Pharmacy Medical Necessity Guidelines: Factor Products

Effective: March 14, 2016

<table>
<thead>
<tr>
<th>Prior Authorization Required</th>
<th>TYPE OF REVIEW – CARE MANAGEMENT</th>
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<th>Not Covered</th>
<th>TYPE OF REVIEW – CLINICAL REVIEW</th>
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<td>MED</td>
<td>PRECERT/MM</td>
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This Pharmacy Medical Necessity Guideline applies to the following:

**Tufts Health Plan Commercial Plans**
- Tufts Health Plan Commercial Plans – large group plans
- Tufts Health Plan Commercial Plans – small group and individual plans

**Tufts Health Public Plans**
- Tufts Health Direct – Health Connector
- Tufts Health Together – A MassHealth Plan

**Tufts Health Freedom Plan products**
- Tufts Health Freedom Plan - large group plans
- Tufts Health Freedom Plan - small group plans

Fax Numbers:
- All plans except Tufts Health Direct – Health Connector: PRECERT:617.972.9409
- Tufts Health Direct – Health Connector only: MM:888.415.9055

**Note:** For Tufts Health Plan Medicare Preferred Members, please refer to the Tufts Health Plan Medicare Preferred Prior Authorization Criteria. Background, applicable product and disclaimer information can be found on the last page.

**OVERVIEW**

The plan covers factor products (monoclonal and recombinant) for factor VIII deficiency (classic hemophilia), for factor IX deficiency (Christmas factor deficiency), for factor VII deficiency (extrinsic factor deficiency), for hereditary factor X deficiency, for factor XIII deficiency (also known as fibrin-stabilizing factor deficiency), and for von Willebrand disease. The plan also covers recombinant coagulation factor VIIa (NovoSeven®) for acquired hemophilia.

**Antihemophilic Coagulation Factor VIII (Recombinant) agents**
- Advate, Adynovate, Afstyla®, Eloctate®, Helixate® FS, Kogenate® FS, Kovaltry®, Novoeight®, Nuwiq®, Obizur®, Recombinate, and Xyntha®

**Antihemophilic Coagulation Factor VIII (Plasma-derived) agents**
- Hemoﬁl M, Koate® DVI, and Monoclate-P®

**Antihemophilic Coagulation Factor VIII/von Willebrand factor Complex (Plasma-derived) agents**
- Alphanate®, Humate-P®, and Wilate®

**Coagulation Factor IX (Recombinant) agents**
- Alprolix®, BeneFIX®, Idelvion®, Ixinity®, and Rixubis

**Coagulation Factor IX (Plasma-derived) agents**
- AlphaNine® SD and Mononine®

**Factor IX Complex (Plasma-derived) agents**
- Bebulin® and Profilnine® SD

**Coagulation Factor X (Plasma-derived) agent**
- Coagadex®

**Factor XIII Concentrate (Recombinant) agent**
- Tretten®

**Factor XIII Concentrate (Plasma-derived) agent**
- Corifact®

**Coagulation Factor VIIa (Recombinant) agent**
- NovoSeven® RT

**Anti-inhibitor Coagulant Complex (Plasma-derived) agent**
- FEIBA NF

**Von Willebrand factor (Recombinant) agent**
- Vonvendi
Hemophilia is one of the most common congenital bleeding disorders known to be due to defects in distinct and unrelated genes. Hemophilia is a clinically heterogeneous disorder resulting in deficiency of plasma factor VIII (FVIII) or factor IX (FIX) coagulant activity. The worldwide prevalence of hemophilia is estimated to be about 400,000 people and is estimated to affect approximately 20,000 people in the United States. There are two main types of hemophilia: hemophilia A (also known as antihemophilic factor [AHF] deficiency, FVIII deficiency, or classic hemophilia) and hemophilia B (also known as FIX deficiency or Christmas disease). Both types of hemophilia are X-linked bleeding disorders almost solely affecting males. The incidence of hemophilia A is 1:5,000 male births whereas the incidence of hemophilia B is approximately one-fourth that of hemophilia A. There are no significant racial differences in the incidence of hemophilia. A quantitative deficiency of AHF or FVIII may be caused by a genetic mutation; deletion and nonsense mutations are often associated with the more severe forms of hemophilia because no functional FVIII is produced. Both FVIII and FIX deficiencies increase the risk of bleeding by reducing the amount of activated factor X (FX) and thrombin available to make a stable fibrin clot. Depending on the severity of the disease, a hemorrhage can occur spontaneously or can be precipitated by trauma.

Acquired hemophilia is an autoimmune disorder where inhibitors/antibodies directed against FVIII or von Willebrand Factor (vWF) develops in patients without hemophilia. The incidence is approximately one to four cases per million per year. Acquired hemophilia A generally occurs in older adults with no underlying bleeding disorder and is commonly associated with pregnancy, malignancy, pemphigoid, rheumatoid arthritis, systemic lupus erythematosus, and other autoimmune diseases. Soft tissue and systemic bleeding rather than joint hemorrhages are the hallmark of acquired hemophilia A compared with congenital hemophilia A. Diagnosis is based on the finding of a low factor VIII level associated with the presence of a time-dependent inhibitor in the plasma.

Factor products are proteins in blood plasma that are responsible for effective clotting of blood (coagulation). Because clinically hemophilia A and B appear alike, special laboratory tests are required to identify the type of coagulation disorder that a Member has. The diagnosis is usually made in the first year or two of life. Hemophilia is a lifelong disorder with no cure at the present time. Studies using gene therapy are showing promising results, providing hope that a cure will be available in the future.

The severity of bleeding in hemophilia is directly related to the degree of factor deficiency. Severity of hemophilia A and B factor deficiency is classified as severe, moderate, or mild, depending on the degree of factor levels present and relating directly to the expected frequency of bleeding. Normal factor levels are 40-200%. Severe hemophilia A or B is defined as a factor level of less than 1%; moderate hemophilia A or B is defined as a factor level of 1-5%; and mild hemophilia is defined as a factor level of >5 and <30%.

Inherited factor VII (FVII) deficiency is a rare autosomal recessive hemorrhagic disorder. Clinical bleeding can be highly variable and may not correlate well with the level of FVII coagulant activity measured in plasma. Inherited FVII deficiency can be classified as type 1 or type 2, depending on the absence or presence of FVII antigen in plasma. The type 1 deficiencies result from decreased biosynthesis or accelerated clearance; the type 2 abnormalities represent a dysfunctional molecule. FVII deficiency is considered rare, affecting an estimated one in 500,000 people. The male-to-female ratio is 1:1. However, women are more likely to be symptomatic because of menorrhagia.

Congenital Factor X deficiency (also known as hereditary Factor XIII deficiency or Stuart-Prower Factor deficiency) is caused by mutations in the F10 gene, which provides instructions for making a protein called coagulation factor X. The incidence of Factor X deficiency is estimated at 1 in 500,000 to 1 in a million. It is inherited in an autosomal recessive fashion, meaning both parents must carry the gene to pass it on to their children; it affects men and women equally. Reduced quantity or function of coagulation factor X prevents blood from clotting normally, causing episodes of abnormal bleeding that can be severe.

Congenital Factor XIII deficiency (also known as fibrin-stabilizing factor deficiency) is rare and affects 1 out of every 3 million to 5 million people in the United States and an incidence in the U.S. of approximately 150 people. Patients with congenital Factor XIII deficiency do not make enough Factor XIII, a substance that circulates in the blood and is important for normal clotting. Without treatment, people with the condition are at risk for life-threatening bleeding. The deficiency may lead to soft tissue bruising, mucosal bleeding and fatal intracranial bleeding.

Another hereditary bleeding disorder is von Willebrand disease, the most common hereditary bleeding disorder, affecting approximately 1% of the population in the United States. Manifestations of the
disease are mild for most people who have this disorder; however, there are about 2,000 people who have severe forms of the disease in which bleeding can be excessive if not treated. Von Willebrand disease affects men and women equally. Vonvendi is the first and only recombinant von Willebrand factor product. Alphanate®️, Humate®, and Wilate®️ are plasma derived von Willebrand factor products. Currently available plasma derived von Willebrand factor products are available in combination with coagulation factor VIII. Alphanate®️ and Humate®️ are indicated for von Willebrand disease and hemophilia A. Wilate®️ and Vonvendi are only indicated for von Willebrand disease. Per package labeling for Vonvendi, administration of recombinant factor VIII may be required to control bleeding episodes.

**COVERAGE GUIDELINES**

This policy supersedes **ALL** Factor Products for treatment of Blood Coagulation Disorders Policies prior to September 2001.

Coverage for factor products may be provided by the plan for Members with a diagnosis of hemophilia A, hemophilia B, or von Willebrand disease who meet any one of the criteria described below:

1. Treatment and/or management of acute bleeding in Members with severe hemophilia, and maintenance therapy as needed to maintain trough factor levels at 1% or greater
   OR
2. Treatment and/or management of acute bleeding episodes for Members with mild hemophilia (factor levels > 5% and <30%) or moderate hemophilia (factor levels of 1% - 5%), such as bleeding episodes associated with surgery or trauma
   OR
3. Treatment and/or management of acute bleeding in Members with von Willebrand disease, and in clinical situations in which patients with von Willebrand disease are at increased risk of bleeding (i.e., surgery or trauma)
   OR
4. Treatment and/or management of significant menorrhagia in women with von Willebrand disease

**Note:** There are no widely accepted severity categories for von Willebrand disease as there are for Hemophilia.

**NovoSeven®️ or Novoseven RT (Coagulation Factor VIIa [recombinant])**

In addition to the above criteria, the plan may cover NovoSeven®️ or Novoseven RT (Coagulation Factor VIIa [recombinant]) for Members with acquired hemophilia or congenital factor VII deficiency when either of the following criteria is met:

1. Treatment and/or management of acute bleeding episodes for Members with acquired hemophilia, and in clinical situations in which patients with acquired hemophilia are at increased risk of bleeding (i.e. surgery or trauma)
   OR
2. Treatment and/or management of acute bleeding in Members with congenital factor VII deficiency, and in clinical situations in which patients with congenital factor VII deficiency are at increased risk of bleeding (i.e., surgery or trauma)

**Coagadex®️ (Coagulation Factor X [Human])**

Coverage for Factor X [Human] (Coagadex) may be provided by the plan for adult and pediatric Members age 12 and older with a diagnosis of hereditary Factor X (FX) deficiency when either of the following criteria is met:

1. On-demand treatment and control of bleeding episodes
   OR
2. Perioperative management of bleeding in patients with mild hereditary Factor X deficiency

**Corifact®️ (Factor XIII Concentrate [Human])**

Coverage for Factor XIII Concentrate [Human] (Corifact) may be provided by the plan for Members with a diagnosis of congenital Factor XIII (FXIII) deficiency when either of the following criteria is met:

1. Routine prophylactic treatment of congenital FXIII deficiency in clinical situations in which Members with congenital Factor XIII deficiency are at increased risk of bleeding (i.e., surgery)
   OR
2. Peri-operative management of surgical bleeding in adult and pediatric Members with congenital factor XIII (FXIII) deficiency
**Tretten® (Coagulation Factor XIII A-Subunit [Recombinant])**
Coverage for Coagulation Factor XIII A-Subunit [Recombinant] (Tretten) may be provided by the plan for Members with a diagnosis of congenital factor XIII A-subunit deficiency when the following criterion is met:

1. Routine prophylaxis of bleeding in Members with confirmed congenital factor XIII A-subunit deficiency

**Vonvendi (von Willebrand Factor [Recombinant])**
Coverage for Von Willebrand factor [Recombinant] (Vonvendi) may be provided by the plan for Members with a diagnosis of von Willebrand disease when the following criterion is met:

1. Documentation from the provider why treatment with Alphanate®, Humate-P®, and Wilate® is not clinically inappropriate

**LIMITATIONS**

1. The quantity of factor product dispensed should be a reasonable estimation of a 30-day supply based on the patient’s current utilization and packaging restrictions.

   **Note:** The designated provider will contact a Tufts Health Plan Care Manager when they identify that a Member does not meet the Tufts Health Plan Clinical Criteria, or if the Member has severe disease with an inhibitor titer, frequent bleeding episodes and/or frequency hospitalization, or who may benefit from case management services.

2. Coverage of Tretten (Coagulation Factor XIII A-Subunit [Recombinant]) will not be authorized for the diagnosis of congenital factor XIII B-subunit deficiency.

3. Coverage of Coagadex (Coagulation Factor X [Human]) will not be authorized for perioperative management of bleeding in major surgery in members with moderate and severe hereditary Factor X deficiency.

**CODES**
The following HCPCS/CPT code(s) are:

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<th>Code</th>
<th>Description</th>
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<tr>
<td>C9140</td>
<td>Injection, factor VIII (antihemophilic factor, recombinant) (Afstyla), 1 IU</td>
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<tr>
<td>J7175</td>
<td>Injection, factor X, (human), 1 IU (Coagadex)</td>
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<td>J7179</td>
<td>Injection, Von Willebrand Factor (recombinant), (Vonvendi), 1 IU VWF:RCo</td>
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<td>Injection, factor IX, albumin fusion protein, (recombinant), Idelvion, 1 IU</td>
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<td>Injection, factor VIII, (antihemophilic factor, recombinant), pegylated, 1 IU (Adynovate)</td>
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<td>J7209</td>
<td>Injection, factor VIII, (antihemophilic factor, recombinant), (Nuwig), 1 IU</td>
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<td>J7180</td>
<td>Injection, factor XIII (antihemophilic factor, human), 1 IU</td>
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<td>J7181</td>
<td>Injection, factor XIII A-subunit, (recombinant), per IU</td>
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<td>Injection, factor VIII, (antihemophilic factor, recombinant), (Novoeight), per IU</td>
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<td>Injection, von Willebrand factor complex (human), Wilate, 1 IU VWF:RCO</td>
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<td>Injection, factor VIII (antihemophilic factor, recombinant) (Xyntha), per IU</td>
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<td>Injection, factor VIII (antihemophilic factor, recombinant), (Obizur), per IU</td>
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<td>Factor VIIa (antihemophilic Factor, recombinant), per 1mcg</td>
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<tr>
<td>J7190</td>
<td>Factor VIII (antihemophilic factor [human]) per IU</td>
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<td>J7192</td>
<td>Factor VIII (antihemophilic factor, recombinant) per IU, not otherwise specified</td>
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<td>J7193</td>
<td>Factor IX (antihemophilic factor, purified, non-recombinant) per IU</td>
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<td>J7194</td>
<td>Factor IX, complex, per IU</td>
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<td>Factor IX (antihemophilic factor, recombinant) per IU</td>
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<td>J7198</td>
<td>Anti-inhibitor, per IU</td>
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<td>J7199</td>
<td>Hemophilia clotting factor, not otherwise classified</td>
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<td>Injection, factor IX, Fc fusion protein (recombinant), Alprolix, per IU</td>
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<tr>
<td>Q9975</td>
<td>Injection, factor VIII, Fc fusion protein, (recombinant), per IU</td>
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REFERENCES
27. FEIBA NF [package insert]. Westlake Village, CA; Baxter Healthcare Corporation; 2013 November.
41. IXinity [package insert]. Winnipeg, Manitoba, Canada: Cangene Corporation; 2015 April.
77. Profilnine SD [package insert]. Los Angeles, CA; Grifols Biologics Inc.; 2014 May.


APPROVAL HISTORY
December 1999: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:
- December 14, 2004: Addition of the criteria of "Documented definitive diagnosis by a hematologist of Hemophilia A or Hemophilia B."
- December 13, 2005: No changes
- November 14, 2006: Added "Congenital Factor VII deficiency" to title. Added criteria for the coverage of NovoSeven (Coagulation Factor VIIa [recombinant]) for acquired hemophilia and congenital factor VII deficiency to the pharmacy coverage guidelines.
- November 13, 2007: No changes
- September 9, 2008: Added Novoseven RT to criteria for Members with acquired hemophilia or congenital factor VII deficiency.
- September 8, 2009: No changes
- January 1, 2010: Removal of Tufts Medicare Preferred language (separate criteria have been created specifically for Tufts Medicare Preferred)
- July 13, 2010: Administrative updates: removed code J7191, product has been discontinued. Added C9267, J7185 and J7186.
- July 12, 2011: Added coverage guidelines for factor XIII deficiency. Changed title from "Factor Products for the Treatment of Hemophilia, Congenital Factor VII Deficiency, and Von Willebrand Disease" to "Factor Products”.
- January 1, 2012: Administrative updates: Added reimbursement codes J7180 and J7183 to policy.
- June 12, 2012: Administrative updates: Removed deleted codes J7184 and Q2041 from policy.
- April 9, 2013: Added Peri-operative management of surgical bleeding to covered uses of Corifact.
- April 8, 2014: No changes.
- October 1, 2014: Administrative update: Added reimbursement codes C9134 and C9135.
- April 1, 2015: Administrative updates: Added reimbursement code Q9975.
- May 12, 2015: No changes
- February 9, 2016: Added coverage guidelines for Coagulation Factor X [Human] (Coagadex).
- April 1, 2016: Administrative update: Added reimbursement codes C9137 and C9138.
- October 1, 2016: Administrative update: Added reimbursement code C9139.
- October 18, 2016: Added Vonvendi to the criteria.
- January 1, 2017: Administrative update: added new C (C9140) and J codes (J7175, J7179, J7202, J7207, J7209) to Medical Necessity Guideline, updated description of J Code J7201, and removed expired C codes (C9137, C9138, C9139).
- March 14, 2017: No changes.

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION
Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. They are used in conjunction with a member’s benefit document and in
coordination with the member’s physician(s). The plan makes coverage decisions on a case-by-case basis considering the individual member’s health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

This Pharmacy Medical Necessity Guideline does not apply to Uniformed Services Family Health Plan members or to certain delegated service arrangements. Unless otherwise noted in the member’s benefit document or applicable Pharmacy Medical Necessity Guideline, Pharmacy Medical Necessity Guidelines do not apply to CareLink℠ members. For self-insured plans, drug coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a coverage guideline and a self-insured member’s benefit document, the provisions of the benefit document will govern. Applicable state or federal mandates will take precedence.

For Tufts Health Plan Medicare Preferred, please refer to Tufts Health Plan Medicare Preferred Prior Authorization Criteria.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.