Medical Drug Clinical Criteria

Subject:	Select Clotting Agents for Bleeding Disorders		
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Overview

This document addresses select clotting factor replacement treatments for various hereditary blood disorders. Fibrin products, fibrin sealants and blood products provided by blood banks are not included in this document. Non-bypassing factor products for hemophilia A and hemophilia B, as well as Hemlibra and agents for von Willebrand disease are addressed in other documents.

Factor replacement treatments can be created from blood products (human plasma-derived) and others that are manufactured (recombinant). Replacement therapy may be given on a routine, preventive basis which is also called prophylactic therapy. The infusion of factor replacements given to stop a bleeding episode is called on-demand or episodic therapy.

Products in this document include:

- Anti-inhibitor Coagulant Complex
  - FEIBA
- Coagulation Factor X, Human plasma-derived
  - Coagadex
- Factor VIIa Recombinant
  - Novoseven RT
  - SevenFact
- Factor XIII
  - Factor XIII Human plasma-derived ---Corifact
  - Factor XIII A subunit Recombinant ---Tretten
- Fibrinogen Concentrate
  - Human plasma-derived---RiaSTAP
  - Human fibrinogen ---Fibryga

Factor X (FX), also called Stuart-Prower factor, can affect females and males equally. The factor X protein is involved in enzyme activation to help produce blood clots.

Factor XIII (FXIII), also called fibrin stabilizing factor, is considered the rarest factor deficiency, and can affect both genders equally. FXIII is responsible for stabilization of blood clots so that the clot doesn't break down and cause recurrent bleeds. FXIII circulates in plasma as FXIII A-subunits and FXIII B-subunits held together by strong bonds. FXIII A is the active unit in the coagulation cascade, while FXIII B acts as only the carrier molecule for subunit A. FXIII B itself does not provide any activity to correct B-subunit deficiencies.

Fibrinogen deficiencies are caused by a deficiency in factor I and includes three forms – afibrinogenemia (absent fibrinogen), hypofibrinogenemia (low levels of fibrinogen), and dysfibrinogenemia (abnormally functioning fibrinogen). Fibrinogen is normally produced in the liver and circulates in the body to help form clots and prevent bleeding. Factor I deficiencies can affect men and women equally.

Inhibitor development is the most common and a severe complication of factor replacement treatment, developing in approximately 15-20% of people with hemophilia (CDC, 2014). Inhibitors are antibodies to replacement factors which reduce response to factor replacement therapy and may result in need for higher doses of factor products. In addition, the use of other agents, such as bypassing agents, does not replace the missing factor "but go around or (bypass) the factors that are blocked by the inhibitor to help the body form a normal clot" (CDC, 2014) to control bleeding episodes. The FDA-approved bypassing agents are FEIBA, NovoSeven RT, and SevenFact.

FEIBA, NovoSeven RT, and SevenFact all have black box warnings for thromboembolic events, particularly after high doses and/or in patients with thrombotic risk factors. Monitoring for signs and symptoms of thromboembolic events is recommended.

Clinical Criteria

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

Coagadex (Human-plasma derived Coagulation Factor X)

Initial requests for Coagadex (Human-plasma derived Coagulation Factor X) may be approved if the following criteria are met:

I. Individual has a diagnosis of severe or moderate hereditary Factor X deficiency (defined as less than 5 IU/dL or 5% endogenous Factor X) (NHf, Srivastava 2020); **AND**
II. Individual is using for one of the following:
    A. Treatment of acute bleeding episodes; **OR**
    B. Peri-procedural management for surgical, invasive or interventional radiology procedures; **OR**
    C. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes;

OR

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

Continuation requests for Coagadex (Human-plasma derived Coagulation Factor X) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Coagadex (Human-plasma derived Coagulation Factor X) may not be approved for the following:

I. Individual with severe hereditary Factor X deficiency is using for perioperative management of bleeding in major surgery; **OR**
II. When the above criteria are not met and for all other indications.

FEIBA (Anti-inhibitor Coagulant Complex)

Initial requests for FEIBA (Anti-inhibitor Coagulant Complex) may be approved if the following criteria are met:

I. Individual has a diagnosis of hemophilia A or B with inhibitors to Factor VIII or Factor IX; **AND**
II. Individual is using for one of the following:
    A. Treatment of bleeding episodes; **OR**
    B. Peri-procedural operative management for surgical, invasive, or interventional radiology procedures; **OR**
    C. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes.

Continuation requests for FEIBA (Anti-inhibitor Coagulant Complex) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

FEIBA (Anti-inhibitor Coagulant Complex) may not be approved for the following:

I. Individual is using to treat bleeding episodes resulting from coagulation factor deficiencies in the absence of inhibitors to coagulation Factor VIII or coagulation Factor IX; **OR**
II. When the above criteria are not met and for all other indications.

NovoSeven RT (Factor VIIa Recombinant)

Initial requests for NovoSeven RT (Factor VIIa recombinant) may be approved if the following criteria are met:

I. Individual has one of the following diagnoses:
   A. Hemophilia A or B with inhibitors to Factor VIII or Factor IX; **OR**
   B. Acquired hemophilia; **OR**
   C. Congenital Factor VII deficiency; **AND**
II. Individual is using for one of the following:
   A. Individual is using for treatment of bleeding episodes; **OR**
   B. Individual is using in the prevention of bleeding in surgical interventions or invasive procedures;

OR

III. Individual has a diagnosis of Glanzmann's thrombasthenia; **AND**
IV. Individual is using for the treatment of bleeding episodes and peri-operative management related to diagnosis; **AND**
V. Individual has documented refractoriness to platelet transfusions with or without antibodies to platelets.

Continuation requests for NovoSeven RT (Factor VIIa recombinant) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

NovoSeven RT (Factor VIIa recombinant) may not be approved when the above criteria are not met and for all other indications.

RiaSTAP (Human plasma-derived Fibrinogen concentrate) or Fibryga (Human fibrinogen)

Initial requests for RiaSTAP (Human plasma-derived Fibrinogen concentrate) or Fibryga (Human fibrinogen) may be approved if the following criteria are met:

I. Individual has a diagnosis of congenital fibrinogen deficiency (afibrinogenemia or hypofibrinogenemia); **AND**
II. Individual is using for the treatment of acute bleeding episodes.

Continuation requests for RiaSTAP (Human plasma-derived Fibrinogen concentrate) or Fibryga (Human fibrinogen) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

RiaSTAP (Human plasma-derived Fibrinogen concentrate) or Fibryga (Human fibrinogen) may not be approved for the following:

I. Individual has a diagnosis of dysfibrinogenemia; **OR**
II. When the above criteria are not met and for all other indications.

SevenFact (Factor VIIa Recombinant)

Initial requests for SevenFact (Factor VIIa Recombinant) may be approved if the following criteria are met:

I. Individual is 12 years of age or older; **AND**
II. Individual has a diagnosis of hemophilia A or B with inhibitors to Factor VIII or Factor IX; **AND**
III. Individual is using for the treatment and control of bleeding episodes.

Continuation requests for SevenFact (Factor VIIa Recombinant) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

SevenFact (Factor VIIa Recombinant) may not be approved for the following:

I. Individual is using for the treatment of congenital factor VII deficiency; **OR**
II. Individual is using to treat bleeding episodes resulting from coagulation factor deficiencies in the absence of inhibitors to coagulation Factor VIII or coagulation Factor IX; **OR**
III. When the above criteria are not met and for all other indications.

Tretten or Corifact (Factor XIII)

Initial requests for Corifact (Human Plasma-derived, Factor XIII) may be approved if the following criteria are met:

I. Individual has a diagnosis of Factor XIII deficiency; **AND**
II. Individual is using for routine prophylactic treatment to prevent or reduce the frequency of bleeding episodes; **OR**
III. Individual is using for peri-procedural management for surgical, invasive or interventional radiology procedures.

Initial requests for Tretten (Recombinant Factor XIII A-Subunit) may be approved if the following criteria are met:

I. Individual has a diagnosis of congenital Factor XIII A-Subunit deficiency; **AND**
II. Individual is using as routine prophylaxis for bleeding.

Continuation requests for Corifact (Human Plasma-derived, Factor XIII) or Tretten (Recombinant Factor XIII A-Subunit) may be approved if the following criteria are met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

Corifact (Human Plasma-derived, Factor XIII) may not be approved for the following:

I. When the above criteria are not met and for all other indications.

Tretten (Recombinant Factor XIII A-Subunit) may not be approved for the following:

II. Individual with congenital Factor XIII B-subunit deficiency; **OR**
III. When the above criteria are not met and for all other indications.

Coding

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

Anti-inhibitor Coagulant Complex (FEIBA)

HCPCS	
J7198	Anti-inhibitor; per IU [FEIBA]

ICD-10 Diagnosis	
D66	Hereditary factor VIII deficiency [hemophilia A]
D67	Hereditary factor IX deficiency [hemophilia B]
D68.311	Acquired hemophilia
D68.318	Other hemorrhagic disorder due to intrinsic circulating anticoagulants, antibodies, or inhibitors
Z29.8	Encounter for other specified prophylactic measure
Z79.899	Other long term (current) drug therapy [prophylactic]

Factor VIIa Recombinant (NovoSeven RT)

HCPCS	
J7189	Factor VIIa (Anti-hemophilic factor, recombinant), per 1 microgram [NovoSeven RT]

ICD-10 Diagnosis	
D66	Hereditary factor VIII deficiency [hemophilia A]
D67	Hereditary factor IX deficiency [hemophilia B]
D68.2	Hereditary deficiency of other clotting factors
D68.311	Acquired hemophilia

D68.318	Hemorrhagic disorder due to intrinsic circulating anticoagulants
D68.4	Acquired coagulation factor deficiency
D69.1	Qualitative platelet defects [when specified as Glanzmann's thrombasthenia]
Z79.899	Other long term (current) drug therapy

Factor X (Coagadex)

HCPCS

J7175	Injection, factor X, (human), 1 I.U. [Coagadex]

ICD-10 Diagnosis

D68.2	Hereditary deficiency of other clotting factors
D68.8	Other coagulation defects
D68.9	Coagulation defect, unspecified

Factor XIII (Corifact, Tretten)

HCPCS

J7180	Injection, factor XIII (Anti-hemophilic factor, human), 1 I.U. [Corifact]
J7181	Injection, factor XIII A-subunit, (recombinant), per IU [Tretten]

ICD-10 Diagnosis

D68.2	Hereditary deficiency of other clotting factors
Z29.8	Encounter for other specified prophylactic measure
Z79.899	Other long term (current) drug therapy [prophylactic]

Fibrinogen Concentrate, Human plasma-derived (RiaSTAP); Human fibrinogen (Fibryna)

HCPCS

J7177	Injection, human fibrinogen concentrate, 1 mg [Fibryga]
J7178	Injection, human fibrinogen concentrate, 1 mg [RiaSTAP]

ICD-10 Diagnosis

D68.2	Hereditary deficiency of other clotting factors

SevenFact (Factor VIIa Recombinant)

HCPCS

J7212	Factor viia (antihemophilic factor, recombinant)-jncw (sevenfact), 1 microgram

ICD-10 Diagnosis

D66	Hereditary factor VIII deficiency
D67	Hereditary factor IX deficiency
D68.0	Von Willebrand's disease
D68.2	Hereditary deficiency of other clotting factors
D68.311	Acquired hemophilia
D69.1	Qualitative platelet defects

Document History

Revised: 06/12/2023
Document History:

- 06/12/2023 – Select Review: Update Coagadex for new FDA indication. Coding Reviewed: No changes.
- 11/18/2022 – Annual Review: Update do not approve criteria for Corifact, modify prophylaxis criteria for Coagadex, wording and formatting. Coding Reviewed: No changes.
- 11/19/2021 – Annual Review: Add continuation criteria to all agents. Coding Reviewed: No changes.
- 11/20/2020 – Annual Review: Update Coagadex criteria to allow for prophylactic use in those with mild to moderate disease with severe phenotype hemophilia per guidelines. Add new clinical criteria for SevenFact. Updated references. Wording and formatting changes. Coding Reviewed: Added ICD-10-CM D68.8, D68.9, removed Z79.899 for Coagadex. Added HCPCS J7189, Added ICD-10-CM D66,D67, D68.0, D68.2, D68.311, D69.1 for SevenFact. Effective 1/1/2021 Added HCPCS J7212, Removed J7189 for SevenFact only.
- 11/15/2019 – Annual Review: Create new clinical criteria document for select clotting agents for bleeding disorders (FEIBA, Coagadex, Corifact, NovoSeven RT, Tretten, RiaSTAP, and Fibryna removed from ING-CC-0065). Update Coagadex criteria to remove moderate factor X deficiency from the non-approvable criteria for use in perioperative management of bleeding in major surgery per label. Clarified Coagadex criteria for control and prevention of acute bleeding episodes and replaced with “treatment”. Changed name of Fibryna to Fibryga per manufacturer update. Wording and formatting changes for clarity and consistency. Coding Reviewed. No changes.

References

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