

Pharmacy Medical Necessity Guidelines: Factor Products

Effective: November 16, 2020

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	
Pharmacy (RX) or Medical (MED) Benefit	MED	Department to Review	PRECERT /MM
<p>These pharmacy medical necessity guidelines apply to the following:</p> <p>Commercial Products</p> <ul style="list-style-type: none"> <input checked="" type="checkbox"/> Tufts Health Plan Commercial products – large group plans <input checked="" type="checkbox"/> Tufts Health Plan Commercial products – small group and individual plans <input checked="" type="checkbox"/> Tufts Health Freedom Plan products – large group plans <input checked="" type="checkbox"/> Tufts Health Freedom Plan products – small group plans • CareLinkSM – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization <p>Tufts Health Public Plans Products</p> <ul style="list-style-type: none"> <input checked="" type="checkbox"/> Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product) <input checked="" type="checkbox"/> Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans <input checked="" type="checkbox"/> Tufts Health RITogether – A Rhode Island Medicaid Plan 		<p>Fax Numbers:</p> <p>All plans except Tufts Health Public Plans: PRECERT:617.972.9409</p> <p>Tufts Health Public Plans: MM:888.415.9055</p>	

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

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[®], Espercot[®], Helixate[®] FS, Jivi[®], 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[®], Rebinyn[®], 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, Sevenfact[®]

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.

Helixate[®] FS (antihemophilic coagulation factor VIII [Recombinant])

In addition to the above criteria, the plan may cover Helixate[®] FS for Members when the following criteria is met:

1. The provider has indicated clinical inappropriateness of treatment with Kogenate[®] FS

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 appropriate

LIMITATIONS

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

Code	Description
J7175	Injection, factor X, (human), 1 IU (Coagadex)
J7179	Injection, Von Willebrand Factor (recombinant), (Vonvendi), 1 IU VWF:RCo
J7180	Injection, factor XIII (antihemophilic factor, human), 1 IU
J7181	Injection, factor XIII A-subunit, (recombinant), per IU
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
J7186	Injection, antihemophilic factor VIII/Von Willebrand factor complex (human), per factor VIII I.U.
J7187	Injection, Von Willebrand factor complex (Humate-P), per IU, VWF:RCo
J7188	Injection, factor VIII (antihemophilic factor, recombinant), (Obizur), per IU
J7189	Factor VIIa (antihemophilic Factor, recombinant), per 1mcg
J7190	Factor VIII (antihemophilic factor [human]) per IU
J7192	Factor VIII (antihemophilic factor, recombinant) per IU, not otherwise specified
J7193	Factor IX (antihemophilic factor, purified, non-recombinant) per IU
J7194	Factor IX, complex, per IU
J7195	Factor IX (antihemophilic factor, recombinant) per IU

Code	Description
J7198	Anti-inhibitor, per IU
J7199	Hemophilia clotting factor, not otherwise classified
J7200	Injection, factor IX, (antihemophilic factor, recombinant), Rixubis, per IU
J7201	Injection, factor IX, Fc fusion protein (recombinant), Alprolix, per IU
J7202	Injection, factor IX, albumin fusion protein, (recombinant), Idelvion, 1 IU
J7203	Injection factor ix, (antihemophilic factor, recombinant), glycopegylated, (rebinyn), 1 iu
J7205	Injection, factor VIII, Fc fusion protein, (recombinant), per IU
J7207	Injection, factor VIII, (antihemophilic factor, recombinant), pegylated, 1 IU (Adynovate)
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 IU
J7211	Injection, factor VIII, (antihemophilic factor, recombinant), (Kovaltry), 1 IU
J7204	Injection, Factor VIII, antihemophilic factor (recombinant), (Esperoct), glycopegylated-exei, per IU
J7212	Factor viia (antihemophilic factor, recombinant)-jncw (sevenfact), 1 microgram

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APPROVAL HISTORY

December 1999: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

1. December 14, 2004: Addition of the criteria of "Documented definitive diagnosis by a hematologist of Hemophilia A or Hemophilia B."
2. December 13, 2005: No changes
3. 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.
4. November 13, 2007: No changes
5. September 9, 2008: Added Novoseven RT to criteria for Members with acquired hemophilia or congenital factor VII deficiency.
6. September 8, 2009: No changes
7. January 1, 2010: Removal of Tufts Medicare Preferred language (separate criteria have been created specifically for Tufts Medicare Preferred)
8. July 13, 2010: Administrative updates: removed code J7191, product has been discontinued. Added C9267, J7185 and J7186.
9. January 1, 2011: Administrative updates: replaced temporary code C9267 with code J7184. Added J7198.
10. 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".
11. January 1, 2012: Administrative updates: Added reimbursement codes J7180 and J7183 to policy.
12. June 12, 2012: Administrative updates: Removed deleted codes J7184 and Q2041 from policy.
13. April 9, 2013: Added Peri-operative management of surgical bleeding to covered uses of Corifact.
14. January 1, 2014: Administrative update: Added reimbursement code C9133.
15. April 8, 2014: No changes.
16. May 13, 2014: Added coverage guidelines for Coagulation Factor XIII A-Subunit [Recombinant] (Tretten).
17. October 1, 2014: Administrative update: Added reimbursement codes C9134 and C9135.
18. January 1, 2015: Administrative update: Removed reimbursement codes C9133, C9134 and C9135. Added reimbursement codes C9136, J7181, J7182, J7200 and J7201.
19. April 1, 2015: Administrative updates: Added reimbursement code Q9975.
20. May 12, 2015: No changes
21. January 1, 2016: Administrative updates: Removed reimbursement code C9136. Added reimbursement codes J7188 and J7205. Changed to rebranded template.
22. February 9, 2016: Added coverage guidelines for Coagulation Factor X [Human] (Coagadex).
23. April 1, 2016: Administrative update: Added reimbursement codes C9137 and C9138.
24. October 1, 2016: Administrative update: Added reimbursement code C9139.
25. October 18, 2016: Added Vonvendi to the criteria.

26. 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).
27. March 14, 2017: No changes.
28. April 11, 2017: Administrative update, Adding Tufts Health RITogether to the template.
29. October 17, 2017: Effective 1/1/18, criteria updated to require clinical inappropriateness of Kogenate FS prior to approval of Helixate FS.
30. April 1, 2018: Administrative update: Added new C Code C9468 to Medical Necessity Guideline.
31. May 8, 2018: Administrative update: Added Rebinyn to the list of available Coagulation Factor IX (Recombinant) agents in the Overview section.
32. July 10, 2018: Effective October 1, 2018 the Medical Necessity Guideline applies to Tufts Health Together and Tufts Health RITogether.
33. January 1, 2019: Administrative update: added new J code J7203 to the Medical Necessity Guideline and removed expired C code C9468 from the Medical Necessity Guideline.
34. February 12, 2019: Added Jivi (antihemophilic factor [recombinant], PEGylated-aucl) to the Medical Necessity Guideline. Administrative update: removed deleted Q code Q9975 and deleted C code C9140 from the Medical Necessity Guideline. Administrative update: added J codes J7210 and J7211 to the Medical Necessity Guideline.
35. July 1, 2019: Administrative update: Added new J Code J7208 to Medical Necessity Guideline. Administrative update: Removed expired code C9141 from Medical Necessity Guideline.
36. January 14, 2020: No changes.
37. March 10, 2020: Added Espercot to the Medical Necessity Guideline.
38. November 10, 2020: Added Sevenfact to the Medical Necessity Guideline.

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. 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.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

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.