BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

FEIBA® (anti-inhibitor coagulant complex)
NOVOSEVEN RT® (coagulation Factor VIIa recombinant)
SEVENFACT® [coagulation Factor VIIa (recombinant)-jncw]
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

FEIBA (anti-inhibitor coagulant complex)

➢ **Criteria for initial therapy:** Feiba (anti-inhibitor coagulant complex) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Hematologist

2. Individual has a confirmed diagnosis of Hemophilia A or B with inhibitors (to factor VIII or factor IX) and request is for **ONE** of the following:

a. Control and prevention of bleeding episodes
b. Perioperative management
c. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes

3. Individual does not have bleeding episodes resulting from coagulation factor deficiencies in the absence of inhibitors to factor VIII or factor IX

4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

5. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation

6. There are **NO** FDA-label contraindications such as:
   a. History of anaphylactic or severe hypersensitivity reactions to FEIBA or any of its components, including factors of the kinin generating system
   b. Disseminated intravascular coagulation (DIC)
   c. Acute thrombosis or embolism (including myocardial infarction)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Feiba (anti-inhibitor coagulant complex) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Hematologist

2. Individual has a confirmed diagnosis of Hemophilia A or B with inhibitors (to factor VIII or factor IX) and request is for **ONE** of the following:
   a. Control and prevention of bleeding episodes
   b. Perioperative management
   c. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes

3. Individual does not have bleeding episodes resulting from coagulation factor deficiencies in the absence of inhibitors to factor VIII or factor IX

4. Individual's condition has responded while on therapy with response defined as hemostasis has been achieved and maintained as needed for clinical condition being treated

5. Individual has been adherent with the medication

6. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

7. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:
    a. Thromboembolic event including venous thrombosis, pulmonary embolism, myocardial infarction, and stroke
    b. Anaphylaxis or severe hypersensitivity

8. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

NOVOSEVEN RT (coagulation Factor VIIa, recombinant)

- **Criteria for initial therapy:** Novoseven RT (coagulation Factor VIIa, recombinant) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Hematologist

2. Individual has a confirmed diagnosis of **ONE** of the following:
    a. Congenital Hemophilia A or B with Inhibitors
    b. Congenital Factor VII Deficiency
    c. Acquired Hemophilia
    d. Glanzmann's thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets

3. Request is for **ONE** of the following:

a. Treatment of bleeding episodes and perioperative management in adults and children with hemophilia A or B with inhibitors, congenital Factor VII (FVII) deficiency, and Glanzmann's thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets
b. Treatment of bleeding episodes and perioperative management in adults with acquired hemophilia

4. For Factor VII deficiency: Individual has a **baseline** prothrombin time and Factor VII (FVII) coagulant activity to monitor for antibody formation with continued monitoring of the individual as clinically appropriate

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation such as:
   a. Simultaneous use of activated prothrombin complex concentrates (aPCCs)
   b. Administration with coagulation factor XIII (FXIII)

7. There are **NO** FDA-label contraindications such as:
   a. Serious arterial and venous thrombotic events in individuals at risk for developing thrombotic events (see Definitions section)
   b. Hypersensitivity reactions, including anaphylaxis especially in those with known hypersensitivity to mouse, hamster, or bovine proteins

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Novoseven RT (coagulation Factor VIIa, recombinant) and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Hematologist

2. Individual has a confirmed diagnosis of **ONE** of the following:
   a. Congenital Hemophilia A or B with Inhibitors
   b. Congenital Factor VII Deficiency
   c. Acquired Hemophilia
   d. Glanzmann's thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets

3. Request is for **ONE** of the following:
    a. Treatment of bleeding episodes and perioperative management in adults and children with hemophilia A or B with inhibitors, congenital Factor VII (FVII) deficiency, and Glanzmann's thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets
    b. Treatment of bleeding episodes and perioperative management in adults with acquired hemophilia

4. Individual's condition has responded while on therapy with response defined as hemostasis has been achieved and maintained as needed for clinical condition being treated

5. Individual has been adherent with the medication

6. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

7. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:
    a. Serious arterial and venous thrombotic events in individuals at risk for developing thrombotic events (see Definitions section)
    b. Hypersensitivity reactions, including anaphylaxis especially in those with known hypersensitivity to mouse, hamster, or bovine proteins

8. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation such as:
    a. Simultaneous use of activated prothrombin complex concentrates (aPCCs)
    b. Administration with coagulation factor XIII (FXIII)

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

    1. **Off-Label Use of Non-Cancer Medications**

    2. **Off-Label Use of Cancer Medications**

SEVENFACT [coagulation Factor VIIa (recombinant)-jncw]

- **Criteria for initial therapy:** Sevenfact [coagulation factor VIIa (recombinant)-jncw] and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Hematologist
2. Individual has a confirmed diagnosis of hemophilia A or B with inhibitors
3. Request is for treatment and control of bleeding episodes in hemophilia A or B with inhibitors
4. Request is not for treatment of congenital factor VII deficiency
5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)
6. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation
7. Individual does **NOT** have the FDA-label contraindication of known allergy to rabbits or rabbit proteins

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Sevenfact [coagulation factor VIIa (recombinant)-jncw] and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Hematologist
2. Individual has a confirmed diagnosis of hemophilia A or B with inhibitors
3. Request is for treatment and control of bleeding episodes in hemophilia A or B with inhibitors
4. Request is not for treatment of congenital factor VII deficiency
5. Individual's condition has responded while on therapy with response defined as hemostasis has been achieved and maintained as needed for clinical condition being treated
6. Individual has been adherent with the medication
7. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)
8. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:

a. Serious arterial and venous thrombotic events in individuals at risk for developing thrombotic events (see Definitions section)
b. Hypersensitivity reactions, including anaphylaxis

9. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Feiba (anti-inhibitor coagulant complex) is indicated for use in hemophilia A and B individuals with inhibitors for: 1) control and prevention of bleeding episodes; 2) perioperative management; and 3) routine prophylaxis to prevent or reduce the frequency of bleeding episodes. Dosage and duration of treatment depend on the location and extent of bleeding, and the individual's clinical condition and clinical response. FEIBA contains factor VIII inhibitor bypassing activity. Clinical response to treatment with FEIBA may vary by individual and may not correlate with the individual's inhibitor titer. Feiba is not indicated for the treatment of bleeding episodes resulting from coagulation factor deficiencies in the absence of inhibitors to coagulation factor VIII and coagulation factor IX. The mechanism of action of Feiba is unknown. Feiba contains multiple components, mainly non-activated factors II, IX, X and mainly activated factor VII (aVII). In addition, it contains factor VIII coagulant antigen (FVIII C:Ag) and trace amounts of factors of the kinin generating system. These factors can interact with plasma coagulation factors and platelets to increase the impaired thrombin generation of hemophilia patients with inhibitors, leading to hemostasis.

Novoseven RT (coagulation Factor VIIa, recombinant, rFVIIa) is a vitamin K-dependent glycoprotein indicated for treatment of: 1) bleeding episodes and peri-operative management in adults and children with hemophilia A or B with inhibitors; 2) congenital Factor VII (FVII) deficiency; 3) Glanzmann's thrombasthenia (GT) with refractoriness to platelet transfusions, with or without antibodies to platelets; and 4) bleeding episodes and peri-operative management in adults with acquired hemophilia. Platelet transfusions are the primary treatment in patients with GT without refractoriness to platelets or in patients without platelet specific antibodies.

GT is an inherited platelet function disorder where platelets lack the alpha-IIb beta-3 integrin (previously called the glycoprotein [GP] IIb/IIIa receptor), which is the platelet receptor for fibrinogen. When these individuals have bleeding or require surgery, platelet transfusions can be used. However, individuals with GT develop alloantibodies against GPIIb/IIIa and/or against human leukocyte (HLA) antigens, resulting in bleeding refractory to platelet transfusions. Avoiding platelet transfusions for minor bleeding is desirable which would then, allow

platelet transfusions to be reserved for life-threatening or major bleeding. Use of rFVIIa can be used to treat bleeding or to prevent surgical bleeding in individuals who have become refractory to platelet transfusion due to alloantibodies or in an approach to avoid development of alloantibodies in individuals who have not received platelet transfusion.

Sevenfact [coagulation factor VIIa (recombinant)-jncw, rFVIIa)] is a vitamin K-dependent glycoprotein indicated for the treatment and control of bleeding episodes occurring in adults and adolescents (12 years of age and older) with hemophilia A or B with inhibitors. Sevenfact is not indicated for the treatment of patients with congenital Factor VII deficiency

Novoseven RT and Sevenfact complex with tissue factor to activate coagulation Factor X to Factor Xa. Factor Xa, in complex with other factors, converts prothrombin to thrombin, which leads to the formation of a hemostatic plug by converting fibrinogen to fibrin inducing local hemostasis. This process may also occur on the surface of activated platelets.

Inhibitors are antibodies directed against infused clotting factors that prevent the functional activity or pharmacokinetics of the factor against which they are directed. Inhibitors occur most often in severe hemophilia (factor VIII or IX <1percent) and are more common in hemophilia A than hemophilia B. They may be discovered when factor infusions become unsuccessful in treating or preventing bleeding or in raising the factor level. In addition, infusion reactions may occur to infused factor. Inhibitors are confirmed using the Bethesda assay (with Nijmegen modification). This establishes the diagnosis of an inhibitor and quantifies the titer. Titers greater than or equal to 5 Bethesda units (BU) are considered high titer, and high titer inhibitors are considered high responding, even if they subsequently decline to below 5 BU. Individuals with high titer inhibitors usually require a bypassing agent or an alternative product. Individuals with low titer inhibitors may be treated with higher doses of factor to overcome the inhibitor. The number of exposure days correlates with the risk of inhibitor development. For hemophilia A, the majority of inhibitors develop within the first 20 exposure days. Data on development of inhibitors in hemophilia B are few with one review indicating inhibitor development occurs at a median of 11 exposure days.

Immune tolerance induction (ITI), also called immune tolerance therapy [ITT] or inhibitor eradication) is the primary method used to eliminate or control inhibitors. It involves administration of frequent, regularly scheduled doses of the deficient factor to reset the individual's immune system and reduce or ablate production of the antibody.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Novoseven: Risk factors for developing thrombotic events
Patients with congenital hemophilia receiving concomitant treatment with activated prothrombin complex concentrates (aPCCs), older patients particularly with acquired hemophilia and receiving other hemostatic agents, or patients with a history of cardiac, vascular disease

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Sevenfact: Risk factors for developing thrombotic events

History of congenital or acquired hemophilia receiving concomitant treatment with activated or non-activated prothrombin complex (aPCC/PCC) or other hemostatic agents
History of atherosclerotic disease, coronary artery disease, cerebrovascular disease, crush injury, septicemia, or thromboembolism

Resources:

Feiba (anti-inhibitor coagulant complex) product information, revised by Takeda Pharmaceuticals America, Inc. 03-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 19, 2024.

Novoseven RT (coagulation Factor VIIa, recombinant) product information, revised by Novo Nordisk 07-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 19, 2024.

Sevenfact [coagulation factor VIIa (recombinant)-jncw] product information, revised by Laboratoire Français du Fractionnement et des Biotechnologies Société Anonyme (LFB S.A.). 11-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 19, 2024.

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Hoffman M, Konkle BA. Recombinant factor VIIa: Administration and adverse effects. In: UpToDate, Leung LLK, Tirnauer JS (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through May 2024. Last updated March 02, 2023. Accessed June 20, 2024.

Menegatti M, Peyvandi F. Treatment of rare factor deficiencies other than hemophilia. Blood 2019;133(5):415-424. Accessed June 16, 2024.

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Konkle BA, Nakaya Fletcher S. Hemophilia B. 2000 Oct 2 [Updated 2024 Jun 6]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1495/. Accessed June 08, 2024.