CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

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

REVIEW DATE: 12/04/2024

OVERVIEW

NovoSeven RT is indicated for the treatment of bleeding episodes and perioperative management in the following conditions:[1]

- **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.

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 Bleeding Disorders Foundation Medical and Scientific Advisory Council (MASAC) guidelines (updated October 2024) 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 Bleeding Disorders MASAC guidelines (updated October 2024) 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]

Dosing Information

Dosing of clotting factor concentrates is highly individualized. MASAC provides recommendations regarding doses of clotting factor concentrate in the home (2016).[9] The number of required doses varies greatly and is dependent on the severity of the disorder and the prescribed regimen. Per MASAC guidance, patients on prophylaxis should also have a minimum of one major dose and two minor doses on hand for

breakthrough episodes in addition to the prophylactic doses used monthly. 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 prophylactic dosing plus three days of acute episodes or perioperative management per 28 days. Doses exceeding this quantity will be reviewed on a case-by-case basis by a clinician.

Dosing considerations for individual indications are as follows:

- **Congenital Factor VII Deficiency:** In the routine prophylactic setting, recombinant Factor VIIa dosing of up to 30 mcg/kg three times weekly has been described in the literature.[10] Per prescribing information, dosing for bleeding episodes and perioperative management ranges up to 30 mcg/kg up to every 4 hours (180 mcg/kg daily dose).[1]
- **Glanzmann's Thrombasthenia:** Prophylactic dosing is not routine. Per the prescribing information, dosing up to 90 mcg/kg every 2 hours may be used for acute episodes or perioperative management (1,080 mcg/kg daily dose).[1]
- **Hemophilia, Acquired:** Data are limited describing prophylactic use of recombinant Factor VIIa in acquired hemophilia; dosing is generally similar to what is used for congenital hemophilia A and B with inhibitors. Per the prescribing information, dosing up to 90 mcg/kg every 2 hours may be used for acute episodes or perioperative management (1,080 mcg/kg daily dose).[1]
- **Hemophilia A with Inhibitors** and **Hemophilia B with Inhibitors:** For congenital hemophilia A and B with inhibitors, MASAC recommendations note that doses of up to 270 mcg/kg per day have been found to be effective.[7] Per the prescribing information, dosing up to 50 mcg/kg per hour by continuous infusion may be used in the perioperative setting (1,200 mcg/kg daily dose).[1]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of NovoSeven RT. 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 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.

   Dosing. Approve up to 900 mcg/kg intravenously per 28 days.

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

   Dosing. Approve up to 3,240 mcg/kg intravenously per 28 days.

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

   Dosing. Approve up to 10,800 mcg/kg intravenously per 28 days.

4. **Hemophilia A with Inhibitors.** Approve for 1 year if the patient meets BOTH of the following (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.

   Dosing. Approve up to 11,160 mcg/kg intravenously per 28 days.

5. **Hemophilia B with Inhibitors.** Approve for 1 year if the patient meets BOTH of the following (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 history 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.

   Dosing. Approve up to 11,160 mcg/kg intravenously per 28 days.

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.[11,12] 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.[13]

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

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	11/08/2023
Annual Revision	No criteria changes.	12/04/2024