PRIOR AUTHORIZATION POLICY

POLICY: Hemophilia – Eptacog Products – NovoSeven RT Prior Authorization Policy
- NovoSeven® RT (coagulation Factor VIIa [recombinant] intravenous infusion – Novo Nordisk)

REVIEW DATE: 11/02/2022

OVERVIEW

NovoSeven RT is indicated for the treatment of bleeding episodes and perioperative management in the following conditions:

- **Congenital Factor VII deficiency** in adults and children;
- **Glanzmann's thrombasthenia** with refractoriness to platelet transfusions in adults and children, with or without antibodies to platelets;
- **Hemophilia, acquired** in adults; and
- **Hemophilia A or B with inhibitors** in adults and children.[1]

Of note, off-label use of NovoSeven RT in the general population has been suggested in a variety of acute bleeding scenarios (e.g., trauma, intracranial hemorrhage). A 2012 Cochrane Review concluded that the effectiveness of recombinant activated Factor VIIa as a general hemostatic drug in non-hemophiliac patients remains unproven and that use outside its licensed indications should be limited to clinical trials.[2] Various reviews and clinical practice guidelines concur that the evidence is insufficient to support use of NovoSeven RT as a hemostatic agent outside of its labeled uses.[3-5]

Guidelines

The National Hemophilia Foundation Medical and Scientific Advisory Council (MASAC) guidelines (updated March 2022) support NovoSeven RT as a treatment option for inherited **hemophilia A or B with inhibitors**, **acquired hemophilia A** (other forms of acquired hemophilia not addressed), and **Factor VII deficiency**.[6] Glanzmann's thrombasthenia is not addressed in the guideline. MASAC recommendations (2013) also state that recombinant Factor VIIa has demonstrated efficacy and safety for prophylactic use for patients with inhibitors in hemophilia A and hemophilia B.[7]

Regarding **hemophilia A and B with inhibitors**, World Federation of Hemophilia guidelines (2020) support recombinant Factor VIIa for patients with high-titer inhibitors who require acute treatment or around surgery/invasive procedures.[8] 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. National Hemophilia Foundation MASAC guidelines (updated August 2020) have similar recommendations: treatment for patients with inhibitors depends on multiple factors, including type of inhibitor (high- or low-responding), current titer, location of bleed, and previous response.[6]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of NovoSeven RT. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with NovoSeven RT as well as the monitoring required for adverse events and

long-term efficacy, approval requires NovoSeven RT to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Congenital Factor VII Deficiency.** Approve for 1 year if NovoSeven RT is prescribed by or in consultation with a hemophilia specialist.

2. **Glanzmann's Thrombasthenia.** Approve for 1 year if the patient meets the following criteria (A and B):
   - **A)** Patient is refractory to platelet transfusions; AND
   - **B)** The medication is prescribed by or in consultation with a hematologist.

3. **Hemophilia, Acquired.** Approve for 1 year if the patient meets the following criteria (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** The medication is prescribed by or in consultation with a hemophilia specialist.

4. **Hemophilia A with Inhibitors.** Approve for 1 year if the patient meets the following criteria (A and B):
   - **A)** 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 an inhibitor with 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 an inhibitor with refractory hemostatic response to increased Factor VIII dosing, which, according to the prescriber, precludes the use of Factor VIII replacement to treat bleeding episodes; AND
   - **B)** The medication is prescribed by or in consultation with a hemophilia specialist.

5. **Hemophilia B with Inhibitors.** Approve for 1 year if the patient meets the following criteria (A and B):
   - **A)** 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 an inhibitor with 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 of an inhibitor with refractory hemostatic response to increased Factor IX dosing, which, according to the prescriber, precludes the use of Factor IX replacement to treat bleeding episodes; AND
   - **B)** The medication is prescribed by or in consultation with a hemophilia specialist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of NovoSeven RT is not recommended in the following situations:

1. **Bleeding Associated with Liver Disease.** Randomized trials have failed to show benefit of NovoSeven RT in controlling upper gastrointestinal bleeding and variceal bleeding in patients with advanced liver disease.[9,10] American Association for the Study of Liver Disease guidelines for portal hypertensive bleeding in cirrhosis (2016) state that recombinant Factor VIIa should not be used to correct coagulopathy in this scenario.[11]

2. 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. NovoSeven® RT intravenous infusion [prescribing information]. Plainsboro, NJ: Novo Nordisk; July 2020.
2. Simpson E, Lin Y, Stanworth S, et al. Recombinant factor VIIa for the prevention and treatment of bleeding in patients without haemophilia. *Cochrane Database Syst Rev.* 2012;3:CD005011.
3. Cannon JW, Khan MA, Raja AS, et al. Damage control resuscitation in patients with severe traumatic hemorrhage: a practice management guideline from the Eastern Association for the Surgery of Trauma. *J Trauma Acute Care Surg.* 2017;82(3):605-617.
4. Hemphill JC 3rd, Greenberg SM, Anderson CS, et al.; American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2015;46(7):2032-60.
5. Yank V, Tuohy CV, Logan AC, et al. Comparative effectiveness of in-hospital use of recombinant factor VIIa for off-label indications vs. usual care [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US). Updated May 2010. Available at: https://www.ncbi.nlm.nih.gov/books/NBK98697/. Accessed on October 28, 2022.
6. MASAC (Medical and Scientific Advisory Council) recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders (Revised March 2022). MASAC Document #272. Adopted on April 27, 2022. Available at: https://www.hemophilia.org/healthcare-professionals/guidelines-on-care/masac-documents/masac-document-272-masac-recommendations-concerning-products-licensed-for-the-treatment-of-hemophilia-and-other-bleeding-disorders. Accessed on October 28, 2022.
7. MASAC (Medical and Scientific Advisory Council) recommendation regarding prophylaxis with bypassing agents in patients with hemophilia and high titer inhibitors. MASAC Document #220. Adopted on October 6, 2013. Available at: https://www.hemophilia.org/sites/default/files/document/files/masac220.pdf. Accessed on October 28, 2022.
8. Srivastava A, Santagostino E, Dougall A, et al. WFH guidelines for the management of hemophilia, 3rd edition. *Haemophilia*. 2020;26 Suppl 6:1-158.
9. Bosch J, Thabut D, Bendtsen F, et al; European Study Group on rFVIIa in UGI Haemorrhage. Recombinant Factor VIIa for upper gastrointestinal bleeding in patients with cirrhosis: a randomized, double-blind trial. *Gastroenterology.* 2004;127(4):1123-30.
10. Bosch J, Thabut D, Albillos A, et al; International Study Group on rFVIIa in UGI Hemorrhage. Recombinant factor VIIa for variceal bleeding in patients with advanced cirrhosis: a randomized, controlled trial. *Hepatology.* 2008;47(5):1604-14.
11. Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. *Hepatology.* 2017;65(1):310-335.