāte® (antihemophilic Factor [Human]) Lyophilized powder for solution for intravenous injection	• Control or prevention of bleeding episodes or in order to perform emergency and elective surgery on individuals with hemophilia Limitations of Use: Koāte is not indicated for the treatment of von Willebrand disease	Human Plasma-Derived Immunoaffinity-Purified Factor VIII concentrate	10
Kogenate FS® (antihemophilic Factor [recombinant	• 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	Recombinant Factor VIII concentrate	11

Agent(s)	FDA Indication(s)	Notes	Ref#
], formulated with sucrose) Lyophilized powder for reconstitution with vial adapter for intravenous use	• 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 Kogenate FS is not indicated for the treatment of von Willebrand disease		
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 Kovaltry is not indicated for the treatment of von Willebrand disease	Recombinant Factor VIII concentrate	12
NovoEight® (antihemophilic Factor [recombinant]) Lyophilized powder for solution for intravenous use	• Adults and children with hemophilia A for: o On-demand control and prevention of bleeding o Perioperative management o Routine prophylaxis to prevent or reduce the frequency of bleeding episodes. NovoEight is not indicated for the treatment of von Willebrand disease	Recombinant Factor VIII concentrate	13
Nuwiq® (antihemophilic Factor [recombinant]) Lyophilized powder for solution for intravenous injection	• Adults and children with Hemophilia A for: o On-demand treatment and control of bleeding episodes o Perioperative management of bleeding o Routine prophylaxis to reduce the frequency of bleeding episodes Nuwiq is not indicated for the treatment of von Willebrand disease.	Recombinant Factor VIII concentrate	14
Recombinate® (antihemophilic Factor [recombinant]) Lyophilized powder for reconstitution for	• Hemophilia A (classical hemophilia) for the prevention and control of hemorrhagic episodes • Perioperative management of patients with hemophilia A (classical hemophilia) • Recombinate can be of therapeutic value in patients with acquired Factor VIII inhibitors not exceeding 10 Bethesda Units per mL Recombinate is not indicated for the treatment of von Willebrand disease.	Recombinant Factor VIII concentrate	15

Agent(s)	FDA Indication(s)	Notes	Ref#
intravenous injection			
Vonvendi® (von Willebrand Factor [recombinant]) Solution for intravenous use	• Adults (age 18 and older) diagnosed with von Willebrand disease (VWD) for: o On-demand treatment and control of bleeding episodes o Perioperative management of bleeding o Routine prophylaxis to reduce the frequency of bleeding episodes in patients with severe Type 3 von Willebrand disease receiving on-demand therapy	Recombinant von Willebrand Factor	16
Wilate® (von Willebrand Factor/Coagulation Factor VIII Complex [human]) Lyophilized powder for solution for intravenous use	• On-demand treatment and control of bleeding episodes in children and adults with von Willebrand disease (VWD) • Perioperative management of bleeding in children and adults with VWD • Routine prophylaxis to reduce the frequency of bleeding episodes in adolescents and adults with hemophilia A • On-Demand treatment and control of bleeding episode in adolescents and adults with hemophilia A	Human plasma-derived, sterile, purified, fouble virus inactivated von Willebrand Factor/Coagulation Factor VIII complex	17
Xyntha®/Xyntha® Solofuse® (antihemophilic Factor [recombinant]) Lyophilized powder for solution for intravenous injection	• Indicated for use in adults and children with hemophilia A for: o On-demand treatment for control and prevention of bleeding episodes o Perioperative management o Routine prophylaxis to reduce the frequency of bleeding episodes Xyntha/Xyntha Solofuse is not indicated in patients with von Willebrand's disease	Recombinant Factor VIII concentrate	18

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Hemophilia A	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.(19) 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.(25) The main goal of any therapy is to completely prevent bleeding. The current World Hemophilia Federation Guidelines for the Management of Hemophilia state:(26) • 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 National Hemophilia Foundation Medical and Scientific Advisory Council (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. 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.(20) 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.).(20) 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.(22) 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 standard of care therapy for individuals with severe hemophilia A (FVIII less than 1%) including those with inhibitors. Prophylactic therapy may also be considered for persons with moderate and mild hemophilia with a severe phenotype. Prophylactic therapy should be instituted early (prior to the onset of frequent bleeding).(35) 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.(25,27) The National Hemophilia Foundation classifies inhibitors as low responding and high responding in addition to low titer (less than 5 BU) and high titer (greater than or equal to 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 month, 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.(26) ITI can take several months to several years to be effective. The recommendation is 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.(23) 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.(24) 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)].(24) 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:(30) • 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
von Willebrand disease	von Willebrand disease (VWD) is a common, inherited bleeding disorder. VWD affects males and females equally in up to 1% of the population. There are several classification types of VWD which includes types 1 and 2 which are characterized by quantitative deficiencies of von Willebrand Factor (VWF) and types 2A, 2B, 2M, and 2N which are qualitative variants. Clinically, VWD patients experience several symptoms including: (32) • Excessive mucocutaneous bleeding including heavy menstrual bleeding • Epistaxis • Easy bruising • Prolonged bleeding from minor wounds and the oral cavity • Gastrointestinal bleeding • Bleeding after dental work, childbirth, and surgery • Musculoskeletal bleeding in severe cases Persons with type 1, 2A, 2M and 2N VWD may be treated with desmopressin (DDAVP Injection or Stimate Nasal Spray) if they have been shown by a DDAVP trial to be responsive. Response to DDAVP should be assessed one and four hours after DDAVP; the one-hour assessment is particularly important for patients suspected of having type 1 C VWD. A desmopressin response requires an increase of at least greater than 2 times the baseline VWF activity level and a sustained increase of both VWF and Factor VIII:C levels greater than 0.50 IU/mL for at least 4 hours.(33) Persons with type 2B and type 3 VWD and those with type 1, 2A, 2M, and 2N who have been shown to be nonresponsive to DDAVP, should be treated with a Factor VIII/VWF concentrate that is known to contain the higher molecular weight multimers of von Willebrand Factor and that has been virally attenuated to eliminate transmission of HIC and hepatitis A, B, and C.(33) In patients with VWD with a history of major and frequent bleeds, the American Society of Hematology (ASH), the International Society for Thrombosis and Haemostasis (ISTH), the National Hemophilia Foundation (NHF), and the World Federation of Hemophilia (WFH) guideline panel suggests using long-term prophylaxis with Factor replacement rather than no prophylaxis. Prophylaxis in VWD is defined as a period of at least 3 months of treatment of VWF concentrate at least once weekly, or for women with heavy menstrual bleeding, the use of VWF concentrate at least once per menstrual cycle.(33)

	Prior to surgery in a patient with VWD, consultation should be obtained with a pediatric or adult hematologist who specializes in the management of individuals with inherited bleeding disorders. This consultation should cover risk of bleeding with procedure and duration of risk. Treatment plan should be developed including such issues as the need for a DDAVP trial; type of fluid replacement or fluid restriction; dose and duration of DDAVP to be used; appropriate dose, timing, and duration of factor replacement therapy; and use of adjunctive medications (antifibrinolytics and topical agents). The ASH ISRH NHF WFH 2021 guidelines on the management of VWD conditionally recommend that desmopressin should not be used for major surgery and factor replacement should contain both FVIII and VWF activity levels of 0.50 IU/mL for at least 3 days after surgery.(33)

Safety	• **Advate** is contraindicated in:(1)
	  • 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:(2)
	  • 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:(3)
	  • Patients who have had life-threatening hypersensitivity reactions, including anaphylaxis to Afstyla or its excipients, or hamster proteins
	• **Alphanate** is contraindicated in:(4)
	  • Patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product of its components
	• **Altuviiio** is contraindicated in:(34)
	  o Patients who have had severe hypersensitivity reactions, including anaphylaxis, to Altuviio or excipients of Altuviio
	• **Eloctate** is contraindicated in:(5)
	  • 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:(6)
	  • Patients who have known hypersensitivity to Esperoct or its components, including hamster protein
	• **Hemofil M** is contraindicated in:(7)
	  • Patients with a known hypersensitivity to the active substance, to excipients, or to mouse proteins
	• **Humate-P** is contraindicated in:(8)
	  • Anaphylactic or severe systemic reaction to antihemophilic factor or VWF preparations
	• **Jivi** is contraindicated in:(9)
	  • 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:(10)
	  • Patients who have had hypersensitivity reactions, including anaphylaxis, to Koāte or its components
	• **Kogenate FS** is contraindicated in:(11)
	  • Patients who have life-threatening hypersensitivity reactions, including anaphylaxis to mouse or hamster protein or other constituents of the product
	• **Kovaltry** is contraindicated in:(12)
	  • Patients who have history of hypersensitivity reactions to the active substance, mouse or hamster protein, or other constituents of the product
	• **NovoEight** is contraindicated in:(13)

	• Patients who have had life-threatening hypersensitivity reactions, including anaphylaxis, to NovoEight or its components, including hamster proteins • **Nuwiq** is contraindicated in:(14) • Patients who have manifested life-threatening hypersensitivity reactions, including anaphylaxis, to the product or its components • **Recombinate** is contraindicated in:(15) • Patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product or its components, including bovine, mouse or hamster protein • **Vonvendi** is contraindicated in:(16) • Patients who have had life-threatening hypersensitivity reactions to Vonvendi or its components (tri-sodium citrate dihydrate, glycine, mannitol, trehalose-dihydrate polysorbate 80m and hamster or mouse proteins) • **Wilate** is contraindicated in:(17) • Patients with known hypersensitivity reactions, including anaphylactic or severe systemic reaction, to human plasma-derived products, any ingredient in the formulation, or components of the container • **Xyntha** is contraindicated in:(18) • Patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product or its components, including hamster proteins

REFERENCES

Number	Reference
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2	Adynovate prescribing information. Takeda Pharmaceuticals America, Inc. August 2023.
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4	Alphanate prescribing information. Grifols USA LLC. November 2022.
5	Eloctate prescribing information. Bioverity Therapeutics Inc. May 2023.
6	Esperoct prescribing information. Novo Nordisk. July 2024.
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8	Humate-P prescribing information. Takeda Pharmaceuticals America, Inc. March 2023.
9	Jivi prescribing information. Bayer HealthCare LLC. August 2018.
10	Koāte prescribing information. Kedrion Biopharma, Inc. January 2022.
11	Kogenate FS prescribing information. Bayer HealthCare LLC. December 2019.
12	Kovaltry prescribing information. Bayer HealthCare LLC. December 2022.
13	NovoEight prescribing information. Novo Nordisk. July 2020.
14	Nuwiq prescribing information. Octapharma USA Inc. June 2021.
15	Recombinate prescribing information. Takeda Pharmaceuticals America, Inc. March 2023.
16	Vonvendi prescribing information. Takeda Pharmaceuticals America, Inc. March 2023.
17	Wilate prescribing information. Octapharma USA Inc. November 2019.
18	Xyntha prescribing information. Wyeth BioPharma Division of Wyeth Pharmaceuticals LLC. July 2022.
19	National Hemophilia Foundation. Bleeding disorders A-Z/Types/Hemophilia A. https://www.hemophilia.org/bleeding-disorders-a-z/types/hemophilia-a
20	Medical and Scientific Advisory Committee. MASAC recommendation regarding doses of clotting factor concentrate in the home. MASAC Document #242. June 2016.
21	Reference no longer used

Number	Reference
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25	National Hemophilia Foundation. One Size Does Not Fit All: Individualized Therapy. Dr Steven Pipe. February 2017. https://www.hemophilia.org/educational-programs/education/online-education/one-size-does-not-fit-all-individualized-therapy
26	Srivastave A, Santagostino E, Dougall A, et al. World Federation of Hemophilia Guidelines for the Management of Hemophilia. 3rd edition. August 2020.
27	CDC Centers for Disease Control and Prevention. Inhibitors and Hemophilia. https://www.cdc.gov/ncbddd/hemophilia/inhibitors.html
28	National Hemophilia Foundation Bleeding Disorders A-Z Overview Inhibitors Treatment for Inhibitors. https://www.hemophilia.org/bleeding-disorders-a-z/overview/inhibitors/treatment-for-inhibitors
29	National Hemophilia Foundation. Bleeding Disorders A-Z/ Overview/ Inhibitors/ Immune Tolerance. https://www.hemophilia.org/bleeding-disorders-a-z/overview/inhibitors/immune-tolerance
30	Clinicatrials.gov. NCT04023019. Treatment of Hemophilia A Patients With FVIII Inhibitors (MOTIVATE). https://clinicaltrials.gov/ct2/show/NCT04023019?term=NCT04023019&draw=2&rank=1
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32	James PD, Connell NT, Ameer B, et al. ASH ISTH NHF WFH 2021 guidelines on the diagnosis of von Willebrand disease. Blood Advances 12 January 2021. Volume 5, Number 1. 280-300.
33	Medical and Scientific Advisory Committee. MASAC Document 266 - MASAC Recommendations Regarding the Treatment of von Willebrand Disease. March 2021.
34	Altuviiio prescribing information. Bioverativ Therapeutics Inc. March 2023.
35	Medical and Scientific Advisory Council. MASAC Document 267 - Recommendation Concerning Prophylaxis for Hemophilia A and B with and without inhibitors. April 2022.

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
J7192	Advate	antihemophilic factor rahf-pfm for inj ; antihemophilic factor recomb (rahf-pfm) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	M ; N ; O ; Y	N		
J7207	Adynovate	antihemophilic factor recomb pegylated for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 500 UNIT ; 750 UNIT	M ; N ; O ; Y	N		
J7210	Afstyla	antihemophilic fact rcmb single chain for inj kit	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 2500 UNIT ;	M ; N ; O ; Y	N		

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
			3000 UNIT ; 500 UNIT				
J7186 ; J7190	Alphanate	antihemophilic factor/vwf (human) for inj	1000 UNIT ; 1000-2400 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 250-600 UNIT ; 500 UNIT ; 500-1200 UNIT	M ; N ; O ; Y	N		
J7214	Altuviiio	antihemophilic fact rcmb fc-vwf-xten-ehtl for inj	1000 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT ; 750 UNIT	M ; N ; O ; Y	N		
J7192 ; J7205	Eloctate	antihemophilic factor rcmb (bdd-rfviiifc) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT ; 5000 UNIT ; 6000 UNIT ; 750 UNIT	M ; N ; O ; Y	N		
J7204	Esperoct	antihemophilic factor recomb glycopeg-exei for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	M ; N ; O ; Y	N		
J7190	Hemofil m ; Koate ; Koate-dvi	antihemophilic factor (human) for inj	1000 UNIT ; 1700 UNIT ; 250 UNIT ; 500 UNIT	M ; N ; O ; Y	N		
J7187 ; J7190	Humate-p	antihemophilic factor/vwf (human) for inj	1000 UNIT ; 1000-2400 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 250-600 UNIT ; 500 UNIT ; 500-1200 UNIT	M ; N ; O ; Y	N		
J7208	Jivi	antihemophil fact rcmb(bdd-rfviii peg-aucl) for inj ; antihemophil fact rcmb(bdd-rfviii peg-aucl)for inj	1000 UNIT ; 2000 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	M ; N ; O ; Y	N		
J7192	Kogenate fs	antihemophilic factor recomb (rfviii) for inj kit	1000 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 500 UNIT	M ; N ; O ; Y	N		
J7211	Kovaltry	antihemophilic factor recomb (rahf-pfm) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	M ; N ; O ; Y	N		
J7182	Novoeight	antihemophilic fact rcmb (bd trunc-rfviii) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 500 UNIT	M ; N ; O ; Y	N		
J7209	Nuwiq	antihemophil fact rcmb (bdd-rfviii,sim) for inj kit ; antihemophil fact	1000 UNIT ; 1500 UNIT ; 2000 UNIT ;	M ; N ; O ; Y	N		

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
		rcmb(bdd-rfviii,sim) for inj kit	250 UNIT ; 2500 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT				
J7209	Nuwiq	antihemophilic fact rcmb (bdd-rfviii,sim) for inj ; antihemophilic factor rcmb (bdd-rfviii,sim) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 2500 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	M ; N ; O ; Y	N		
J7192	Recombinate	antihemophilic factor recomb (rfviii) for inj	1241 -1800 UNIT ; 1801 - 2400 UNIT ; 220 -400 UNIT ; 401 -800 UNIT ; 801 - 1240 UNIT	M ; N ; O ; Y	N		
J7179	Vonvendi	von willebrand factor (recombinant) for inj	1300 UNIT ; 650 UNIT	M ; N ; O ; Y	N		
J7183 ; J7190	Wilate	antihemophilic factor/vwf (human) for inj	1000 UNIT ; 1000-1000 UNIT ; 1000-2400 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 250-600 UNIT ; 500 UNIT ; 500-1200 UNIT ; 500-500 UNIT	M ; N ; O ; Y	N		
J7185	Xyntha ; Xyntha solofuse	antihemophil fact rcmb (bdd-rfviii,mor) for inj kit ; antihemophil fact rcmb(bdd-rfviii,mor) for inj kit	1000 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 500 UNIT	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Advate	antihemophilic factor rahf-pfm for inj ; antihemophilic factor recomb (rahf-pfm) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Adynovate	antihemophilic factor recomb pegylated for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 500 UNIT ; 750 UNIT	Commercial ; HIM ; ResultsRx
Afstyla	antihemophilic fact rcmb single chain for inj kit	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 2500 UNIT ; 3000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Alphanate	antihemophilic factor/vwf (human) for inj	1000 UNIT ; 1000-2400 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 250-600 UNIT ; 500 UNIT ; 500-1200 UNIT	Commercial ; HIM ; ResultsRx
Altuviiio	antihemophilic fact rcmb fc-vwf-xten-ehtl for inj	1000 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT ; 750 UNIT	Commercial ; HIM ; ResultsRx
Eloctate	antihemophilic factor rcmb (bdd-rfviiifc) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 4000 UNIT ;	Commercial ; HIM ; ResultsRx

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
		500 UNIT ; 5000 UNIT ; 6000 UNIT ; 750 UNIT	
Esperoct	antihemophilic factor recomb glycopeg-exei for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Hemofil m ; Koate ; Koate-dvi	antihemophilic factor (human) for inj	1000 UNIT ; 1700 UNIT ; 250 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Humate-p	antihemophilic factor/vwf (human) for inj	1000 UNIT ; 1000-2400 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 250-600 UNIT ; 500 UNIT ; 500-1200 UNIT	Commercial ; HIM ; ResultsRx
Jivi	antihemophil fact rcmb(bdd-rfviii peg-aucl) for inj ; antihemophil fact rcmb(bdd-rfviii peg-aucl)for inj	1000 UNIT ; 2000 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Kogenate fs	antihemophilic factor recomb (rfviii) for inj kit	1000 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Kovaltry	antihemophilic factor recomb (rahf-pfm) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Novoeight	antihemophilic fact rcmb (bd trunc-rfviii) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Nuwiq	antihemophil fact rcmb (bdd-rfviii,sim) for inj kit ; antihemophil fact rcmb(bdd-rfviii,sim) for inj kit	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 2500 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Nuwiq	antihemophilic fact rcmb (bdd-rfviii,sim) for inj ; antihemophilic factor rcmb (bdd-rfviii,sim) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 2500 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Recombinate	antihemophilic factor recomb (rfviii) for inj	1241 -1800 UNIT ; 1801 -2400 UNIT ; 220 -400 UNIT ; 401 -800 UNIT ; 801 -1240 UNIT	Commercial ; HIM ; ResultsRx
Vonvendi	von willebrand factor (recombinant) for inj	1300 UNIT ; 650 UNIT	Commercial ; HIM ; ResultsRx
Wilate	antihemophilic factor/vwf (human) for inj	1000 UNIT ; 1000-1000 UNIT ; 1000-2400 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 250-600 UNIT ; 500 UNIT ; 500-1200 UNIT ; 500-500 UNIT	Commercial ; HIM ; ResultsRx
Xyntha ; Xyntha solofuse	antihemophil fact rcmb (bdd-rfviii,mor) for inj kit ; antihemophil fact rcmb(bdd-rfviii,mor) for inj kit	1000 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Advate ; Kovaltry	antihemophilic factor recomb (rahf-pfm) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Adynovate	antihemophilic factor recomb pegylated for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 500 UNIT ; 750 UNIT	Commercial ; HIM ; ResultsRx
Afstyla	antihemophilic fact rcmb single chain for inj kit	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 2500 UNIT ; 3000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Alphanate ; Humate-p	antihemophilic factor/vwf (human) for inj	1000 UNIT ; 1000-2400 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 250-600 UNIT ; 500 UNIT ; 500-1200 UNIT	Commercial ; HIM ; ResultsRx

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Altuviiio	antihemophilic fact rcmb fc-vwf-xten-ehtl for inj	1000 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT ; 750 UNIT	Commercial ; HIM ; ResultsRx
Eloctate	antihemophilic factor rcmb (bdd-rfviiifc) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT ; 5000 UNIT ; 6000 UNIT ; 750 UNIT	Commercial ; HIM ; ResultsRx
Esperoct	antihemophilic factor recomb glycopeg-exei for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Hemofil m ; Koate ; Koate-dvi	antihemophilic factor (human) for inj	1000 UNIT ; 1700 UNIT ; 250 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Jivi	antihemophil fact rcmb(bdd-rfviii peg-aucl) for inj ; antihemophil fact rcmb(bdd-rfviii peg-aucl)for inj	1000 UNIT ; 2000 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Kogenate fs	antihemophilic factor recomb (rfviii) for inj kit	1000 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Novoeight	antihemophilic fact rcmb (bd trunc-rfviii) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Nuwiq	antihemophil fact rcmb (bdd-rfviii,sim) for inj kit ; antihemophil fact rcmb(bdd-rfviii,sim) for inj kit	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 2500 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Nuwiq	antihemophilic fact rcmb (bdd-rfviii,sim) for inj ; antihemophilic factor rcmb (bdd-rfviii,sim) for inj	1000 UNIT ; 1500 UNIT ; 2000 UNIT ; 250 UNIT ; 2500 UNIT ; 3000 UNIT ; 4000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx
Recombinate	antihemophilic factor recomb (rfviii) for inj	1241 -1800 UNIT ; 1801 -2400 UNIT ; 220 -400 UNIT ; 401 -800 UNIT ; 801 -1240 UNIT	Commercial ; HIM ; ResultsRx
Vonvendi	von willebrand factor (recombinant) for inj	1300 UNIT ; 650 UNIT	Commercial ; HIM ; ResultsRx
Wilate	antihemophilic factor/vwf (human) for inj	1000-1000 UNIT ; 500-500 UNIT	Commercial ; HIM ; ResultsRx
Xyntha ; Xyntha solofuse	antihemophil fact rcmb (bdd-rfviii,mor) for inj kit ; antihemophil fact rcmb(bdd-rfviii,mor) for inj kit	1000 UNIT ; 2000 UNIT ; 250 UNIT ; 3000 UNIT ; 500 UNIT	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** All target agents are eligible for continuation of therapy 1. The patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR** 2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR**

Module	Clinical Criteria for Approval
	B. BOTH of the following: 1. ONE of the following: A. The patient has a diagnosis of hemophilia A (also known as Factor VIII deficiency or classic hemophilia) AND ONE of the following: 1. The patient is currently experiencing a bleed AND BOTH of the following: A. The patient is out of medication **AND** B. The patient needs to receive a ONE TIME emergency supply of medication **OR** 2. ALL of the following: A. The requested agent is FDA labeled or compendia supported for a diagnosis of hemophilia A **AND** B. The requested agent is being used for ONE of the following: 1. Prophylaxis AND the patient will NOT be using the requested agent in combination with Hemlibra (emicizumab-kxwh) **OR** 2. As a component of Immune Tolerance Therapy (ITT)/Immune Tolerance Induction (ITI) AND BOTH of the following: A. The patient will NOT be using the requested agent in combination with Hemlibra (emicizumab-kxwh) **AND** B. ONE of the following: (medical records required) 1. The patient has NOT had more than 33 months of ITT/ITI therapy **OR** 2. There is support for the continued use of ITT/ITI therapy (i.e., the patient has had a greater than or equal to 20% decrease in inhibitor level over the last 6 months and needs further treatment to eradicate inhibitors) **OR** 3. On-demand use for bleeds **OR** 4. Peri-operative management of bleeding **AND** C. If the client has a preferred agent(s), then ONE of the following: 1. The requested agent is a preferred agent **OR** 2. The patient has tried and had an inadequate response to ALL of the preferred agent(s) **OR** 3. The patient has an intolerance or hypersensitivity to ALL of the preferred agent(s) **OR** 4. The patient has an FDA labeled contraindication to ALL of the preferred agents **OR** B. The patient has a diagnosis of von Willebrand disease (VWD) AND ALL of the following:

Module	Clinical Criteria for Approval
	1. The requested agent is FDA labeled or compendia supported for a diagnosis of von Willebrand disease **AND** 2. ONE of the following: A. The patient is currently experiencing a bleed AND BOTH of the following: 1. The patient is out of medication **AND** 2. The patient needs to receive a ONE TIME emergency supply of medication **OR** B. The patient has type 1, 2A, 2M or 2N VWD AND ONE of the following: 1. The patient has tried and had an inadequate response to desmopressin (e.g., DDAVP injection, Stimate nasal spray) **OR** 2. The patient did not respond to a DDAVP trial with 1 and 4 hour post infusion bloodwork **OR** 3. The patient has an intolerance or hypersensitivity to desmopressin **OR** 4. The patient has an FDA labeled contraindication to desmopressin **OR** 5. The patient cannot use desmopressin (e.g., shortage in marketplace) **OR** C. The patient has type 2B or 3 VWD **AND** 3. The requested agent will be used for ONE of the following: A. Prophylaxis AND ONE of the following: 1. The requested agent is Vonvendi AND ONE of the following: A. The patient has severe Type 3 VWD **OR** B. The patient has another subtype of VWD AND the subtype is FDA labeled for prophylaxis use **OR** 2. The requested agent is NOT Vonvendi **OR** B. On-demand use for bleeds **OR** C. Peri-operative management of bleeding **AND** 4. If the client has a preferred agent(s), then ONE of the following: A. The requested agent is a preferred agent **OR** B. The patient has tried and had an inadequate response to ALL of the preferred agent(s) for the requested indication **OR** C. The patient has an intolerance or hypersensitivity to ALL of the preferred agent(s) for the requested indication **OR** D. The patient has an FDA labeled contraindication to ALL of the preferred agents for the requested indication **AND** 2. If the patient has an FDA labeled indication, ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 2. The prescriber is a specialist in the area of the patient's diagnosis [e.g., prescriber working in a hemophilia treatment center (HTC), hematologist with hemophilia experience] or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND**

Module	Clinical Criteria for Approval
	3. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 4. The prescriber must provide the actual prescribed dose with ALL of the following: A. Patient's weight **AND** B. Intended use/regimen: (e.g., prophylaxis, ITT/ITI, on-demand, peri-operative) **AND** C. If the patient has a diagnosis of hemophilia A BOTH of the following: 1. Severity of the factor deficiency (i.e., severe is less than 1% factor activity, moderate is greater than or equal to 1 to less than or equal to 5% factor activity, mild is greater than 5 to 40% factor activity) **AND** 2. Inhibitor status **AND** 5. ONE of the following: A. The patient will NOT be using the requested agent in combination with another agent in the same category (e.g., Factor VIII agents, Factor VIII and von Willebrand Factor combination agents) included in this program **OR** B. There is support for the use of more than one unique agent in the same category (medical records required) **AND** 6. ONE of the following: A. The requested quantity (dose) does NOT exceed the program quantity limit defined by BOTH of the following: 1. The requested dose is within the FDA labeled dosing **AND** 2. The requested quantity (number of doses) is appropriate based on intended use (e.g., prophylaxis, ITT/ITI, on-demand) **OR** B. The prescriber has provided clinical reasoning for exceeding the appropriate quantity limit based on the FDA labeled dose and/or intended use (medical records required) **Compendia Allowed:** AHFS, or DrugDex 1 or 2a level of evidence **Length of Approval:** One time emergency use: up to 2 weeks, Peri-operative dosing: 1 time per request. On-demand: up to 3 months, Prophylaxis: up to 12 months, ITT/ITI: up to 6 months - or up to a total of 33 months of ITT/ITI therapy, or requested duration whichever is shortest **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Medical Drug Review process (if current request is for ONE TIME emergency use or if patient ONLY has previous approval(s) for emergency use, must use Initial Evaluation) (Note: patients not previously approved for the requested agent will require initial evaluation review) **AND** 2. If the patient is using the requested agent for prophylaxis, then ONE of the following: A. The patient has a diagnosis of hemophilia A AND the patient will NOT be using the requested agent in combination with Hemlibra (emicizumab-kxwh) **OR** B. The patient has another diagnosis **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis [e.g., prescriber working in a hemophilia treatment center (HTC), hematologist with hemophilia experience] or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 5. The prescriber must provide the actual prescribed dose with ALL of the following: A. Patient's weight **AND** B. Intended use/regimen: (e.g., prophylaxis, ITT/ITI, on-demand, peri-operative) **AND**

Module	Clinical Criteria for Approval
	C. If the patient has a diagnosis of hemophilia A BOTH of the following: 1. Severity of the factor deficiency (i.e., severe is less than 1% factor activity, moderate is greater than or equal to 1 to less than or equal to 5% factor activity, mild is greater than 5 to 40% factor activity) **AND** 2. Inhibitor status **AND** 6. ONE of the following: A. The prescriber communicated with the patient (via any means) regarding the frequency and severity of the patient's bleeds and has verified that the patient does not have greater than 5 on-demand doses on hand **OR** B. There is support for the patient having more than 5 on-demand doses on hand **AND** 7. ONE of the following: A. The patient will NOT be using the requested agent in combination with another agent in the same category (e.g., Factor VIII agents, Factor VIII and von Willebrand Factor combination agents) included in this program **OR** B. There is support for the use of more than one unique agent in the same category (medical records required) **AND** 8. If the patient is using Immune Tolerance Therapy (ITT)/Immune Tolerance Induction (ITI), then BOTH of the following: A. The patient will NOT be using the requested agent in combination with Hemlibra (emicizumab-kxwh) **AND** B. ONE of the following: (medical records required) 1. The patient has NOT had more than 33 months of ITT/ITI therapy **OR** 2. There is support for the continued use of ITT/ITI therapy (i.e., the patient has had a greater than or equal to 20% decrease in inhibitor level over the last 6 months and needs further treatment to eradicate inhibitors) **AND** 9. ONE of the following: A. The requested quantity (dose) does NOT exceed the program quantity limit defined by BOTH of the following: 1. The requested dose is within the FDA labeled dosing **AND** 2. The requested quantity (number of doses) is appropriate based on intended use (e.g., prophylaxis, ITT/ITI, on-demand, peri-operative) **OR** B. The prescriber has provided clinical reasoning for exceeding the appropriate quantity limit based on the FDA labeled dose and/or route of administration (medical records required) **Length of Approval:** Peri-operative dosing: 1 time per request, On-demand: up to 3 months, Prophylaxis: up to 12 months, ITT/ITI: up to 6 months -or up to a total of 33 months of ITT/ITI therapy, or requested duration, whichever is shortest