Medical Policy Bulletin
Title:
Coagulation Factors
Policy #:
MA08.004z

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

This policy uses coverage criteria primarily based on applicable Medicare statutes, regulations, NCDs, LCDs, CMS manuals and other applicable Medicare coverage documents. In the absence of fully established coverage criteria from these Medicare coverage documents for a specific medical service or item, the criterion/indication/service indicated by an asterisk below (*) is based on internal coverage criteria developed by the Company in consideration of peer-reviewed medical literature, clinical practice guidelines, regulatory status, and/or expert opinion.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY
*US Food and Drug Administration (FDA) 04/2025.

HEMOPHILIA A (FACTOR VIII DEFICIENCY)
The following coagulation factors are considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with hemophilia A (factor VIII deficiency):

- Human preparations: Alphanate, Koate-DVI, Hemofil M, Humate-P, and Wilate
- Recombinant preparations: Advate, Adynovate, Afstyla, Altuviiio, Eloctate, Esperoct, Jivi, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, and Xyntha/Xyntha Solofuse
- Human monoclonal antibody: Alhemo, Hemlibra, Hympavzi
- Small interfering ribonucleic acid: Qfitlia

HEMOPHILIA B (FACTOR IX DEFICIENCY)
The following coagulation factors are considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with hemophilia B (factor IX deficiency):

- Human preparations: Alphanine SD, Profilnine
- Recombinant preparations: Alprolix, BeneFIX, Idelvion, Ixinity, Rebinyn, and Rixubis
- Human monoclonal antibody: Alhemo, Hympavzi
- Small interfering ribonucleic acid: Qfitlia

HEMOPHILIA C (FACTOR XI DEFICIENCY)
Factor XI concentrates are not currently available in the United States.

HEMOPHILIA WITH INHIBITORS TO FACTORS VIII OR IX
The following coagulation factors are considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with hemophilia with inhibitors to factors VIII or IX:

- Human and recombinant factors VIII or IX (see Hemophilia A and B above)
- FEIBA (human plasma-derived activated prothrombin complex concentrate [APCC])
- Recombinant activated coagulation factor VIIa (e.g., NovoSeven RT, Sevenfact)
- Human monoclonal antibody
    - Alhemo for hemophilia with inhibitors to factor VIII, or IX
    - Hemlibra for hemophilia with inhibitors to factor VIII
- Small interfering ribonucleic acid: Qfitlia

FACTOR I DEFICIENCY, ACQUIRED
Fibryga (fibrinogen concentrate [Human]) is considered medically necessary and, therefore, covered for the treatment of bleeding episodes in individuals with acquired fibrinogen deficiency (AFD).

FACTOR I DEFICIENCY, CONGENITAL
Fibryga and RiaSTAP (fibrinogen concentrate [Human]) are considered medically necessary and, therefore, covered for the treatment of bleeding episodes in individuals with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia. NOTE: See EXPERIMENTAL/INVESTIGATIONAL section regarding dysfibrinogenemia.

FACTOR VII DEFICIENCY, CONGENITAL
NovoSeven RT (recombinant-activated coagulation factor VIIa) is considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with congenital factor VII deficiency.

FACTOR VIII DEFICIENCY, ACQUIRED
The following coagulation factors are considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with acquired factor VIII deficiency:

- Factor VIII concentrates, including Obizur
- Alphanate (antihemophilic factor VIII/von Willebrand factor complex [human])
- NovoSeven RT (recombinant-activated coagulation factor VIIa)
- FEIBA (human plasma-derived APCC)

FACTOR X DEFICIENCY, ACQUIRED OR CONGENITAL
Coagadex is considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with factor X deficiency.

FACTOR XIII DEFICIENCY, ACQUIRED OR CONGENITAL
The following coagulation factors are considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with acquired or congenital factor XIII deficiency:

- Corifact (factor XIII Concentrate [Human])
- Tretten (factor XIII A-Subunit [Recombinant])

GLANZMANN THROMBASTHENIA (GLYCOPROTEIN COMPLEX IIb/IIIa DEFICIENCY)
NovoSeven RT (recombinant-activated coagulation factor VIIa) is considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with Glanzmann thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets.

VON WILLEBRAND DISEASE
The following coagulation factors are considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with von Willebrand disease when the use of desmopressin (1-desamino-8-D-arginine vasopressin [DDAVP]) is known or suspected to be ineffective or contraindicated:

- Human preparations: Alphanate, Humate-P, Wilate
- Recombinant preparation: Vonvendi

EXPERIMENTAL/INVESTIGATIONAL

In addition to indications that are not described in the Medically Necessary section, Fibryga and RiaSTAP are also

considered experimental/investigational for the treatment of dysfibrinogenemia and, therefore, not covered because the safety and/or effectiveness of this service cannot be established by review of the available published peer-reviewed literature.

All other uses for coagulation factors other than FDA-labeled indications are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

NOT ELIGIBLE FOR REIMBURSEMENT

Bebulin, Helixate FS, Hyate:C, Monoclate-P, Mononine, NovoSeven, Profilnine SD, and ReFacto are no longer manufactured and have been withdrawn from market; therefore, they are not eligible for reimbursement.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

BILLING REQUIREMENTS

If there is no specific Healthcare Common Procedure Coding System (HCPCS) code available for the drug administered, then the drug must be reported with the most appropriate unlisted code along with the corresponding National Drug Code (NDC).

Guidelines

This policy is consistent with Medicare's coverage determination for coagulation factors. The Company’s payment methodology may differ from Medicare.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable Evidence of Coverage, coagulation factors are covered under the medical benefits of the Company’s Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

Certain drugs are available only through the member's medical benefit (Part B benefit), depending on how the drug is prescribed, dispensed, or administered. For Medicare Advantage members, coagulation factors are covered ONLY under a member's medical benefit (Part B benefit).

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

There are numerous drugs approved by the FDA for the prevention and treatment of bleeding due to a factor deficiency.

Description

Hemophilia and von Willebrand disease (VWD) are the most common congenital bleeding disorders. Bleeding disorders are a group of conditions that result when the blood cannot clot properly. In normal clotting, platelets stick together and form a plug at the site of vascular damage. Proteins in the blood called coagulation factors then interact in a series of physiological processes to form an insoluble fibrin clot that holds the platelets in place and allows

healing to occur at the site of the injury while preventing blood from escaping the blood vessel. The coagulation factors are indicated by Roman numerals (e.g., VII, VIII, and IX).

HEMOPHILIA TYPES A, B, C

Hemophilia is a rare, typically inherited bleeding disorder that can range from mild to severe, depending on how much clotting factor is present in the blood. Hemophilia A is considered the classic form of the disease and is a consequence of a congenital deficiency of factor VIII. Hemophilia B, also called Christmas disease, is the result of a congenital deficiency of factor IX. Hemophilia C, a rare form of hemophilia, is the result of a congenital deficiency of factor XI. The defect results in the insufficient generation of thrombin by factor VIIIa, factor IX, or factor XI complex by means of the intrinsic pathway of the coagulation cascade. Individuals with less than 1% normal factor are considered to have severe hemophilia. Individuals with 1% to 5% normal factor are considered to have moderately severe hemophilia marked by spontaneous bleeding from the oral mucosa, joint bleeding, and bleeding from minor trauma. Individuals with more than 5% but less than 40% normal factor are considered to have mild hemophilia. Clinical bleeding symptom criteria have also been used for hemophilia classification when individuals have bleeding symptoms different than what would be expected from the plasma coagulant levels.

Because blood does not clot properly without enough clotting factor, any cut or injury carries the risk of excessive bleeding. The hallmark of congenital hemophilia is hemorrhage into the joints, or hemarthrosis. Synovial cells in joints synthesize high levels of tissue factor inhibitor, which predisposes hemophilic joints to bleed. This bleeding leads to progressive inflammation, deterioration, and deformities of the joint. In addition, people with hemophilia may suffer from internal bleeding that can damage organs and tissues over time.

TREATMENT
Treatment options include fresh frozen plasma and clotting factor products that are made from human blood products such as donated plasma, or synthetic (recombinant) products. The administration of antihemophilic factor products temporarily replaces the missing clotting factor to treat or prevent bleeding episodes. Human preparations are manufactured from human plasma obtained and screened from tested United States donors for use in the treatment of bleeding episodes. Improved screening techniques and specific viral-inactivation treatments have made these products safer. A major breakthrough has enabled scientists to create synthetic blood factors, called recombinants, in the laboratory by cloning the genes responsible for specific clotting factors. Today’s factor replacement therapies are much safer, reducing the risk of viral pathogens such as hepatitis B, hepatitis C, and human immunodeficiency virus (HIV) infection.

Hemophilia A (Factor VIII Deficiency)

Some examples of the human preparations of coagulation factor VIII for the treatment of hemophilia A include Alphanate, Koate-DVI, Hemofil M, Humate-P, and Wilate. Recombinant antihemophilic factor products for use in those with hemophilia A include Advate, Adynovate, Afstyla, Altuviiio, Eloctate, Esperoct, Jivi, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, and Xyntha/Xyntha Solofuse. Additionally, Alhemo, Hemlibra and Hympavzi are examples of humanized monoclonal antibodies. Qfitlia (fitusiran) is an antithrombin-directed small interfering ribonucleic acid (siRNA). These products have various US Food and Drug Administration (FDA)–labeled indications, depending on the specific product, which may include prevention and control of bleeding episodes; short-term routine prophylactic treatment to reduce or prevent spontaneous musculoskeletal bleeding episodes and the risk of joint damage; and/or prevention or control of bleeding in surgical procedures in certain individuals with hemophilia A.

Jivi is not indicated for use in previously untreated individuals, and it also is not indicated for use in children younger than 7 years of age due to a greater risk for hypersensitivity reactions and/or loss of efficacy.

Hemophilia B (Factor IX Deficiency)

For the treatment of hemophilia B, human preparations of coagulation factor IX include Alphanine SD and Profilnine. Recombinant antihemophilic factor IX products include Alprolix, BeneFIX, Idelvion, Ixinity, Rebinyn, Rixubis. Additionally, **Alhemo and** Hympavzi are examples of humanized monoclonal antibodies. Qfitlia (fitusiran) is an antithrombin-directed siRNA. These products have various FDA-labeled indications, depending on the specific product, which may include the prevention or control of bleeding during surgical procedures. In addition to those indications, Alprolix, Rebinyn, and Rixubis also have an FDA approval for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in individuals with hemophilia B.

Hemophilia C (Factor XI Deficiency)

For the treatment of hemophilia C, replacement therapy via factor XI concentrates are not currently available in the United States.

HEMOPHILIA WITH INHIBITORS TO FACTORS VIII OR IX

Some individuals with severe forms of hemophilia A or hemophilia B develop autoantibody inhibitors that can neutralize factor VIII or factor IX, respectively. They neutralize the coagulant effects of replacement therapy. The levels of factor inhibitors are often measured by using the Bethesda method. The Bethesda method quantitates the inhibitor titer.

TREATMENT
Treatment of hemophilia with inhibitors to factors VIII or IX is complex and ranges from products that increase factor levels to factor-bypassing agents. Several different immune tolerance therapy regimens have been developed. For example, if attempts to lower antibody levels with immunosuppressants or corticosteroids have been unsuccessful, large doses of replacement factor VIII or factor IX can be used to try to produce inhibitor suppression, or eradication can be utilized. In addition, genetically engineered or recombinant antihemophilic factor
VIII (e.g., Advate, Kogenate FS, Recombinate) has the same biological effects as human factor VIII and has FDA-approved indications for certain individuals with factor VIII inhibitor disorder with inhibitor titers less than 10 Bethesda units per milliliter.

Additionally, FEIBA is a human plasma–derived activated prothrombin complex concentrate (APCC); its factor VIII inhibitor–bypassing activity controls spontaneous bleeding episodes and is also used during surgical interventions in individuals who have hemophilia A and hemophilia B with inhibitors. In December 2013, FEIBA received FDA approval for use as routine prophylaxis to prevent or reduce the frequency of bleeding episodes in individuals with hemophilia A or B who have developed inhibitors.

Recombinant activated coagulation factor VIIa (e.g., NovoSeven RT, Sevenfact) has FDA-labeled indications for use in the treatment of bleeding episodes or for the prevention or control of bleeding in surgical interventions and invasive procedures in certain individuals with hemophilia who have inhibitors to factor VIII or factor IX.

Emicizumab-kxwh (Hemlibra) is a human monoclonal antibody that was approved by the FDA for the treatment of hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.
Concizumab-mtci (Alhemo) is a human monoclonal antibody that was approved by the FDA for the treatment of hemophilia A or B with or without factor VIII or IX inhibitors.
Qfitlia (fitusiran) is an antithrombin-directed siRNA that was approved by the FDA for the treatment of hemophilia A or B with or without factor VIII or IX inhibitors.

FACTOR I DEFICIENCY, ACQUIRED

Fibrinogen is a soluble protein in the bloodstream that is required to form clots. Fibrinogen is broken down to fibrin by the enzyme thrombin. Acquired fibrinogen deficiency (AFD) may be caused by hypofibrinogenemia (e.g., liver disease, plasma exchange therapy, disseminated intravascular coagulation [DIC], hemophagocytic lymphohistiocytosis [HLH]), inflammation, malignancy, or certain medications (e.g., fibrinolytic agents, isotretinoin, valproic acid). AFD is more common than congenital because liver disease and DIC are common. Individuals with AFD can be asymptomatic or present with either bleeding and/or thrombotic events.

TREATMENT

Fibryga (fibrinogen concentrate [Human]) was approved by the FDA for fibrinogen supplementation in bleeding individuals with AFD. In 2019, Callum et al. found that it was noninferior to cryoprecipitate with regard to number of blood components transfused in a 24-hour period after cardiac bypass surgery.

FACTOR I DEFICIENCY, CONGENITAL

Fibrinogen is a soluble protein in the bloodstream that is required to form clots. Fibrinogen is broken down to fibrin by the enzyme thrombin. Factor I (fibrinogen) deficiency is a rare inherited bleeding disorder that is composed of an absence of fibrinogen (afibrinogenemia), a low level of fibrinogen (hypofibrinogenemia), or fibrinogen of low quality that does not clot properly (dysfibrinogenemia).

TREATMENT
Management of acute hemorrhage includes cryoprecipitate or fresh frozen plasma. Additionally, there are FDA-approved fibrinogen concentrates (human), Fibryga and RiaSTAP, indicated for the treatment of acute bleeding episodes in individuals with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia. (NOTE: Fibryga and RiaSTAP are not indicated for dysfibrinogenemia.)

FACTOR VII DEFICIENCY, CONGENITAL

Factor VII is one of the vitamin K–dependent coagulation factors synthesized in the liver. Plasma factor VII predominately exists in an inactive form; however, approximately 1% circulates in the activated form as factor VIIa. In response to injury or inflammation, factor VIIa activates other clotting factors, initiating the coagulation cascade. Congenital factor VII deficiency is a rare hemorrhagic disorder. The severity of the bleeding manifestations in affected individuals varies from mild to severe.

TREATMENT
Management of acute hemorrhage primarily consists of administration of factor VII to treat bleeding episodes. Because of the short half-life of factor VII, a treatment alternative may include recombinant-activated coagulation factor VIIa (NovoSeven RT), which is similar to human plasma–derived factor VIIa, with FDA-labeled indications that include the treatment of bleeding episodes and the prevention or control of bleeding in surgical interventions or invasive procedures in certain individuals who have a factor VII deficiency. The need for prophylaxis is determined by the individual's clinical presentation and the number of clinically significant bleeding episodes requiring intervention.

FACTOR VIII DEFICIENCY, ACQUIRED

Acquired hemophilia A is the development of factor VIII inhibitors (autoantibodies) in persons without a history of factor VIII deficiency. It develops with a frequency of one case per one million population per year. Although the disorder is rare, it is known to cause significant morbidity and mortality. It may be associated with other disease cond itions (e.g., collagen vascular disease, drug reaction, lymphoproliferative malignancies), or it can be idiopathic.

TREATMENT
Early treatment is directed toward achieving hemostasis and inhibitor eradication. Appropriate options for the treatment of bleeding episodes or for the prevention or control of bleeding in surgical procedures will depend on clinical presentation, and may include the use of immunosuppressive agents, desmopressin (1-desamino-8-D-arginine vasopressin [DDAVP]), Obizur and other factor VIII concentrates, antihemophilic factor VIII/von Willebrand factor complex (human) (Alphanate), recombinant-activated coagulation factor VIIa (NovoSeven RT), or FEIBA.

FACTOR VIII DEFICIENCY, CONGENITAL

See HEMOPHILIA A section (above).

FACTOR IX DEFICIENCY

See HEMOPHILIA B section (above).

FACTOR X DEFICIENCY, ACQUIRED OR CONGENITAL

Factor X is a vitamin K–dependent factor that is the first step in the common pathway to thrombus formation. Factor X can be activated by either the intrinsic or extrinsic clotting cascades. Factor X clotting deficiency may be acquired or congenital.

TREATMENT
Treatment options include fresh frozen plasma or plasma-derived prothrombin complex concentrates (plasma products containing a combination of vitamin K–dependent proteins) to stop or prevent bleeding.
Additionally, Coagadex is the first human factor X concentrate approved by the FDA for the treatment of hereditary factor X deficiency. It is indicated for routine prophylaxis to reduce the frequency of bleeding episodes, on-demand treatment and control of bleeding episodes, and for perioperative (period extending from the time of hospitalization for surgery to the time of discharge) management of bleeding in individuals with mild, moderate, and severe hereditary factor X deficiency.

FACTOR XI DEFICIENCY, ACQUIRED OR CONGENITAL

See HEMOPHILIA C section (above).

FACTOR XIII DEFICIENCY

ACQUIRED FACTOR XIII DEFICIENCY
Acquired factor XIII deficiency has been described in association with a variety of diseases such as hepatic failure, inflammatory bowel disease, and myeloid leukemia. Deficiency of factor XIII can be corrected with infusions of fresh frozen plasma, cryoprecipitate, or factor XIII concentrates.

CONGENITAL FACTOR XIII DEFICIENCY
Factor XIII is the protein responsible for stabilizing the formation of a blood clot. Congenital factor XIII deficiency is known as fibrin-stabilizing factor deficiency. In the absence of factor XIII, a clot will still develop, but it will remain unstable. This condition, a rare autosomal disease, is perhaps the rarest of all factor deficiencies. It is a potentially life-threatening bleeding disorder in which the blood clots normally but the clots formed are unstable, leading to recurrent bleeding. It is estimated that the condition affects one in every three million to five million births. It affects men and women equally. Most individuals with factor XIII deficiency experience symptoms from birth, often bleeding from the umbilical cord stump. Symptoms such as menorrhagia, bleeding in soft tissue, abnormal bleeding during or after injury or surgery, and hemarthrosis tend to continue throughout life but may be managed prophylactically.

Treatment

Treatment options for factor XIII deficiency include cryoprecipitate or fresh frozen plasma, which are made from human blood products such as donated plasma. In February 2011, factor XIII concentrate (Human) (Corifact) was approved by the FDA for routine prophylactic treatment of congenital factor XIII deficiency and was later indicated for the perioperative management of surgical bleeding in adult and pediatric individuals with congenital factor XIII deficiency. Additionally, in December 2013, the FDA approved the first recombinant product, Tretten®, for use in the routine prevention of bleeding in those who have congenital factor XIII A-subunit deficiency.

GLYCOPROTEIN COMPLEX IIb/IIIa DEFICIENCY

Glanzmann thrombasthenia is a rare inherited bleeding disorder caused by an abnormality in the glycoprotein complex IIb/IIIa. This disorder prevents platelets from initiating clot formation.

TREATMENT
Treatment options for Glanzmann thrombasthenia include blood platelet transfusions and recombinant-activated coagulation factor VIIa (NovoSeven RT). NovoSeven RT was approved by the FDA for the treatment of bleeding episodes and perioperative management in adults and children with Glanzmann thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets.

VON WILLEBRAND DISEASE (VWD)

VWD is a congenital condition that results when there is an abnormality, either quantitative or qualitative, of von Willebrand factor. von Willebrand factor is required for normal platelet adhesion: it functions in both primary (involving platelet adhesion) and secondary (involving factor VIII) hemostasis. In primary hemostasis, von Willebrand factor attaches onto the platelet surface and acts as an adhesive bridge between the platelets and the damaged subendothelium at the site of vascular injury. In secondary hemostasis, von Willebrand factor protects factor VIII from degradation and delivers it to the site of injury. Bleeding tendency is usually mild and is characterized by a tendency for easy bruising, frequent epistaxis, and menorrhagia. VWD is classified into three different types (types 1, 2, and 3), based on the levels of von Willebrand factor and factor VIII activity in the blood. Type 1 is the mildest and most common form; type 3 is the most severe and least common form.

TREATMENT
Desmopressin (DDAVP) is a synthetic vasopressin analogue that has become a mainstay of therapy for most individuals with mild VWD. At appropriate doses, desmopressin causes a two-fold to five-fold increase in plasma von Willebrand factor and factor VIII concentrations in individuals who are healthy and responsive. Desmopressin can be used to treat bleeding complications or to prepare individuals with VWD for surgery. In a subtype of VWD (type IIB), desmopressin may cause a paradoxical drop in the platelet count and should not be used in a therapeutic setting without prior testing to see how the individual responds.

The goal of therapy is to correct the defect in platelet adhesiveness (by raising the level of effective von Willebrand factor) and to correct the defect in blood coagulation (by raising the level of factor VIII). Products such as von Willebrand factor/coagulation factor VIII complex (human) (Wilate) and antihemophilic factor/von Willebrand factor complexes (human) (Alphanate and Humate-P) are developed from human plasma consisting of two different

proteins (factor VIII and von Willebrand factor).

Wilate has been FDA-approved for the treatment of spontaneous or trauma-induced bleeding episodes in certain individuals with severe VWD, as well as individuals with mild or moderate VWD in whom desmopressin is known or suspected to be ineffective or contraindicated. Wilate is indicated for the perioperative management of bleeding. Additionally, Wilate is indicated for routine prophylaxis in children 6 years of age and older and adults with von Willebrand disease to reduce the frequency of bleeding episodes.

Alphanate has been FDA approved for surgical and/or invasive procedures in individuals with VWD in whom desmopressin (DDAVP) is either ineffective or contraindicated. This product is not indicated for individuals with severe VWD (type 3) undergoing major surgery.

Humate-P has been approved by the FDA for the treatment of spontaneous and trauma-induced bleeding episodes and for the prevention of excessive bleeding related to surgery in adult and pediatric individuals with VWD. This includes individuals with severe VWD, as well as individuals with mild to moderate VWD for whom desmopressin is known or suspected to be ineffective. In addition, Humate-P is the first product specifically FDA-approved for individuals with severe VWD who are undergoing major surgery.

A synthetic (recombinant) product, Vonvendi, has been approved by the FDA for adult and pediatric individuals with VWD for on-demand treatment and control of bleeding episodes and perioperative management of bleeding. Additionally, it is FDA approved for routine prophylaxis to reduce the frequency of bleeding episodes in adult patients only.

OFF-LABEL INDICATIONS

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)
N/A

ICD - 10 Procedure Code Number(s)
N/A

ICD - 10 Diagnosis Code Number(s)
Report the most appropriate diagnosis code in support of medical necessity as listed in the policy.

HCPCS Level II Code Number(s)
J7170 Injection, emicizumab-kxwh, 0.5 mg
J7172 Injection, marstacimab-hncq, 0.5 mg
J7174 Injection, fitusiran, 0.04 mg
J7177 Injection, human fibrinogen concentrate (fibryga), 1 mg
J7179 Injection, von Willebrand factor (recombinant), (Vonvendi), 1 IU VWF:RCo
J7182 Injection, factor VIII, (antihemophilic factor, recombinant), (NovoEight), per IU
J7183 Injection, von Willebrand factor complex (human), Wilate, 1 IU vWF:RCo
J7185 Injection, factor VIII (antihemophilic factor, recombinant) (Xyntha), per IU
J7187 Injection, von Willebrand factor complex (Humate-P), per IU VWF:RCO
J7189 Factor viia (antihemophilic factor, recombinant), (novoseven rt), 1 microgram
J7200 Injection, factor IX, (antihemophilic factor, recombinant), Rixubis, per IU
J7201 Injection, factor IX, Fc fusion protein, (recombinant), Alprolix, 1 IU
J7202 Injection, factor IX, albumin fusion protein, (recombinant), Idelvion, 1 IU
J7203 Injection factor ix, (antihemophilic factor, recombinant), glycopegylated, (rebinyn), 1 iu
J7204 Injection, factor viii, antihemophilic factor (recombinant), (esperoct), glycopegylated-exei, per iu
J7208 Injection, factor viii, (antihemophilic factor, recombinant), pegylated-aucl, (jivi), 1 i.u.
J7209 Injection, factor VIII, (antihemophilic factor, recombinant), (Nuwiq), 1 IU
J7210 Injection, factor viii, (antihemophilic factor, recombinant), (Afstyla), 1 I.U.
J7211 Injection, factor viii, (antihemophilic factor, recombinant), (Kovaltry), 1 I.U.
J7212 Factor viia (antihemophilic factor, recombinant)-jncw (sevenfact), 1 microgram
J7213 Injection, coagulation factor ix (recombinant), ixinity, 1 i.u.
J7214 Injection, Factor VIII/von Willebrand factor complex, recombinant (Altuviiio), per Factor VIII IU

THE FOLLOWING CODE IS USED TO REPRESENT Coagadex®:
J7175 Injection, factor X, (human), 1 IU

THE FOLLOWING CODE IS USED TO REPRESENT RiaSTAP®:

J7178 Injection, human fibrinogen concentrate, not otherwise specified, 1 mg

THE FOLLOWING CODE IS USED TO REPRESENT Corifact®:
J7180 Injection, factor XIII (antihemophilic factor, human), 1 IU

THE FOLLOWING CODE IS USED TO REPRESENT Tretten®:
J7181 Injection, factor XIII A-subunit, (recombinant), per IU

THE FOLLOWING CODE IS USED TO REPRESENT Alphanate®:
J7186 Injection, antihemophilic factor VIII/von Willebrand factor complex (human), per factor VIII i.u.

THE FOLLOWING CODE IS USED TO REPRESENT Obizur:
J7188 Injection, factor VIII (antihemophilic factor, recombinant), per IU

THE FOLLOWING CODE IS USED TO REPRESENT Koate®DVI and Hemofil M:
J7190 Factor VIII (antihemophilic factor, human) per IU

THE FOLLOWING CODE IS USED TO REPRESENT Advate®, Kogenate FS®, and Recombinate®:
J7192 Factor VIII (antihemophilic factor, recombinant) per IU, not otherwise specified

THE FOLLOWING CODE IS USED TO REPRESENT Alphanine® SD:
J7193 Factor IX (antihemophilic factor, purified, nonrecombinant) per IU

THE FOLLOWING CODE IS USED TO REPRESENT Profilnine®:
J7194 Factor IX complex, per IU

THE FOLLOWING CODE IS USED TO REPRESENT BeneFIX®:
J7195 Injection, factor IX (antihemophilic factor, recombinant) per IU, not otherwise specified

THE FOLLOWING CODE IS USED TO REPRESENT FEIBA (human plasma-derived activated prothrombin complex concentrate [APCC]):
J7198 Antiinhibitor, per IU

THE FOLLOWING CODE IS USED TO REPRESENT Eloctate®:
J7205 Injection, factor VIII Fc fusion protein (recombinant), per IU

THE FOLLOWING CODE IS USED TO REPRESENT Adynovate:
J7207 Injection, factor VIII, (antihemophilic factor, recombinant), PEGylated, 1 IU

THE FOLLOWING CODES ARE USED TO REPRESENT Concizumab-mtci (Alhemo):
C9399 Unclassified drugs or biologicals
J3590 Unclassified biologics

NOT ELIGIBLE FOR REIMBURSEMENT

THE FOLLOWING CODES REPRESENT BEBULIN, HELIXATE® FS, HYATE:C®, MONOCLATE-P®, MONONINE®, NOVOSEVEN®, PROFILNINE®SD, AND REFACTO® WHICH ARE NO LONGER MANUFACTURED AND HAVE BEEN WITHDRAWN FROM THE MARKET:

J7189 Factor VIIa (atihemophilic factor, recombinant), per 1 mcg
J7190 Factor VIII (antihemophilic factor, human) per IU
J7191 Factor VIII (antihemophilic factor (porcine), per IU
J7192 Factor VIII (antihemophilic factor, recombinant) per IU, not otherwise specified
J7193 Factor IX (antihemophilic factor, purified, nonrecombinant) per IU
J7194 Factor IX complex, per IU

Revenue Code Number(s)

N/A

Coding And Billing Requirements

BILLING REQUIREMENTS

If there is no specific HCPCS code available for the drug administered, then the drug must be reported with the most appropriate unlisted code along with the corresponding National Drug Code (NDC).

Policy History

Revisions From MA08.004z:

03/20/2026	This version of the policy will become effective 03/20/2026. This policy has been updated to communicate the coverage position for the following two new products: • Concizumab-mtci (Alhemo). Monoclonal antibody for the treatment of hemophilia A and B with or without FVIII and FIX inhibitors. • Fitusiran (Qfitlia). Small interfering ribonucleic acid for the treatment of hemophilia A or B with or without factor VIII or IX inhibitors. The following HCPCS code has been added to this policy for fitusiran (Qfitlia): J7174 Injection fitusiran 0.04 mg THE FOLLOWING CODES ARE USED TO REPRESENT Concizumab-mtci (Alhemo): C9399 Unclassified drugs or biologicals J3590 Unclassified biologics All of the ICD-10 CM codes have been removed from this policy. Report the most appropriate diagnosis code in support of medically necessary criteria as listed in the policy.

Revisions from MA08.004y:

09/16/2025	This version of the policy will become effective 09/16/2025. The following HCPCS code has been added to this policy: J7172 Injection, marstacimab-hncq, 0.5 mg The following HCPCS codes have been removed from this policy for marstacimab-hncq (Hympavzi): C9399 Unclassified drugs or biologicals J3590 Unclassified biologics

Revisions from MA08.004x:

06/13/2025	This version of the policy will become effective 06/13/2025. The following HCPCS code has been added to this policy: C9304 Injection, marstacimab-hncq, 0.5 mg The following HCPCS code has been removed from this policy for marstacimab-hncq (Hympavzi): C9399 Unclassified drugs or biologicals.

Revisions from MA08.004w:

03/28/2025	This version of the policy will become effective 03/28/2025. This policy has been updated to communicate the coverage position for the following, in consideration of revisions within the US Food and Drug Administration (FDA) labeling: • The new product, marstacimab-hncq (Hympavzi) was added to this policy for the treatment of hemophilia A and B. • Mononine has been discontinued by the pharmaceutical company • Fibryga (fibrinogen concentrate [Human]) is covered for the treatment of bleeding episodes in individuals with acquired fibrinogen deficiency (AFD). • Coagadex is covered for the prevention and/or treatment of bleeding episodes in individuals with mild, moderate, or severe factor X deficiency. • Wilate is covered for routine prophylaxis in children 6 years of age and older and adults with von Willebrand disease to reduce the frequency of bleeding episodes. The following changes to coding have been made: • All of the ICD-10 CM codes have been removed from this policy, because they are informational. • The following HCPCS codes have been added to this policy for marstacimab-hncq (Hympavzi): C9399 Unclassified drugs or biologicals J3590 Unclassified biologics • Mononine was discontinued. HCPCS code "J7193 Factor IX (antihemophilic factor, purified, nonrecombinant) per IU" will be considered Not Eligible for Reimbursement.

Revisions from MA08.004v:

01/02/2024	This version of the policy will become effective 01/02/2024. This policy was updated to communicate the coverage position for Altuviiio, represented by HCPCS J7214, for the treatment for Hemophilia A.

Revisions from MA08.004u:

07/01/2023	This version of the policy will become effective 07/01/2023. The following HCPCS code has been replaced by the following code for Ixinity. (Ixinity will no longer be represented by J7195, but will remain in the policy for Benefix.): **Removed:** J7195 Injection, factor IX (antihemophilic factor, recombinant) per IU, not otherwise specified **Replaced With:** J7213 Injection, coagulation factor ix (recombinant), ixinity, 1 i.u.

Revisions From MA08.004t:

11/02/2022	The policy has been reviewed and reissued to communicate the Company's continuing position on Coagulation Factors. This policy has been updated in consideration of revisions within the US Food and Drug Administration (FDA) labeling: • The new product, Xyntha Solofuse, was added to this policy for the treatment of hemophilia A. It is represented by HCPCS J7185, which already exists in the policy. • Rebinyn received a supplemental FDA-approval for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in individuals with hemophilia B.
10/01/2022	This version of the policy will become effective 10/01/2022. The following ICD-10 CM code has been **termed** (no longer valid codes) and removed from this policy: D68.0 Von Willebrand's disease The following ICD-10 CM codes have been **added** to this policy:

	D68.00 Von Willebrand disease, unspecified D68.01 Von Willebrand disease, type 1 D68.020 Von Willebrand disease, type 2A D68.021 Von Willebrand disease, type 2B D68.022 Von Willebrand disease, type 2M D68.023 Von Willebrand disease, type 2N D68.029 Von Willebrand disease, type 2, unspecified D68.03 Von Willebrand disease, type 3 D68.04 Acquired von Willebrand disease D68.09 Other von Willebrand disease

Revisions From MA08.004s:

10/25/2021	This version of the policy will become effective 10/25/2021. This policy was updated to clarify the coverage position for the following: • Hemophil M was misspelled. Revised to be Hemofil M. • Profilnine was added to the policy as Medically Necessary. HCPCS code J7194 Factor IX complex, per IU • Profilnine SD was discontinued. HCPCS code J7194 Factor IX complex, per IU will be considered Not Eligible for Reimbursement.

Revisions From MA08.004r:

01/01/2021	This policy was updated to communicate the coverage position for the following: • New FDA-approved product: Name changed from Eptacog Beta to Sevenfact® (HCPCS J7189). • New indication: Wilate® in individuals with hemophilia A • Products discontinued by the Pharmaceutical Companies and are not eligible for reimbursement: Helixate® FS (HCPCS J7192), Monoclate-P® (HCPCS J7190), NovoSeven® (HCPCS J7189), ReFacto® (HCPCS J7192) • Coagadex® updated per FDA - not indicated for perioperative in severe disease. • Categorization of Hemlibra® changed from a recombinant preparation for hemophilia to a human monoclonal antibody for hemophilia A. • Tretten® expanded for use in those with acquired or congenital factor XIII deficiency • Afstyla HCPCS code change from J7192 to J7210. The effective date of this policy has been revised from 12/28/2020 to 01/01/2021, to include to quarterly code updates. The following HCPCS narrative has been **revised** in this policy: **FROM:** J7189 Factor VIIa (antihemophilic factor, recombinant), per 1 mcg **TO:** J7189 Factor viia (antihemophilic factor, recombinant), (novoseven rt), 1 microgram The following HCPCS code has been **removed** for **Sevenfact** and is replaced by the following HCPCS code: **REMOVED:** J7189 Factor VIIa (antihemophilic factor, recombinant), per 1 mcg **REPLACED WITH:** J7212 Factor viia (antihemophilic factor, recombinant)-jncw (sevenfact), 1 microgram

Revisions From MA08.004q:

07/01/2020	This policy has been identified for the HCPCS code update, effective 07/01/2020. The following code has been **removed** from this policy to represent Esperoct, and is replaced by

	the following HCPCS code: **REMOVED:** J7192 Factor VIII (antihemophilic factor, recombinant) per IU, not otherwise specified **REPLACED WITH:** J7204 Injection, factor viii, antihemophilic factor (recombinant), (esperoct), glycopegylated-exei, per iu

Revisions From MA08.004p:

10/21/2019	This policy has been updated to communicate the coverage criteria for two products: • Medically Necessary coverage criteria has been added for a new hemophilia A recombinant product, Esperoct • Bebulin changed from Medically Necessary to Not Eligible For Reimbursement, since withdrawn from the market Additionally, ICD-10 D68.1 Hereditary factor XI deficiency has been removed, since there are no FDA-approved products for hemophilia C.

Revisions From MA08.004o:

07/01/2019	This policy has been identified for the HCPCS code update, effective 07/01/2019. **The following HCPCS code has been added to this policy as Medically Necessary:** J7208 Injection, factor viii, (antihemophilic factor, recombinant), pegylated-aucl, (jivi), 1 i.u. • **Note:** This code no longer represents Jivi: J7207 Injection, factor VIII, (antihemophilic factor, recombinant), PEGylated, 1 IU **The following HCPCS code has been removed from this policy:** C9141 Injection, factor viii, (antihemophilic factor, recombinant), pegylated-aucl (jivi), 1 i.u

Revisions From MA08.004n:

04/01/2019	This policy has been identified for the HCPCS code update, effective 04/01/2019. **The following HCPCS code has been added to this policy as Medically Necessary:** C9141 Injection, factor viii, (antihemophilic factor, recombinant), pegylated-aucl (jivi), 1 i.u.

Revisions From MA08.004m:

01/01/2019	This version of the policy will become effective 01/01/2019.
	
	This policy has been updated in consideration of revisions within the US Food and Drug Administration (FDA) labeling.
	• Jivi®, a recombinant DNA-derived Factor VIII product, has been added to this policy as Medically Necessary.
	• The coverage of Hemlibra® has been updated to include the new indication of hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.
	• There has been a brand name change: FROM: Fibryna TO: Fibryga
	
	The following HCPCS codes have been added/revised/deleted:
	
	• Fibryga HCPCS Code Change:
	  ○ FROM: J7178 Injection, human fibrinogen concentrate, 1 mg
	  ○ TO: J7177 Injection, human fibrinogen concentrate (fibryga), 1 mg
	• Riastap HCPCS Narrative Change:
	  ○ FROM: J7178 Injection, human fibrinogen concentrate, 1 mg
	  ○ TO: J7178 Injection, human fibrinogen concentrate, not otherwise specified, 1 mg
	• Rebinyn HCPCS coding changes
	  ○ Delete: C9468 Injection, factor ix (antihemophilic factor, recombinant), glycopegylated, Rebinyn, 1 i.u.
	  ○ Update:
	  ▪ FROM: J7195 Injection, factor IX (antihemophilic factor, recombinant) per IU, not otherwise specified

	▪ TO: J7203 Injection factor ix, (antihemophilic factor, recombinant), glycopegylated, (rebinyn), 1 iu • Hemlibra HCPCS coding changes o FROM: Q9995 Injection, emicizumab-kxwh, 0.5 mg o TO: J7170 Injection, emicizumab-kxwh, 0.5 mg

Revisions From MA08.004l:

07/01/2018	This policy has been identified for the HCPCS code update, effective 04/01/2018. The following HCPCS code has been **added** and the corresponding non-specific code **removed** from this policy: **ADDED:** Q9995 Injection, emicizumab-kxwh, 0.5 mg **REMOVED:** J7199 Hemophilia clotting factor, not otherwise classified

Revisions From MA08.004k:

05/28/2018	This policy has been updated in consideration of revisions within the US Food and Drug Administration (FDA) labeling. Eptacog Beta and emicizumab-kxwh (Hemlibra®) have been added to this policy as Medically Necessary. Fibryna® and RiaSTAP® have been updated as experimental/investigational for the treatment of dysfibrinogenemia.

Revisions From MA08.004j:

04/01/2018	This policy has been updated in consideration of revisions within the US Food and Drug Administration (FDA) labeling. Eptacog Beta and emicizumab-kxwh (Hemlibra®) have been added to this policy as Medically Necessary. Fibryna® and RiaSTAP® have been updated as experimental/investigational for the treatment of dysfibrinogenemia.

Revisions From MA08.004i:

01/01/2018	This policy has been identified for the HCPCS code update, effective 01/01/2018. The following HCPCS code has been **removed** from this policy: C9140 Injection, factor VIII (antihemophilic factor, recombinant) (Afstyla), 1 IU The following ICD-10 CM codes have been **added** to this policy: J7210 Injection, factor viii, (antihemophilic factor, recombinant), (afstyla), 1 i.u. J7211 Injection, factor viii, (antihemophilic factor, recombinant), (kovaltry), 1 i.u.

Revisions From MA08.004h:

10/30/2017	This policy was updated to communicate the coverage of the following new products, Fibryna® and Rebinyn®. Additionally, Hyate:C® is not eligible for reimbursement since it is no longer manufactured and has been withdrawn from market.

Revisions From MA08.004g:

01/01/2017	This policy has been identified for the HCPCS code update, effective 01/01/2017. The following HCPCS codes have been **added** and the corresponding non-specific code **removed** from this policy: **ADDED:** J7175 Injection, factor x, (human), 1 i.u. **REMOVED:** J7199 Hemophilia clotting factor, not otherwise classified **ADDED:** J7179 Injection, von willebrand factor (recombinant), (vonvendi), 1 i.u. vwf:rco **REMOVED:** J7199 Hemophilia clotting factor, not otherwise classified The following HCPCS codes have been **added** to this policy:

	C9140 Injection, factor viii (antihemophilic factor, recombinant) (afstyla), 1 i.u. J7202 Injection, factor ix, albumin fusion protein, (recombinant), idelvion, 1 i.u. J7207 Injection, factor viii, (antihemophilic factor, recombinant), pegylated, 1 i.u. J7209 Injection, factor viii, (antihemophilic factor, recombinant), (nuwiq), 1 i.u. The following HCPCS narrative has been **revised** in this policy: **FROM:** J7201 INJECTION, FACTOR IX, FC FUSION PROTEIN (RECOMBINANT), PER IU **TO:** J7201 Injection, factor ix, fc fusion protein, (recombinant), alprolix, 1 i.u. The following HCPCS codes have been **deleted** from this policy: C9137, C9138, C9139 **Note:** Due to the addition of C9140, the product, Afstyla®, was added as an example of a recombinant Factor VIII to the **Description Section** and **Policy Section.**

Revisions From MA08.004f:

10/01/2016	This policy has been identified for the HCPCS code update, effective 10/01/2016. The following HCPCS code has been **added** to this policy: C9139 Injection, Factor IX, albumin fusion protein (recombinant), Idelvion, 1 i.u.

Revisions From MA08.004e:

08/08/2016	The title of this policy has changed due to the scope of products included in this policy: **FROM:** Coagulation Factors for Hemophilia **TO:** Coagulation Factors This policy has been updated to reflect changes in Novitas Solutions, Inc. *Local Coverage determination (LCD).* L35111: Hemophilia Factor Products, updated 04/14/2016. This policy has been updated to include coverage information for the following products that are new to market: • Hemophilia A products: Adynovate, Kovaltry, Lonoctocog alfa, Nuwiq® • Factor X deficiency: Coagadex® • Hemophilia B products: Ixinity®, Idelvion® • von Willebrand disease: Vonvendi This policy has also been updated to include coverage information for Factor I (Fibrinogen) deficiency product, RiaSTAP®. Trade names of some existing Factor Products have been revised.

Revisions From MA08.004d:

04/01/2016	This policy has been identified for the HCPCS code update, effective 04/01/2016. The following HCPCS codes have been **added** to this policy: **Healthcare Common Procedure Coding System (HCPCS) C Series Codes can only be reported for outpatient facility services**. **Professional providers should not report HCPCS C Series Codes for professional services regardless of where those services are performed**: C9137 Injection, Factor VIII (antihemophilic factor, recombinant) PEGylated, 1 I.U. C9138 Injection, Factor VIII (antihemophilic factor, recombinant) (Nuwiq), 1 I.U.

Revisions From MA08.004c:

01/01/2016	This policy has been identified for the HCPCS code update, effective 01/01/2016. The following HCPCS code has been **added** to this policy, as Medically Necessary: J7188 Injection, factor viii (antihemophilic factor, recombinant), (obizur), per i.u. J7205 Injection, factor viii fc fusion (recombinant), per iu

	The following HCPCS code has been **termed** from this policy: Q9975 Injection, Factor VIII, FC Fusion Protein (Recombinant), per IU

Revisions From MA08.004b:

04/01/2015	This policy has been identified for the HCPCS code update, effective 04/01/2015. **The following HCPCS code has been termed from this policy:** C9136 Injection, factor viii, fc fusion protein, (recombinant), per i.u. **The following HCPCS code has been added to this policy as Medically Necessary:** Q9975 Injection, Factor VIII, FC Fusion Protein (Recombinant), per IU **The HCPCS for Eloctate has been revised:** **FROM:** J7199 **TO:** Q9975

Revisions From MA08.004a:

01/28/2015	This policy has been updated to include the new porcine factor VIII product, Obizur.

Revisions From MA08.004:

01/01/2015	This is a new policy.

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