

Medical Policy

Healthcare Services Department

Policy Name Agents for Hemophilia A and Von Willebrand Disease	Policy Number MP-RX-FP-02-23	Scope ☒ MMM MA ☒ MMM Multihealth
Service Category ☐ Anesthesia ☐ Surgery ☐ Radiology Procedures ☐ Pathology and Laboratory Procedures ☐ Medicine Services and Procedures ☐ Evaluation and Management Services ☐ DME/Prosthetics or Supplies ☒ Part B Drugs		
Service Description This document addresses the use of <i>Antihemophilic Factor VIII Human plasma derived [Koate, Hemofil-M], Antihemophilic Factor VIII (Recombinant) Plasma/Albumin-Free [Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwix, Recombinate, Xyntha/Xyntha Solofuse], Antihemophilic Factor (factor VIII) – Long acting [Adynovate, Jivi, Eloctate, Esperoct, Altuviiio], 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], Qfitlia (fitsuran),</i> drugs approved by the Food and Drug Administration (FDA) for the treatment of Hemophilia A and von Willebrand Disease. Background Information Agents in this document are used for hereditary or congenital hemophilia A, also called factor VIII (FVIII) deficiency or classic hemophilia. Acquired hemophilia A (also called acquired factor VIII deficiency) is a rare autoimmune disorder, and not a congenital disease. 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. <u>Definitions and Measures:</u> Products in this document include: • Anti-hemophilic factor (factor VIII) Human plasma derived: Hemofil-M, Koate-DVI		

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
• Anti-hemophilic factor (factor VIII) Recombinant: Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiiq, Recombinate, Xyntha/Xyntha Solofuse • Anti-hemophilic factor (factor VIII) – Long acting - o Recombinant, Pegylated – Adynovate, - o Recombinant, Pegylated damactocog alfa pegol – Jivi - o Recombinant Fc Fusion Protein–Eloctate - o Recombinant, Glycopegylated– Esperoct o Recombinant Anti-hemophilic factor Fc-VWF-XTEN Fusion Protein-ehtl – Altuviiio • 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 • Antithrombin-directed small interfering ribonucleic acid: Qfitlia (fitsuran) 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 U.S. National Hemophilia Foundation (NHF) and the World Federation of Hemophilia (Srivastava 2020) both note there is a relationship of bleeding severity to the clotting factor level. Both entities list “severe” hemophilia as a clotting factor level < 1 IU/dl or < 1% of normal. A “mild” bleeding severity 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). <i>Hemophilia severity:</i> - 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. However, more studies are needed to determine if all individuals should remain on therapy as adults (that is, those with severe hemophilia vs.		

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
moderate or mild). The WFH 2020 guidelines have been endorsed by several societies worldwide, including the U.S. NHF. 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 and during 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). Approved Indications i. Indications are drug specific, but in general, these products are used in patients with Hemophilia A and Von Willebrand disease for: A. Control and prevention of acute bleeding in patients with Hemophilia A and Von Willebrand disease. B. Routine prophylaxis to reduce the frequency of bleeding episodes in patients with Hemophilia A. C. Perioperative management of bleeding in patients with Hemophilia A and Von Willebrand disease undergoing surgical or invasive procedures. D. Treatment of bleeding episodes in patients with acquired hemophilia A. E. On-demand therapy for episodic bleeding in patients with Hemophilia A and Von Willebrand disease. F. Routine prophylaxis to prevent or reduce bleeding episodes in patients with Hemophilia A with inhibitors to factor VIII (e.g., using bypassing agents or Hemlibra). G. Control and prevention of bleeding episodes in patients requiring specialized factor VIII products, such as porcine sequence factor VIII (e.g., Obizur). H. Replacement therapy for von Willebrand factor in patients with von Willebrand disease (e.g., using recombinant or plasma-derived products). Other Uses		

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth

i. N/A

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

Anti-hemophilic factor (factor VIII) Human plasma derived: Koate-DVI, Hemofil M

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

ICD-10	Description
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
Z29.8	Encounter for other specified prophylactic measure
Z79.899	Other long term (current) drug therapy [prophylactic]

Anti-hemophilic factor (factor VIII) Recombinant: Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiiq, Recombinate, Xyntha/Xyntha Solofuse

HCPCS	Description
J7192	Factor VIII (Anti-hemophilic factor, recombinant) per IU, not otherwise specified [Advate, Kogenate-FS, Recombinate]
J7182	Injection, factor VIII, (Anti-hemophilic factor, recombinant), (Novoeight), per IU
J7185	Injection, factor VIII (Anti-hemophilic factor, recombinant) (Xyntha) (Xyntha Solofuse), per IU
J7209	Injection, factor VIII, (Anti-hemophilic factor, recombinant), (Nuwiiq), 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	Description
D66	Hereditary factor VIII deficiency [hemophilia A]
D68.00-D68.09	Von Willebrand's disease
D68.311	Acquired hemophilia

Medical Policy

Healthcare Services Department

Policy Name		Policy Number	Scope	
Agents for Hemophilia A and Von Willebrand Disease		MP-RX-FP-02-23	☒ MMM MA	☒ MMM Multihealth
D68.318	Other hemorrhagic disorder due to intrinsic circulating anticoagulants, antibodies, or inhibitors			
D68.4	Acquired coagulation factor deficiency			
Z29.8	Encounter for other specified prophylactic measure			
Z79.899	Other long term (current) drug therapy [prophylactic]			
Anti-hemophilic factor (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	Description			
J7204	Injection, factor viii, (antihemophilic factor (recombinant), glycopegylated-exei, per iu [Esperoct]			
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.			
J7214	Injection, Factor VIII/von Willebrand factor complex, recombinant (Altuviio), per Factor VIII IU			
ICD-10	Description			
D66	Hereditary factor VIII deficiency [hemophilia A]			
D68.00-D68.09	Von Willebrand's disease			
D68.311	Acquired hemophilia			
Z29.8	Encounter for other specified prophylactic measure			
Z79.899	Other long term (current) drug therapy [prophylactic]			
Anti-hemophilic Factor VIII Recombinant, Porcine Sequence (Obizur)				
HCPCS	Description			
J7188	Injection, factor VIII (Anti-hemophilic factor, recombinant), (Obizur), per I.U.			
J7191	Factor VIII, Anti-hemophilic factor (porcine), per IU			
ICD-10	Description			
D68.318	Other hemorrhagic disorder due to intrinsic circulating anticoagulants, antibodies, or inhibitors			
D68.4	Acquired coagulation factor deficiency			
D68.311	Acquired hemophilia			

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
Anti-hemophilic Factor VIII/Von Willebrand Factor Complex (Alphanate, Humate-P, Wilate)		
HCPCS	Description	
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	Description	
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	
Z29.8	Encounter for other specified prophylactic measure	
Z79.899	Other long term (current) drug therapy [prophylactic]	
Von Willebrand factor, Recombinant (Vonvendi)		
HCPCS	Description	
J7179	Injection, Von Willebrand factor (recombinant), (Vonvendi), 1 I.U. VWF:RCO	
ICD-10	Description	
D68.00-D68.09	Von Willebrand's disease	
D68.311	Acquired hemophilia	
Z29.8	Encounter for other specified prophylactic measure	
Hemlibra (emicizumab) - Anti-hemophilic bispecific factor --- Factor IXa and Factor X		
HCPCS	Description	
J7170	Injection, emicizumab-kxwh, 0.5 mg [Hemlibra] [Note: code effective 01/01/2019]	
ICD-10	Description	
D66	Hereditary factor VIII deficiency [hemophilia A]	
D68.00-D68.09	Von Willebrand's disease	
D68.311	Acquired hemophilia	
Z29.8	Encounter for other specified prophylactic measure	
Z79.899	Other long term (current) drug therapy [prophylactic]	

Medical Policy

Healthcare Services Department

Policy Name		Policy Number	Scope	
Agents for Hemophilia A and Von Willebrand Disease		MP-RX-FP-02-23	☒ MMM MA	☒ MMM Multihealth
Qfitlia (fitsuran)- Antithrombin-directed small interfering ribonucleic acid				
HCPCS		Description		
C9399		Unclassified drug or biological		
J3490		Unclassified drugs		
ICD-10		Description		
D66		Hereditary factor VIII deficiency [hemophilia A]		
D68.00-D68.09		Von Willebrand's disease		
D68.311		Acquired hemophilia		
Z29.8		Encounter for other specified prophylactic measure		
Z79.899		Other long term (current) drug therapy [prophylactic]		
Medical Necessity Guidelines				
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.				
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.				
Clinical Criteria				
Hemofil M, Koate/Koate-DVI (Factor VIII Human plasma-derived)				
A. Criteria for Initial Requests				
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 <i>hemophilia A</i> (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				

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
v. Individual has a diagnosis of severe hemophilia A (defined as less than 1 International Unit per deciliter [1IU/dL] or 1% endogenous Factor VIII) (NHF, Srivastava 2020); 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 to moderate hemophilia A (defined as endogenous Factor VIII less than 40 IU/dL [less than 40%], but greater than or equal to 1 IU) (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. B. Criteria for Continuation of Therapy 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 had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes). C. Conditions not Covered Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):		

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
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. D. Authorization Duration i. Initial Approval Duration: Up to 12 months ii. Reauthorization Approval Duration: Up to 12 months Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiiq, Recombinate, Xyntha/Xyntha Solofuse (Factor VIII Recombinant) A. Criteria for Initial Approval Initial requests for Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiiq, Recombinate, or Xyntha/Xyntha Solofuse (Factor VIII recombinant) may be approved if the following criteria are met: i. Individual has a diagnosis of <i>hemophilia A</i> (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 <i>von Willebrand disease</i>; 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 <i>von Willebrand disease</i>; 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).		

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
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 severe hemophilia A (defined as less than 1 International Unit per deciliter [1IU/dL] or 1% endogenous Factor VIII) (NHF, Srivastava 2020); OR iii. Individual has a diagnosis of mild to moderate hemophilia A (defined as endogenous Factor VIII less than 40 IU/dL [less than 40%], but greater than or equal to 1 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 <i>hemophilia A</i> (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 <i>acquired Factor VIII inhibitors</i> not exceeding 10 Bethesda Unit (BU) per milliliter (mL). B. Criteria for Continuation of Therapy		

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
Continuation requests for Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiiq, Recombinate, or Xyntha/Xyntha Solofuse (Factor VIII recombinant) may be approved if the following criteria are met: i. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes). C. Conditions not Covered Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive): Advate, Afstyla, Kogenate FS, Kovaltry, Novoeight, Nuwiiq, 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 <i>von Willebrand disease</i>; OR ii. When the above criteria are not met and for all other indications. D. Authorization Duration i. Initial Approval Duration: Up to 12 months ii. Reauthorization Approval Duration: Up to 12 months Long acting: Adynovate (Factor VIII Long-Acting Recombinant, pegylated), Jivi (Factor VIII Recombinant, PEGylated damactocog alfa pegol), Eloctate (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). A. Criteria for Initial Approval Initial requests for Adynovate (Factor VIII Long-Acting Recombinant, pegylated), Jivi (Factor VIII Recombinant PEGylated damactocog alfa pegol), Eloctate (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 <i>severe hemophilia A</i> (defined as less than 1 International Unit per deciliter [1IU/dL] endogenous Factor VIII) (NHF, Srivastava 2020); 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		

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
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 to <i>moderate hemophilia A</i> (defined as endogenous Factor VIII less than 40 IU/dL [less than 40%], but greater than or equal to 1 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: 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. B. Criteria for Continuation of Therapy Continuation requests for Adynovate (Factor VIII Long-Acting Recombinant, pegylated), Jivi (Factor VIII Recombinant PEGylated damactocog alfa pegol), Eloctate (Factor VIII Recombinant Anti-hemophilic Factor Fc Fusion Protein), Esperoct (Factor VIII Recombinant, glycopegylated), or Altuviiio (Factor VIII Recombinant Antihemophilic Factor FC-VWF-XTEN Fusion Protein) may be approved if the following criteria are met: i. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes). C. Conditions not Covered Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):		

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
Adynovate (Factor VIII Long-Acting Recombinant, pegylated), Jivi (Factor VIII Recombinant PEGylated damactocog alfa pegol), Eloctate (Factor VIII Recombinant Anti-hemophilic Factor Fc Fusion Protein), Esperoct (Factor VIII Recombinant, glycopegylated), or Altuviio (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 <i>von Willebrand disease</i>; OR ii. When the above criteria are not met and for all other indications.		
D. Authorization Duration i. Initial Approval Duration: Up to 12 months ii. Reauthorization Approval Duration: Up to 12 months		
Hemlibra (emicizumab-kxwh) - Anti-hemophilic bispecific factor --- Factor IXa and Factor X		
A. Criteria for Initial Approval Initial requests for Hemlibra (emicizumab-kxwh) may be approved if the following criteria are met: i. Individual has a diagnosis of <i>severe hemophilia A</i> (defined as less than 1 International Unit per deciliter [1IU/dL] endogenous Factor VIII) (NHF, Srivastava 2020); 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 <i>mild to moderate hemophilia A</i> (defined as endogenous Factor VIII less than 40 IU/dL [less than 40%], but greater than or equal to 1 IU) (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		

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
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. B. Criteria for Continuation of Therapy Continuation requests for Hemlibra (emicizumab-kxwh) may be approved if the following criteria are met: i. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes). D. Conditions Not Covered Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive): i. Hemlibra (emicizumab) may not be approved when the above criteria are not met and for all other indications. Obizur (Factor VIII Recombinant, Porcine Sequence) A. Criteria for Initial Approval 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 <i>acquired hemophilia A</i>; 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.		

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
B. Criteria for Continuation of Therapy Continuation requests for Obizur (Recombinant, Porcine Sequence) may be approved if the following criteria are met: i. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes). C. Conditions Not Covered Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive): 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 <i>von Willebrand disease</i>; OR iv. When the above criteria are not met and for all other indications. D. Authorization Duration i. Initial Approval Duration: Up to 12 months ii. Reauthorization Approval Duration: Up to 12 months Alphanate, Humate-P, Wilate (Anti-hemophilic Factor VIII/von Willebrand Factor Complex, Human) A. Criteria for Initial Approval 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 <i>hemophilia A</i> (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 <i>severe hemophilia A</i> (defined as less than 1 International Unit per deciliter [1IU/dL] endogenous Factor VIII) (NHF, Srivastava 2020); AND iv. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; OR		

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
v. Individual has a diagnosis of <i>mild to moderate hemophilia A</i> (defined as endogenous Factor VIII less than 40 IU/dL [less than 40%], but greater than or equal to 1 IU) (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 <i>acquired Factor VIII deficiency</i>; 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 <i>severe von Willebrand disease</i>; 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. B. Criteria for Continuation of Therapy 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 had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).		

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
C. Conditions Not Covered Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive): 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. D. Authorization Duration i. Initial Approval Duration: Up to 12 months ii. Reauthorization Approval Duration: Up to 12 months Vonvendi (Recombinant von Willebrand Factor Complex) A. Criteria for Initial Approval 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 <i>severe von Willebrand disease</i>; OR B. Individual has a diagnosis of <i>mild to moderate von Willebrand disease</i> 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		

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
B. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes receiving on-demand therapy. B. Criteria for Continuation of Therapy Continuation requests for Vonvendi (Recombinant von Willebrand Factor Complex) may be approved if the following criteria are met: i. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes). C. Conditions not Covered Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive): Vonvendi (Recombinant von Willebrand Factor Complex) may not be approved when the above criteria are not met and for all other indications. D. Authorization Duration i. Initial Approval Duration: Up to 12 months ii. Reauthorization Approval Duration: Up to 12 months <i>Qfitlia (fitsuran)</i> A. Criteria For Initial Approval i. Individual is at least 12 years of age or older; AND ii. Individual has a diagnosis of hemophilia A or B; AND iii. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes. B. Criteria For Continuation of Therapy Continuation requests for <i>Qfitlia (fitsuran)</i> may be approved if the following criteria are met: i. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes). C. Authorization Duration a. Initial Approval Duration: Up to 12 months b. Reauthorization Approval Duration: Up to 12 months D. Conditions Not Covered <i>Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):</i>		

Policy Name	Policy Number	Scope
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA ☒ MMM Multihealth
i. <i>Qfitlia (fitsuran)</i> may not be approved when the above criteria are not met and for all other indications.		
Reference Information - Centers for Disease Control and Prevention. Hemophilia Facts. Available at: http://www.cdc.gov/ncbddd/hemophilia/facts.html. - Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2022. URL: http://www.clinicalpharmacology.com. Updated periodically. - DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: September 22, 2022 - DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically. - Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically. - National Hemophilia Foundation (NHF). Available at: http://www.hemophilia.org/. Accessed on September 22, 2022. National Hemophilia Foundation (NHF). Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders. January 2021. Available at https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-andScientific-Advisory-Council-MASAC/MASAC-Recommendations/MASAC-Recommendations-Concerning-Products-Licensed-forthe-Treatment-of-Hemophilia-and-Other-Bleeding-Disorders. Accessed on September 22, 2022. - National Hemophilia Foundation (NHF). Recommendation on the Use and Management of Emicizumab-kxwh (Hemlibra) for Hemophilia A with and without Inhibitors. March 16, 2020. Available at: https://www.hemophilia.org/Researchers-HealthcareProviders/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/Recommendation-on-the-Use-andManagement-of-Emicizumab-kxwh-Hemlibra-for-Hemophilia-A-with-and-without-Inhibitors. Accessed on September 22, 2022. - Srivastava A, Santagostino E, Dougall A, et al. World Federation of Hemophilia. Guidelines for the management of hemophilia. Haemophilia. 3rd edition. August 2020. Available at https://onlinelibrary.wiley.com/doi/epdf/10.1111/hae.14046. Accessed on September 22, 2022. - Vonvendi – von Willebrand factor (recombinant) Package Insert. Baxalta US Inc. 2018. Available at file:///C:/Users/AF38863/Downloads/20190215_53b6d198-6175-4a26-8606-dc0d2a0f12d6%20(1).pdf Accessed on September 22, 2022. - Altuviiiio – antihemophilic factor (recombinant), Fc-VWF-XTEN fusion protein-ehtl Package Insert. Bioverativ Therapeutics Inc. Available at https://www.fda.gov/media/165594/download. Accessed February 23, 2023. - CMS IOM Publication 100-04, Medicare Claims Processing Manual, Chapter 17, Section 80.4 Billing for Hemophilia Clotting Factors, Section 80.4.1 Clotting Factor Furnishing Fee. Billing and Coding: Hemophilia Factor Products, A56482, Revision Effective Date: 10/01/2023.		

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope	
Agents for Hemophilia A and Von Willebrand Disease	MP-RX-FP-02-23	☒ MMM MA	☒ MMM Multihealth

Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Select Review 7/17/2025	Addition of Qfitlia clinical authorization criteria.	7/21/2025	8/8/2025
Annual Review 10/1/2024	Wording and formatting changes. Add Approved Indications, Other Uses, Therapeutic Alternatives. Add to Obizur do not approve criteria. Coding Reviewed: No changes.	2/18/2025	3/6/2025
Policy Inception 10/1/2023	Elevance Health's Medical Policy adoption.	N/A	11/30/2023