



UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hemophilia – Eptacog Products – Sevenfact Utilization Management Medical Policy

- Sevenfact® (Factor VIIa [recombinant]-jncw intravenous infusion – LFB S.A./Hema Biologics)

REVIEW DATE: 11/08/2023

OVERVIEW

Sevenfact, a recombinant Factor VIIa product, is indicated for the treatment and control of bleeding episodes occurring in adults and adolescents (≥ 12 years of age) with **hemophilia A or B with inhibitors**.¹ As a limitation of use, Sevenfact is not indicated for the treatment of patients with congenital Factor VII deficiency.

Disease Overview

In hemophilia A and B, antibodies to exogenous clotting factor, known as “inhibitors”, may develop. Approximately 30% of patients with severe hemophilia A and up to 5% of patients with severe hemophilia B develop inhibitors to Factor VIII or Factor IX during their lifetime.² A high-responding inhibitor (≥ 5 Bethesda Units [BU]) tends to persist, whereas low-responding inhibitors of < 5 BU may wane without changes to the treatment regimen. Presence of inhibitors is associated with higher disease burden, increased risk of musculoskeletal complications, pain, physical limitations, and treatment challenges.^{2,3}

Dosing Information

Sevenfact is only indicated in the acute treatment setting for treatment of bleeding events. In the prescribing information, it is noted that maximum tolerated doses have not been determined for Sevenfact, and cumulative daily doses greater than 900 mcg/kg, which may be associated with greater risk of thromboembolic complications, have not been studied.¹ The National Hemophilia Foundation Medical and Scientific Advisory Council (MASAC) provides recommendations regarding doses of clotting factor concentrate in the home (2016).⁴ Per MASAC guidance, patients on prophylaxis should also have a minimum of one major dose and two minor doses on hand for breakthrough episodes. The guidance also notes that an adequate supply of clotting factor concentrate is needed to accommodate weekends and holidays. Therefore, maximum doses in this policy allow for three days of acute bleeding per 28 days. Doses exceeding this quantity will be reviewed on a case-by-case basis by a clinician.

Guidelines

National Bleeding Disorders Foundation MASAC guidelines (revised August 2023) recognize both Sevenfact and NovoSeven RT® (coagulation Factor VIIa [recombinant] intravenous infusion) as treatments for **hemophilia A or B with inhibitors**.⁵ No preference is stated for one agent over the other. It is noted that choice of product depends on multiple factors, including type of inhibitor (low- or high-responding), current titer, location of bleed, and previous response. Of note, NovoSeven RT, but not Sevenfact, is recognized as a treatment option in other settings, such as acquired hemophilia A and congenital Factor VII deficiency.

World Federation of Hemophilia (WFH) guidelines (2020) support recombinant Factor VIIa for patients with high-titer inhibitors who require acute treatment or around surgery/invasive procedures.³ For low-titer inhibitors, Factor VIII or IX replacement may be used. These products may also be used for patients with a history of a high-titer inhibitor whose titer has fallen to low or undetectable levels. However, once an anamnestic response occurs, further treatment with Factor replacement is typically no longer effective, and bypass agent therapy (e.g., recombinant Factor VIIa) is needed.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Sevenfact. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Sevenfact as well as the monitoring required for adverse events and long-term efficacy, approval requires Sevenfact to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Sevenfact is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. **Hemophilia A with Inhibitors.** Approve for 1 year if the patient meets all of the following (A, B, and C):
 - A) Patient is ≥ 12 years of age; AND
 - B) Patient meets one of the following (i, ii, or iii):
 - i. Patient has a positive inhibitor titer ≥ 5 Bethesda Units; OR
 - ii. Patient has a history of anamnestic response to Factor VIII replacement therapy, which, according to the prescriber, precludes the use of Factor VIII replacement to treat bleeding episodes; OR
 - iii. Patient has a history of refractory response to increased Factor VIII dosing, which, according to the prescriber, precludes the use of Factor VIII replacement to treat bleeding episodes; AND
 - C) The medication is prescribed by or in consultation with a hemophilia specialist.

Dosing. Approve up to 2,700 mcg/kg intravenously per 28 days.

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2. **Hemophilia B with Inhibitors.** Approve for 1 year if the patient meets all of the following (A, B, and C):
 - A) Patient is ≥ 12 years of age; AND
 - B) Patient meets one of the following (i, ii, or iii):
 - i. Patient has a positive inhibitor titer ≥ 5 Bethesda Units; OR
 - ii. Patient has a history of anamnestic response to Factor IX replacement therapy, which, according to the prescriber, precludes the use of Factor IX replacement to treat bleeding episodes; OR
 - iii. Patient has a history of refractory response to increased Factor IX dosing, which, according to the prescriber, precludes the use of Factor IX replacement to treat bleeding episodes; AND
 - C) The medication is prescribed by or in consultation with a hemophilia specialist.

Dosing. Approve up to 2,700 mcg/kg intravenously per 28 days.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Sevenfact is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Sevenfact® intravenous infusion [prescribing information]. Les Ulis, France/Louisville, KY: LFB S.A./Hema Biologics; November 2022.
2. Meeks SL, Leissing CA. The evolution of factor VIIa in the treatment of bleeding in haemophilia with inhibitors. *Haemophilia*. 2019;25(6):911-918.
3. Srivastava A, Santagostino E, Dougall A, et al; WFH Guidelines for the Management of Hemophilia panelists and co-authors. WFH Guidelines for the Management of Hemophilia, 3rd edition. *Haemophilia*. 2020 Aug;26 Suppl 6:1-158.
4. MASAC (Medical and Scientific Advisory Council) recommendations regarding doses of clotting factor concentrate in the home. MASAC Document #242. Adopted on June 7, 2016. Available at: <https://www.hemophilia.org/sites/default/files/document/files/242.pdf>. Accessed on November 5, 2023.
5. National Bleeding Disorders Foundation. MASAC (Medical and Scientific Advisory Council) recommendations concerning products licensed for the treatment of hemophilia and selected disorders of the coagulation system (August 2023). MASAC Document #280. Available at: <https://www.hemophilia.org/sites/default/files/document/files/MASAC-Products-Licensed.pdf>. Accessed on November 5, 2023.

HISTORY

| Type of Revision | Summary of Changes | Review Date |
|------------------|----------------------|-------------|
| Annual Revision | No criteria changes. | 11/02/2022 |
| Annual Revision | No criteria changes. | 11/08/2023 |