

Medical Drug Clinical Criteria

Subject:	Agents for Hemophilia A and von Willebrand Disease		
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Overview

This document addresses select agents for hereditary or congenital hemophilia A, also called factor VIII (FVIII) deficiency or classic hemophilia and select agents for von Willebrand disease. Acquired hemophilia A (also called acquired factor VIII deficiency) is a rare autoimmune disorder, and not a congenital disease. Acquired hemophilia A requires individualized treatment, which is addressed by some of the agents in this document. This document does not address fibrin products, fibrin sealants and blood products provided by blood banks. Bypassing agents (i.e., NovoSeven RT, SevenFact, and FEIBA) for those who develop antibodies or inhibitors to factor products, and Stimate (desmopressin acetate) intranasal spray are discussed in separate documents.

Factor replacement treatments can be created from blood products (human plasma-derived) and others that are manufactured (recombinant). Replacement therapy may be given on a routine, preventive basis which is also called prophylactic therapy. The infusion of factor replacements given to stop a bleeding episode is called on-demand or episodic therapy. While the World Federation of Hemophilia (WFH) (Srivastava 2020) does not place a preference between plasma-derived and recombinant products, the U.S. National Hemophilia Federation (NHF 2020) recommends recombinant over plasma-derived due the possibility of virus transmission. WFH states that the choice between the two classes of products must be made according to the availability, cost, and patient preferences.

Products in this document include:

- Anti-hemophilic factor (factor VIII) Human plasma derived
 - Hemofil-M, Koate-DVI
- Anti-hemophilic factor (factor VIII) Recombinant
 - Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, Xyntha/Xyntha Solofuse
- Anti-hemophilic factor (factor VIII) – Long acting
 - Recombinant, Pegylated – Adynovate,
 - Recombinant, Pegylated damactocog alfa pegol – Jivi
 - Recombinant Fc Fusion Protein–Eloctate
 - Recombinant, Glycopegylated– Esperoct
 - Recombinant Anti-hemophilic factor Fc-VWF-XTEN Fusion Protein-ehtl – Altuviiiio
- Anti-hemophilic bispecific factor (Factor IXa- and Factor X-)
 - Hemlibra (emicizumab-kxwh)
- Anti-hemophilic Factor VIII (Recombinant), Porcine Sequence
 - Obizur
- Anti-hemophilic Factor VIII/von Willebrand Factor Complex
 - Alphanate, Humate-P, Wilate
- von Willebrand factor, Recombinant
 - Vonvendi

Hereditary hemophilia A is the most common type of hemophilia. Although it is usually inherited, about one third of cases are caused by spontaneous mutations. Hemophilia A is related to mutations in the gene coding for coagulation Factor VIII, and it is four times more common than hemophilia B (CDC 2014), the second most common hemophilia type.

The World Federation of Hemophilia (Srivastava 2020) and International Society on Thrombosis and Haemostasis (ISTH) (Rezende 2024) both note there is a relationship of bleeding severity to the clotting factor level. Mild disease is identified as a clotting factor level of >5-40 IU/dl or 5 to < 40% of normal. A bleeding episode for individuals with mild risk includes severe bleeding with major trauma or surgery. Individuals with 1-5 IU/dl or 1-5% of normal are considered “moderate” risk for occasional spontaneous bleeding and prolonged bleeding with minor trauma or surgery (Srivastava 2020). Severe hemophilia is defined as a clotting factor level < 1 IU/dl or < 1% of normal.

Hemophilia severity:

- Severe hemophilia – Severe hemophilia is defined as < 1 percent factor activity, which corresponds to < 1 IU/dL.
- Moderate hemophilia – Moderate hemophilia is defined as a factor activity level ≥ 1 percent of normal and ≤ 5 percent of normal, corresponding to ≥ 1 and ≤ 5 IU/dL.
- Mild hemophilia – Mild hemophilia is defined as a factor activity level > 5 percent of normal and < 40 percent of normal (> 5 and < 40 IU/dL).

World Federation of Hemophilia 2020 Guidelines for treatment of hemophilia state that prophylaxis prevents bleeding and joint destruction, and that prophylaxis should enable those with hemophilia to lead healthy and active lives. Moreover, the updated 2020 guidelines proposes that the definition of prophylaxis be based on outcomes rather than doses or timing of initiation, and treatment regimens that take into account the hemophilic phenotype of the individual in addition to factor levels. The WFH 2020 guidelines have been endorsed by several societies worldwide, including the U.S. NHF. ISTH endorses prophylaxis treatment for individuals with moderate to severe disease (Rezende 2024). Short-term prophylaxis (of 4 to 8 weeks) may interrupt the bleeding cycle and benefit individuals with repeated bleeding into target joints. Prophylaxis does not reverse existing joint damage but reduces bleeding and may slow progression of joint damage. Prophylactic clotting factor administration is recommended prior to the individual engaging in activities with higher risk of injury. Randomized trials of prophylactic therapy of hemophilia have demonstrated a decreased incidence of arthropathy (Gringeri 2011; Manco-Johnson 2007).

Von Willebrand disease (VWD) is the most common inherited bleeding disorder. It is caused by missing or defective von Willebrand factor (VWF), a clotting protein. Unlike hemophilia, which very rarely occurs in females, von Willebrand disease can occur equally in men and women. There are three main types of hereditary VWD – type 1 (most common), type 2, and type 3. The types are classified by their level of VWF in the blood or by the presence or behavior of the VWF chains. VWD can be caused by an autoimmune disorder or as a result of certain medications. This is called acquired von Willebrand disease. Those with VWD can experience frequent nosebleeds, easy bruising, and excessive bleeding after during and after surgical procedures. Women may have heavy and long lasting menstrual periods and hemorrhaging after childbirth (NHF).

Hemlibra has a black box warning for thrombotic microangiopathy and thromboembolism, especially when administered with activated prothrombin complex concentrate (aPCC).

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Hemofil M, Koate/Koate-DVI (Factor VIII Human plasma-derived)

Initial requests for Hemofil M or Koate/Koate-DVI (Factor VIII, human plasma-derived) may be approved if the following criteria are met:

- I. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
- II. Individual is using for the treatment of bleeding episodes;

OR

- III. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
- IV. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
- V. Individual has a diagnosis of moderate to severe hemophilia A (defined as 5 International Units per deciliter [5IU/dL] or 5% or less endogenous Factor VIII) (Rezende 2024);

OR

- VI. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
- VII. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
- VIII. Individual has a diagnosis of mild hemophilia A (defined as endogenous Factor VIII less than 40 IU/dL [less than 40%], but greater than 5 IU/dL) (NHF, Srivastava 2020); **AND**
- IX. Individual has one of the following (NHF, Srivastava 2020):
 - A. One or more episodes of spontaneous bleeding into joint; **OR**
 - B. One or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
 - C. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

Initial requests for Koate/Koate-DVI (Factor VIII, human plasma-derived) may be approved if the following criteria are met:

- I. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
- II. Individual is using for peri-procedural management for surgical, invasive or interventional radiology procedures.

Continuation requests for Hemofil M or Koate/Koate-DVI (Factor VIII, human plasma-derived) may be approved if the following criteria are met:

- I. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
- II. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Hemofil M, Koate/Koate-DVI (Factor VIII, human plasma-derived) may not be approved for the following:

- I. Individual is using for the treatment of von Willebrand disease (VWD); **OR**
- II. When the above criteria are not met and for all other indications.

Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, Xyntha/Xyntha Solofuse (Factor VIII Recombinant)

Initial requests for Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, or Xyntha/Xyntha Solofuse (Factor VIII recombinant) may be approved if the following criteria are met:

- I. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
- II. Individual is using for one of the following:
 - A. Treatment of bleeding episodes; **OR**
 - B. Peri-procedural management for surgical, invasive or interventional radiology procedures;

OR

- III. Individual has a diagnosis of von Willebrand disease; **AND**
- IV. Individual is using for the treatment of bleeding episodes; **AND**
- V. Individual is using in combination with Vonvendi (recombinant von Willebrand factor complex); **AND**
- VI. Individual has a baseline factor VIII level less than 40 IU/dL [less than 40%] or are unknown (Vonvendi 2018);

OR

- VII. Individual has a diagnosis of von Willebrand disease; **AND**
- VIII. Individual is using for peri-procedural management for surgical, invasive or interventional radiology procedures; **AND**
- IX. Individual is using in combination with Vonvendi (recombinant von Willebrand factor complex); **AND**
- X. Individual has a baseline factor VIII level less than 30 IU/dL [less than 30%] or are unknown (Vonvendi 2018).

Initial requests for Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, or Xyntha/Xyntha Solofuse (Factor VIII recombinant) may be approved if the following criteria are met:

- I. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
- II. Individual has a diagnosis of moderate to severe hemophilia A (defined as 5 International Units per deciliter [5IU/dL] or 5% or less endogenous Factor VIII) (Rezende 2024);

OR

- III. Individual has a diagnosis of mild hemophilia A (defined as endogenous Factor VIII less than 40 IU/dL [less than 40%], but greater than 5 IU) (NHF, Srivastava 2020); **AND**
- IV. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
- V. Individual has one of the following:
 - A. One or more episodes of spontaneous bleeding into joint; **OR**
 - B. One or more episodes of severe, life-threatening, spontaneous bleeding as determined by the prescriber ; **OR**
 - C. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

Initial requests for Kogenate FS (Factor VIII recombinant) may be approved if the following criteria are met:

- I. Individual is 16 years of age or younger; **AND**
- II. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
- III. Individual is using as routine prophylaxis to reduce the risk of joint damage in those without pre-existing joint damage.

Initial requests for Recombinate (Factor VIII recombinant) may be approved if the following criteria are met:

- I. Individual is using for the treatment of acquired Factor VIII inhibitors not exceeding 10 Bethesda Unit (BU) per milliliter (mL).

Continuation requests for Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, or Xyntha/Xyntha Solofuse (Factor VIII recombinant) may be approved if the following criteria are met:

- I. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia) or von Willebrand disease (VWD); **AND**
- II. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, or Xyntha/Xyntha Solofuse (Factor VIII recombinant) may not be approved for the following:

- I. Individual is using as monotherapy for the maintenance treatment of von Willebrand disease; **OR**
- II. When the above criteria are not met and for all other indications.

Long Acting Agents: Adynovate (Factor VIII Long-Acting Recombinant, pegylated), Jivi (Factor VIII Recombinant, PEGylated damactocog alfa pegol), Elocate (Factor VIII Recombinant Anti-hemophilic Factor Fc Fusion Protein), Esperoct (Factor VIII Recombinant, glycopegylated), or Factor VIII Recombinant Antihemophilic Factor FC-VWF-XTEN Fusion Protein (Altuviiiio)

Initial requests for Adynovate (Factor VIII Long-Acting Recombinant, pegylated), Jivi (Factor VIII Recombinant PEGylated damactocog alfa pegol), Elocate (Factor VIII Recombinant Anti-hemophilic Factor Fc Fusion Protein), Esperoct (Factor VIII Recombinate, glycopegylated), or Altuviiiio (Factor VIII Recombinant Antihemophilic Factor FC-VWF-XTEN Fusion Protein) may be approved if the following criteria are met:

- I. Individual has a diagnosis of moderate to severe hemophilia A (defined as 5 International Units per deciliter [5IU/dL] or less endogenous Factor VIII) (Rezende 2024); **AND**
- II. Individual is using for one of the following:
 - A. Treatment of acute bleeding episodes; **OR**
 - B. Peri-procedural management for surgical, invasive or interventional radiology procedures; **OR**
 - C. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes;**AND**
- III. If using Jivi, individual is 12 years of age or older and has been previously treated with factor VIII;

- OR**
- IV. Individual has a diagnosis of mild hemophilia A (defined as endogenous Factor VIII less than 40 IU/dL [less than 40%], but greater than 5 IU) (NHF, Srivastava 2020); **AND**
 - V. Individual is using for one of the following:
 - A. Treatment of acute bleeding episodes; **OR**
 - B. Peri-procedural management for surgical, invasive or interventional radiology procedures; **OR**
 - C. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes when one of the following:
 AND
 1. Individual has had one or more episodes of spontaneous bleeding into joint; **OR**
 2. Individual has had one or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
 3. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed;**AND**
 - VI. If using Jivi, individual is 12 years of age or older and has been previously treated with factor VIII.

Continuation requests for Adynovate (Factor VIII Long-Acting Recombinant, pegylated), Jivi (Factor VIII Recombinant PEGylated damactocog alfa pegol), Elocate (Factor VIII Recombinant Anti-hemophilic Factor Fc Fusion Protein), Esperoct (Factor VIII Recombinant, glycopegylated), or Altuviiiio (Factor VIII Recombinant Antihemophilic Factor FC-VWF-XTEN Fusion Protein) may be approved if the following criteria are met:

- I. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
- II. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Adynovate (Factor VIII Long-Acting Recombinant, pegylated), Jivi (Factor VIII Recombinant PEGylated damactocog alfa pegol), Elocate (Factor VIII Recombinant Antihemophilic Factor Fc Fusion Protein), Esperoct (Factor VIII Recombinant, glycopegylated), or Altuviiiio (Factor VIII Recombinant Antihemophilic Factor FC-VWF-XTEN Fusion Protein) may not be approved for the following:

- I. Individual is using for the treatment of von Willebrand disease; **OR**
- II. When the above criteria are not met and for all other indications.

Hemlibra (emicizumab-kxwh) - Anti-hemophilic bispecific factor --- Factor IXa and Factor X

Initial requests for Hemlibra (emicizumab-kxwh) may be approved if the following criteria are met:

- I. Individual has a diagnosis of moderate to severe hemophilia A (defined as 5 International Units per deciliter [5IU/dL] or less endogenous Factor VIII) (Rezende 2024); **AND**
- II. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
- III. Individual has one of the following:
 - A. If switching from factor VIII agents, then individual will discontinue factor VIII agents being used for routine prophylaxis after the first week of Hemlibra initiation; **OR**
 - B. If switching from bypassing agents (i.e., NovoSeven RT, SevenFact, FEIBA), then individual will discontinue bypassing agents being used for routine prophylaxis after 24 hours of Hemlibra initiation;

OR

- IV. Individual has a diagnosis of mild hemophilia A (defined as endogenous Factor VIII less than 40 IU/dL [less than 40%], but greater than 5 IU/dL) (NHF, Srivastava 2020); **AND**
- V. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
- VI. Individual has one of the following:
 - A. One or more episodes of spontaneous bleeding into joint; **OR**
 - B. One or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
 - C. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed; **AND**
- VII. Individual has one of the following:
 - A. If switching from factor VIII agents, then individual will discontinue factor VIII agents being used for routine prophylaxis after the first week of Hemlibra initiation; **OR**
 - B. If switching from bypassing agents, (i.e., NovoSeven RT, SevenFact, FEIBA), then individual will discontinue bypassing agents being used for routine prophylaxis after 24 hours of Hemlibra initiation.

Continuation requests for Hemlibra (emicizumab-kxwh) may be approved if the following criteria are met:

- I. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**
- II. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Hemlibra (emicizumab) may not be approved when the above criteria are not met and for all other indications.

Obizur (Factor VIII Recombinant, Porcine Sequence)

Initial requests for Obizur (Recombinant, Porcine Sequence) may be approved if the following criteria are met:

- I. Individual is 18 years of age or older; **AND**
- II. Individual has a diagnosis of acquired hemophilia A; **AND**
- III. Individual has baseline anti-porcine Factor VIII inhibitor titer less than or equal to 20 BU/mL; **AND**
- IV. Individual is using for the treatment of bleeding episodes.

Continuation requests for Obizur (Recombinant, Porcine Sequence) may be approved if the following criteria are met:

- I. Individual has a diagnosis of acquired hemophilia A; **AND**
- II. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Obizur (Recombinant, Porcine Sequence) may not be approved for the following:

- I. Individual has a diagnosis of congenital hemophilia A with Factor VIII deficiency; **OR**
- II. Individual has a diagnosis of congenital hemophilia A with inhibitors; **OR**
- III. Individual has a diagnosis of von Willebrand disease; **OR**
- IV. When the above criteria are not met and for all other indications.

Alphanate, Humate-P, Wilate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human)

Initial requests for Alphanate, Humate-P, or Wilate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may be approved if the following criteria are met:

- I. Individual has a diagnosis of hemophilia A (also called factor VIII deficiency or classic hemophilia); **AND**

II. Individual is using for the treatment of bleeding episodes;

OR

III. Individual has a diagnosis of moderate to severe hemophilia A (defined 5 International Units per deciliter [5IU/dL] endogenous Factor VIII) (Rezende 2024); **AND**

IV. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes;

OR

V. Individual has a diagnosis of mild hemophilia A (defined as endogenous Factor VIII less than 40 IU/dL [less than 40%], but greater than 5 IU/dL) (NHF, Srivastava 2020); **AND**

VI. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**

VII. Individual has one of the following:

- A. Individual has had one or more episodes of spontaneous bleeding into joint; **OR**
- B. Individual has had one or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
- C. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

Initial requests for Alphanate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may be approved if the following criteria are met:

- I. Individual has a diagnosis with acquired Factor VIII deficiency; **AND**
- II. Individual is using for the control and prevention of bleeding episodes.

Initial requests for Alphanate, Humate-P, Wilate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may be approved if the following criteria are met:

- I. Individual has a diagnosis of severe von Willebrand disease; **OR**
- II. Individual has a diagnosis of mild to moderate von Willebrand disease and use of desmopressin is known or suspected to be inadequate; **AND**
- III. Individual is using for one of the following:
 - A. The treatment of spontaneous or trauma-induced bleeding episodes; **OR**
 - B. Peri-procedural management for surgical, invasive or interventional radiology procedures.

Continuation requests for Alphanate, Humate-P, or Wilate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may be approved if the following criteria are met:

- I. Individual has a diagnosis of hemophilia A, von Willebrand disease, or acquired Factor VIII deficiency; **AND**
- II. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Alphanate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may not be approved for the following:

- I. Individual has a diagnosis for severe (type 3) von Willebrand Disease; **AND**
- II. Individual is undergoing major surgery;

OR

III. Individual is using for prophylaxis of spontaneous bleeding episodes in von Willebrand disease.

Humate-P and Wilate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may not be approved for the following:

- I. Individual is using for prophylaxis of spontaneous bleeding episodes in von Willebrand disease.

Alphanate, Humate-P, Wilate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) may not be approved when the above criteria are not met and for all other indications.

Vonvendi (Recombinant von Willebrand Factor Complex)

Initial requests for Vonvendi (Recombinant von Willebrand Factor Complex) may be approved if the following criteria are met:

- I. Individual is 18 years of age or older; **AND**
- II. Individual is using for one of the following:
 - A. Individual has a diagnosis of severe von Willebrand disease; **OR**

- B. Individual has a diagnosis of mild to moderate von Willebrand disease and use of desmopressin is known or suspected to be inadequate;

AND

- III. Individual is using for one of the following:
 - A. Individual is using to treat spontaneous or trauma-induced bleeding episodes, or for peri-procedural management for surgical, invasive or interventional radiology procedures; **OR**
 - B. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes receiving on-demand therapy.

Continuation requests for Vonvendi (Recombinant von Willebrand Factor Complex) may be approved if the following criteria are met:

- I. Individual has a diagnosis of von Willebrand disease (VWD); **AND**
- II. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Vonvendi (Recombinant von Willebrand Factor Complex) may not be approved when the above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Anti-hemophilic Factor VIII, Human plasma-derived (Hemofil M, Koate-DVI) or Porcine

HCPCS

J7190 Factor VIII Anti-hemophilic factor, human, per IU [Hemofil M, Koate DVI,]

ICD-10 Diagnosis

D66 Hereditary factor VIII deficiency [hemophilia A]
 D68.00-D68.09 Von Willebrand's disease
 D68.311 Acquired hemophilia
 D68.318 Other hemorrhagic disorder due to intrinsic circulating anticoagulants, antibodies, or inhibitors
 D68.4 Acquired coagulation factor deficiency
 Z29.89 Encounter for other specified prophylactic measure
 Z79.899 Other long term (current) drug therapy [prophylactic]

Anti-hemophilic Factor VIII, Recombinant (Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, Xyntha/Xyntha Solofuse)

HCPCS

J7182 Injection, factor VIII, (Anti-hemophilic factor, recombinant), (Novoeight), per IU
 J7185 Injection, factor VIII (Anti-hemophilic factor, recombinant) (Xyntha) (Xyntha Solofuse), per IU
 J7192 Factor VIII (Anti-hemophilic factor, recombinant) per IU, not otherwise specified [Advate, Kogenate-FS, Recombinate]
 J7209 Injection, factor VIII, (Anti-hemophilic factor, recombinant), (Nuwiq), 1 I.U.
 J7210 Injection, factor VIII, (Anti-hemophilic factor, recombinant), (Afstyla), 1 I.U.
 J7211 Injection, factor VIII, (Anti-hemophilic factor, recombinant), (Kovaltry), 1 I.U.

ICD-10 Diagnosis

D66 Hereditary factor VIII deficiency [hemophilia A]
 D68.00-D68.09 Von Willebrand's disease
 D68.311 Acquired hemophilia

D68.318	Other hemorrhagic disorder due to intrinsic circulating anticoagulants, antibodies, or inhibitors
D68.4	Acquired coagulation factor deficiency
Z29.89	Encounter for other specified prophylactic measure
Z79.899	Other long term (current) drug therapy [prophylactic]

Anti-hemophilic Factor VIII, Long Acting Recombinant, pegylated (Adynovate); Jivi (damoctocog alfa pego); Recombinant Anti-hemophilic Factor, Fc Fusion Protein (Elocatate), Factor VIII Recombinant, glycopegylated (Esperoct), glycopegylated (Esperoct), Factor VIII Recombinant Antihemophilic Factor, Fc-VWF-XTEN Fusion Protein (Altuviio)

HCPCS

J7205	Injection, factor VIII Fc fusion protein, (recombinant), per IU [Elocatate]
J7207	Injection, factor VIII, (anti-hemophilic factor, recombinant), pegylated, 1 I.U. [Adynovate]
J7208	Injection, factor viii, (antihemophilic factor, recombinant), pegylated-aucl, [Jivi], 1 i.u.
J7204	Injection, factor viii, (antihemophilic factor (recombinant), glycopegylated-exei, per iu [Esperoct]
J7214	Injection, Factor VIII/von Willebrand factor complex, recombinant (Altuviio), per Factor VIII IU

ICD-10 Diagnosis

D66	Hereditary factor VIII deficiency
D68.00-D68.09	Von Willebrand's disease
D68.311	Acquired hemophilia
Z29.89	Encounter for other specified prophylactic measure
Z79.899	Other long term (current) drug therapy [prophylactic]

Anti-hemophilic Factor VIII Recombinant, Porcine Sequence (Obizur)

HCPCS

J7188	Injection, factor VIII (Anti-hemophilic factor, recombinant), (Obizur), per I.U.
J7191	Factor VIII, Anti-hemophilic factor (porcine), per IU

ICD-10 Diagnosis

D68.311	Acquired hemophilia
D68.318	Other hemorrhagic disorder due to intrinsic circulating anticoagulants, antibodies, or inhibitors
D68.4	Acquired coagulation factor deficiency

Anti-hemophilic Factor VIII/Von Willebrand Factor Complex (Alphanate, Humate-P, Wilate)

HCPCS

J7183	Injection, Von Willebrand factor complex (human) 1 IU VWF:RCO [Wilate]
J7186	Injection, antihemophilic factor VIII/Von Willebrand factor complex (human), per factor VIII I.U. [Alphanate]
J7187	Injection, Von Willebrand factor complex, per IU, VWF:RCO [Humate-P]

ICD-10 Diagnosis

D66	Hereditary factor VIII deficiency
D68.00-D68.09	Von Willebrand's disease
D68.311	Acquired hemophilia
D68.318	Other hemorrhagic disorder due to intrinsic circulating anticoagulants, antibodies, or inhibitors
D68.4	Acquired coagulation factor deficiency
Z29.89	Encounter for other specified prophylactic measure

Z79.899 Other long term (current) drug therapy [prophylactic]

Von Willebrand factor, Recombinant (Vonvendi)

HCPCS

J7179 Injection, Von Willebrand factor (recombinant), (Vonvendi), 1 I.U. VWF:RCO

ICD-10 Diagnosis

D68.00-D68.09 Von Willebrand's disease

D68.311 Acquired hemophilia

Z29.89 Encounter for other specified prophylactic measure

Hemlibra (emicizumab) - Anti-hemophilic bispecific factor --- Factor IXa and Factor X

HCPCS

J7170 Injection, emicizumab-kxwh, 0.5 mg [Hemlibra]

ICD-10 Diagnosis

D66 Hereditary factor VIII deficiency [hemophilia A]

D68.00-D68.09 Von Willebrand's disease

D68.311 Acquired hemophilia

Z29.89 Encounter for other specified prophylactic measure

Z79.899 Other long term (current) drug therapy [prophylactic]

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Document History:

- 04/04/2025 – Coding Update: Removed ICD-10-CM Z29.8 and replaced with Z29.89 for anti-hemophilic factor VIII human plasma-derived or porcine, anti-hemophilic factor VIII recombinant, anti-hemophilic factor VIII long-acting recombinant pegylated, Jivi, Elocate, Esperoct, Altuviio, Alphanate, Humate-P, Wilate, Vonvendi, Hemlibra.
- 11/15/2024 – Annual Review: update continuation criteria to include diagnosis, add moderate disease to prophylaxis treatment. Coding Reviewed: Added header for Hemofil M/Koate-DVI. Remove all diagnoses pend for Altuviio statement. Removed code effective date note from Hemlibra.
- 11/17/2023 – Annual Review: Add to Obizur do not approve criteria. Coding Reviewed: No changes.
- 03/13/2023 – Select Review: Add new FDA approved Altuviio to long-acting agents criteria and step therapy. Coding Reviewed: Added HCPCS J3490, J3590. Effective 7/21/2023 Added HCPCS J7199, C9399 for Altuviio. Removed J3590, J3490. Effective 10/1/2023 Added HCPCS J7214 for Altuviio. Removed HPCS J7199, C9399.
- 11/18/2022 – Annual Review: Add Kogenate FS for prophylaxis, modify prophylaxis language, wording and formatting. Coding Reviewed: Added ICD-10-CM D68.00-D68.09.
- 05/20/2022 Administrative update to remove documentation. Select Review: Update Vonvendi indications to include routine prophylaxis. Coding Reviewed: No changes.
- 11/19/2021 – Annual Review: Remove obsolete agents Helixate FS and Monoclate-P. Add Xyntha Solofuse to document. Clarify use of Hemlibra when switching from factor VIII or bypassing agents. Add continuation criteria for all agents. Wording and formatting changes. Coding reviewed: Removed word Helexate FS from J7192, Removed Monoclate-P from J7186 and J7190. Added Xyntha Solofuse to J7185.
- 08/01/2021 - Administrative update to add documentation.
- 11/20/2020 – Annual Review: Update Factor VIII Human Plasma-derived and Recombinant agents to allow for prophylactic use in those with mild to moderate disease with severe phenotype hemophilia per guidelines. Update Obizur criteria to allow for treatment and control of bleeding episodes per label. Update step therapy criteria to allow override for those with venous access difficulties. Update references. Wording and formatting changes. Coding Reviewed: Added ICD-10-CM D68.311 to Recombinant agents. Effective 1/28/2021 Added ICD-10-CM D68.311 to HCPCS J7170. Added ICD-10-CM codes D66, D68.0, Z29.8, Z79.899 to HCPCS codes J7183, J7186 & J7187.
- 11/15/2019 – Annual Review: Updates as follows:
 - Moved Factor IX agents, FEIBA, NovoSeven RT, Coagadex, Factor XIII, and Fibrinogen Concentrates into separate documents. Renamed document to include only agents for hemophilia A and von Willebrand disease. Coding Review: Added HCPCS J7204 for Esperoct Effective 7/1/2020, Delete term Esperoct from J7192 as of 6/30/2020

- Clarified and updated other names for hemophilia A, and clarified control and prevention of acute bleeding episodes as “treatment”. Coding Reviewed: Added HCPCS J7192 for Esperoct
- Add new criteria and step therapy for Esperoct (recombinant factor VIII, glycopegylated).
- Updated criteria for Anti-hemophilic factor (factor VIII) Recombinant agents in VWD to remove combination use with factor VIII/VWD agents and allow use with non-VWD containing agents only (i.e., Vonvendi) per Vonvendi label.
- Updated criteria for Anti-hemophilic factor (factor VIII) Recombinant agents in VWD to allow use in perioperative management of bleeding.
- Clarified criteria for Anti-hemophilic factor (factor VIII) Recombinant agents in mild to moderate hemophilia A to allow for prophylactic use.
- Updated non-approvable criteria for Anti-hemophilic factor (factor VIII) Recombinant agents in VWD to restrict monotherapy maintenance use.
- Update Hemlibra criteria to restrict combination use with other prophylactic agents except during initiation period.
- Updated Alphanate criteria to allow use for control and prevention of bleeds in acquired hemophilia A per label.
- Updated non-approvable criteria for Alphanate and Wilate to restrict prophylactic use in VWD.
- Clarified Humate-P non-approvable criteria to restrict prophylactic use in VWD.
- Update criteria to allow use of Wilate for hemophilia A per label.
- Wording and formatting changes for clarity and consistency.
- 07/01/2019 – HCPCS and Coding Review: Add J7208 and delete C9141 and J7192 for Jivi.
- 11/16/2018 – Annual review: Initial review of CG-DRUG 78 Hemophilia Agents policy. The following updates are proposed:
 - Jivi (Factor VIII Recombinant PEGylated) was added to the Long-Acting agents override criteria
 - May not approve criteria from the FDA label was added to select agents
 - Hemlibra Prior Authorization for all ages and use in those with hemophilia A for routine prophylaxis to prevent or reduce the frequency of bleeding episodes.
 - Coagadex criteria updated to reflect updated FDA label
 - Included off-label compendia references for override criteria
 - Updated Non-Preferred Anti-Hemophilia Agents Step Therapy with new agents—Jivi and Hemlibra, included separate category for Hemlibra (only SC formulation available), and minor wording and formatting updates to clarify existing override criteria. HCPCS and Coding review: Added HCPCS J7192, J7170, J7183, J7186, J7187, J7203, J7177. Deleted HCPCS Q9995, C9468, J7195. Added ICD-10 D66, D68.0, D68.311, D68.318, D68.4, Z29.8, Z79.899. Deleted ICD-10 D68.0.
 - HCPCS and Coding review: Add C9141 and delete J7192 for Jivi. Re-added J7192 for Jivi.

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