Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO009

Description

FEIBA is an anti-inhibitor complex indicated for use in hemophilia A and B patients with inhibitors. NovoSeven RT is a recombinant coagulation factor VIIa for patients with hemophilia A and B with inhibitors, acquired hemophilia, congenital factor VII deficiency, and Glanzmann's thrombasthenia refractory to platelet transfusions. Sevenfact is a recombinant coagulation factor VIIa for patients with hemophilia A and B with inhibitors.

Length of Authorization

- Initial: 6 months (for on-demand and prophylaxis); 1 month (for perioperative)
- Renewal: 12 months (for prophylaxis); 6 months (for on-demand)

Quantity limits

Product Name	Dosage Form	Indication/ FDA Labeled Dosing	Quantity Limit
FEIBA, anti-inhibitor coagulant complex	500, 1000, 2500 units	**Control and prevention of bleeding – Hemophilia A or B with inhibitors:** Up to 100 units/kg every six to 12 hours until resolution of bleeding **Routine prophylaxis – Hemophilia A or B with inhibitors:** Up to 85 units/kg every other day **Perioperative management – Hemophilia A or B with inhibitors:** Up to 100 units/kg administered as a one-time dose immediately prior to surgery or up to 100 units/kg administered every six to 12 hours postoperatively until resolution of bleed and healing is achieved	**Control and prevention of bleeding – Hemophilia A or B with inhibitors:** Up to the number of doses requested every 28 days **Routine prophylaxis – Hemophilia A or B with inhibitors:** Up to 1,190 units/kg every 28 days **Perioperative management – Hemophilia A or B with inhibitors:** Up to the number of doses requested for 28 days
NovoSeven RT, coagulation factor VIIa (recombinant)	1 mg/vial (1000 mcg/vial) 2 mg/vial (2000 mcg/vial)	**Control and prevention of bleeding – Hemophilia A or B with inhibitors:** Up to 90 mcg/kg every three to six hours until hemostasis is achieved **Control and prevention of bleeding episodes – Acquired hemophilia:**	**Control and prevention of bleeding – Hemophilia A or B with inhibitors:** Up to the number of doses requested every 28 days **Control and prevention of bleeding episodes – Acquired hemophilia:** Up

Product Name	Dosage Form	Indication/ FDA Labeled Dosing	Quantity Limit
	5 mg/vial (5000 mcg/vial) 8 mg/vial (8000 mcg/vial)	Up to 90 mcg/kg every two to three hours until hemostasis is achieved **Control and prevention of bleeding episodes – Factor VII deficiency:** Up to 30 mcg/kg every four to six hours until hemostasis is achieved **Control and prevention of bleeding episodes – Glanzmann's Thrombasthenia:** Up to 90 mcg/kg every two to six hours until hemostasis is achieved **Routine prophylaxis – hemophilia A or B with inhibitors:** 90 mcg/kg once daily **Perioperative management – hemophilia A or B with inhibitors:** Up to 90 mcg/kg immediately before surgery, repeat every two hours during surgery, then up to 90 mcg/kg every two hours after surgery for five days, then every four hours or by continuous infusion, via pump, at 50 mcg/kg/hr until healing occurs **Perioperative management – acquired hemophilia:** Up to 90 mcg/kg immediately before surgery and every two to three hours for the duration of surgery and until hemostasis is achieved **Perioperative management – factor VII deficiency:** Up to 30 mcg/kg immediately before surgery and every four to six hours for the	to the number of doses requested every 28 days **Control and prevention of bleeding episodes – Factor VII deficiency:** Up to the number of doses requested every 28 days **Control and prevention of bleeding episodes – Glanzmann's Thrombasthenia:** Up to the number of doses requested every 28 days **Routine prophylaxis – Hemophilia A or B with inhibitors:** 2,520 mcg/kg per 28 days **Perioperative management – hemophilia A or B with inhibitors:** Up to the number of doses requested for 28 days **Perioperative management – acquired hemophilia:** Up to the number of doses requested for 28 days **Perioperative management – factor VII deficiency:** Up to the number of doses requested for 28 days

Product Name	Dosage Form	Indication/ FDA Labeled Dosing	Quantity Limit
		duration of surgery and until hemostasis is achieved **Perioperative management – Glanzmann's Thrombasthenia:** Up to 90 mcg/kg immediately before surgery and repeat every two hours for the duration of the procedure, then up to 90 mcg/kg every two to six hours to prevent post-operative bleeding	**Perioperative management – Glanzmann's Thrombasthenia:** Up to the number of doses requested for 28 days
Sevenfact, coagulation factor VIIa (recombinant) [eptacog beta]	1 mg/vial (1000 mcg/vial) 2 mg/vial (2000 mcg/vial) 5 mg/vial (5000 mcg/vial)	**Treatment and control of bleeding – Hemophilia A or B with inhibitors:** 75 mcg/kg repeated every 3 hours until hemostasis is achieved Or Initial dose of 225 mcg/kg. If hemostasis is not achieved within 9 hours, additional 75 mcg/kg doses may be administered every 3 hours as needed to achieve hemostasis	**Treatment and control of bleeding – Hemophilia A or B with inhibitors:** Up to the number of doses requested every 28 days

Initial Evaluation

Hemophilia A (congenital factor VIII deficiency)

I. **FEIBA or NovoSeven RT** may be considered medically necessary when the following criteria below are met:
   A. Treatment is prescribed by or in consultation with a hematologist; **AND**
   B. A diagnosis of hemophilia A has been confirmed by blood coagulation testing; **AND**
   C. Clinical documentation confirming that the member has inhibitors to factor VIII [i.e. high anti-FVIII titer (≥ 5 Bethesda units)]; **AND**
   D. Use is planned for one of the following indications:
      1. On-demand treatment and control of bleeding episodes; **OR**
      2. Perioperative management of bleeding; **OR**
      3. Routine prophylaxis to reduce the frequency of bleeding episodes when one of the following is met:

i. Member has had more than one documented episode of spontaneous bleeding; **OR**
ii. Member has had an inadequate response to Immune Tolerance Induction (ITI); **AND**

4. Prior therapy with emiziumab-kxwh (Hemlibra) was ineffective, not tolerated, or contraindicated

II. **Sevenfact** may be considered medically necessary when the following criteria below are met:
   A. Treatment is prescribed by or in consultation with a hematologist; **AND**
   B. A diagnosis of hemophilia A has been confirmed by blood coagulation testing; **AND**
   C. Clinical documentation confirming that the member has inhibitors to factor VIII [i.e. high anti-FVIII titer (≥ 5 Bethesda units)]; **AND**
   D. Use is planned for on-demand treatment and control of bleeding episodes ***only***

<u>Hemophilia B (congenital factor IX deficiency)</u>

I. **FEIBA** or **NovoSeven RT** may be considered medically necessary when the following criteria below are met:
   A. Treatment is prescribed by or in consultation with a hematologist; **AND**
   B. A diagnosis of hemophilia B has been confirmed by blood coagulation testing; **AND**
   C. Clinical documentation confirming that the member has inhibitors to factor VIX [i.e. high anti-IX titer (≥ 5 Bethesda units)]; **AND**
   D. Use is planned for one of the following indications:
      1. On-demand treatment and control of bleeding episodes; **OR**
      2. Perioperative management of bleeding; **OR**
      3. Routine prophylaxis to reduce the frequency of bleeding episodes when one of the following is met:
         i. Member has had more than one documented episode of spontaneous bleeding; **OR**
         ii. Member has had an inadequate response to Immune Tolerance Induction (ITI)

II. **Sevenfact** may be considered medically necessary when the following criteria below are met:
   A. Treatment is prescribed by or in consultation with a hematologist; **AND**
   B. A diagnosis of hemophilia B has been confirmed by blood coagulation testing; **AND**
   C. Clinical documentation confirming that the member has inhibitors to factor VIX [i.e. high anti-IX titer (≥ 5 Bethesda units)]; **AND**
   D. Use is planned for on-demand treatment and control of bleeding episodes ***only***

Acquired Hemophilia

I. **NovoSeven RT** may be considered medically necessary when the following criteria below are met:
   A. Treatment is prescribed by or in consultation with a hematologist; **AND**
   B. A diagnosis of acquired hemophilia has been confirmed by blood coagulation testing; **AND**
   C. Use is planned for one of the following indications:
      1. On-demand treatment and control of bleeding episodes; **OR**
      2. Perioperative management of bleeding

Congenital Factor VII Deficiency

I. **NovoSeven RT** may be considered medically necessary when the following criteria below are met:
   A. Treatment is prescribed by or in consultation with a hematologist; **AND**
   B. A diagnosis of congenital factor VII deficiency has been confirmed by blood coagulation testing; **AND**
   C. Use is planned for one of the following indications:
      1. On-demand treatment and control of bleeding episodes; **OR**
      2. Perioperative management of bleeding

Glanzmann's Thrombasthenia

I. **NovoSeven RT** may be considered medically necessary when the following criteria below are met:
   A. Treatment is prescribed by or in consultation with a hematologist; **AND**
   B. A diagnosis of Glanzmann Thrombasthenia has been confirmed by blood coagulation testing; **AND**
   C. Use is planned for one of the following indications:
      1. On-demand treatment and control of bleeding episodes; **OR**
      2. Perioperative management of bleeding; **AND**
   D. The use of platelet transfusions is known or suspected to be ineffective or contraindicated

II. FEIBA, NovoSeven RT, Sevenfact are considered investigational when used for all other conditions.

Renewal Evaluation

I. Documentation of clinical benefit, including decreased incidence of bleeding episodes or stability of bleeding episodes relative to baseline

Supporting Evidence

I. People with hemophilia A can develop antibodies to the factor replacement product that can interfere with the ability to treat bleeding and achieve adequate homeostasis. These antibodies, called inhibitors, develop in about 23-30% of people with Hemophilia A. Inhibitors often develop during childhood, especially during the first 50 exposure days to factor, with the greatest risk occurring between the first ten to 20 treatments.

II. Patients with hemophilia A or B who develop inhibitors to factor VIII or IX may no longer respond to clotting factor VIII or IX products to prevent or control bleeding episodes.

III. Treatment options for people who develop inhibitors are limited. Immune tolerance induction (ITI) is the main method for inhibitor eradication. It involves the administration of repeated doses of factor to tolerize the individual's immune system to the factor and reduce antibody production.

IV. Other options to treat bleeding in patients with inhibitors include bypassing products [e.g. recombinant activated factor VII (NovoSeven RT), factor eight inhibitor bypassing agent (FEIBA)], plasmapheresis, recombinant coagulation factor VII activated (Sevenfact), and high-dose factor infusion. Emicizumab-kxwh (Hemlibra) is indicated for prophylaxis in patients with hemophilia A and inhibitors. Choice of therapy is individualized and dependent on many factors.

V. A bypassing agent is generally the first choice in a patient with hemophilia A or B who has a high titer inhibitor and requires treatment for bleeding or surgery. Bypassing agents can also be used prophylactically to prevent bleeds. Sevenfact is only indicated for the treatment and control of bleeding episodes at this time. Emicizumab-kxwh (Hemlibra) is only indicated in the setting of prophylaxis.

VI. The bypassing agents contain an activated form of a downstream clotting factor in the coagulation cascade. Activated factor VII (factor VIIa) can directly activate factor X, bypassing the need for factors VIII and IX.

VII. The National Hemophilia Foundation's Medical and Scientific Advisory Council (MASAC) recommends that bypassing agents be used in patients with hemophilia A or B with inhibitors to prevent or control bleeding in settings in which clotting factor VIII or IX would otherwise be used, including before and after surgery and physical therapy.

VIII. In addition, MASAC recommends that prophylaxis with bypassing agents should be considered in patients with inhibitors. Furthermore, any patient with hemophilia A with an inhibitor who is having frequent bleeding episodes and is on either episodic therapy for prophylaxis with bypassing agents will likely derive significant benefit from emicizumab-kxwh (Hemlibra).

IX. Both FEIBA and NovoSeven RT contain activated clotting factors and both are effective for hemostasis in hemophilia. A randomized trial comparing FEIBA and NovoSeven RT demonstrated similar efficacy between the agents for controlling joint bleeds.

X. The safety and efficacy of emicizumab-kxwh (Hemlibra) in adult and pediatric patients with inhibitors was established in two Phase 3 trials (HAVEN 1 and HAVEN 2). Patients treated with

emicizumab-kxwh (Hemlibra) experienced significantly fewer bleeds compared to patients who received no prophylaxis.

XI. Emicizumab-kxwh (Hemlibra) prophylaxis has not been directly compared to any other prophylactic regimen (e.g. bypassing agent, factor VIII replacement); therefore, the comparative safety and efficacy is unknown.

XII. The safety and efficacy of NovoSeven RT for congenital factor VII deficiency, acquired hemophilia, and Glanzmann's Thrombasthenia was established based on small trials, including compassionate use trials and registries. NovoSeven RT was shown to be effective in controlling bleeding episodes.

Investigational or Not Medically Necessary Uses

There is no evidence to support the use of FEIBA, NovoSeven RT or Sevenfact in any other condition in the outpatient setting.

References

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10. UpToDate, Inc. Hemophilia A and B: Routine management including prophylaxis. UpToDate [database online]. Last updated February 11, 2019.
11. UpToDate, Inc. Treatment of bleeding and perioperative management in hemophilia A and B. UpToDate [database online]. Last updated November 26, 2018.

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Policy Implementation/Update:

Action and Summary of Changes	Date
Added 2mg/vial (2000 mcg/vial) Sevenfact product	04/2025
Addition of Sevenfact	08/2020
New policy created for bypassing agents	08/2019