Hemophilia Products – Factor VIIa: NovoSeven RT ™; Sevenfact ® (Intravenous)

Effective Date: 01/01/2020

Review date: 10/02/2019, 12/13/2019, 1/22/20, 6/1/2020, 6/24/2021, 6/16/2022, 6/22/2023, 12/07/2023, 01/10/2024, 08/14/2024

Scope: Medicaid*, Commercial, Medicare-Medicaid Plan (MMP)
***(Medication only available on the Medical Benefit)**

I. Length of Authorization

Unless otherwise specified*, the initial authorization will be provided for 3 months and may be renewed.

Note: The cumulative amount of medication the patient has on-hand will be taken into account for authorizations. Up to 5 'on-hand' doses for the treatment of acute bleeding episodes will be permitted at the time of the authorization request.

** Initial and renewal authorization periods may vary by specific covered indication*

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- NovoSeven RT 1000 mcg vial = 12 vials per 30 days
- NovoSeven RT 2000 mcg vial = 12 vials per 30 days
- NovoSeven RT 5000 mcg vial = 24 vials per 30 days
- NovoSeven RT 8000 mcg vial = 15 vials per 30 days
- Sevenfact 1 mg vial = 48 vials per 30 days
- Sevenfact 5 mg vial = 24 vials per 30 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 120,000 billable units per 30-day supply

III. Summary of Evidence

NovoSeven and Sevenfact are recombinant coagulation factor VIIa indicated for the treatment of bleeding episodes in patients with hemophilia A or B with inhibitors. A double-blind, randomized comparison trial of two dose levels of NovoSeven in the treatment of joint, muscle and mucocutaneous hemorrhages in hemophilia A and B patients with and without inhibitors was conducted in 78 patients who received NovoSeven in treatment centers within 4 to 18 hours after experiencing a bleed. The efficacy and safety of Sevenfact for treatment of bleeding episodes was evaluated in a global, multicenter, randomized, open-label, crossover of two initial dose regimens with 27 subjects with hemophilia A or B with inhibitors. Efficacy for both trials were measured based on a rating scale, specific to each trial. The Sevenfact trial used the primary endpoint of successful treatment of mild or moderate bleeding episode at hour 12 after initial treatment dose. The proportion of mild or moderate bleeding events with hemostatic efficacy at 12 hours was 82% in the 75 mcg/kg dose regimen group and was 91%

in the 225 mcg/kg dose regimen group. Novoseven has further studies indicating its use in Congenital Factor VII Deficiency, Acquired Hemophilia and Glanzmann's Thrombasthenia. Common adverse reactions include headache, dizziness, infusion reactions (hematoma) and thrombotic events.

IV. Initial Approval Criteria [1,2,3,4,9]

Coverage is provided in the following conditions:

- MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

NovoSeven RT ONLY [1]

Hemophilia A (congenital factor VIII deficiency) † Φ

- Diagnosis of congenital factor VIII deficiency has been confirmed by blood coagulation testing; **AND**
- Confirmation Patient has inhibitors to Factor VIII with a current or historical titer of ≥ 5 Bethesda Units (BU)**; **AND**
- Used as treatment in at least one of the following:
  - Treatment and control of acute bleeding episodes (episodic treatment of acute hemorrhage); **OR**
  - Perioperative management *(*Authorizations valid for 1 month)*; **OR**
  - Routine prophylaxis to prevent or reduce the frequency of bleeding episodes when the following criteria are also met:
    - Used as primary prophylaxis in patient with severe factor VIII deficiency (factor VIII level < 1%); **OR**
    - Used as secondary prophylaxis in patients with at least TWO documented episodes of spontaneous bleeding into joints; **OR**
    - Patient has documented trial and failure of Immune Tolerance Induction (ITI); **AND**
      - Patient has documented trial and failure or contraindication to Hemlibra

Acquired Hemophilia †

- Diagnosis of acquired hemophilia has been confirmed by blood coagulation testing; **AND**
- Used as treatment for one of the following:
  - Treatment and control of acute bleeding episodes (episodic treatment of acute hemorrhage); **OR**
  - Perioperative management *(*Authorizations valid for 1 month)*

Hemophilia B (congenital factor IX deficiency aka Christmas disease) † Φ

- Diagnosis of congenital factor IX deficiency has been confirmed by blood coagulation testing; **AND**
- Patient has acquired inhibitors to Factor IX with a current or historical titer of ≥ 5 Bethesda Units (BU)**; **AND**
- Used as treatment for one of the following:

- Treatment and control of acute bleeding episodes (episodic treatment of acute hemorrhage); **OR**
- Perioperative management *(*Authorizations valid for 1 month)*; **OR**
- Routine prophylaxis to prevent or reduce the frequency of bleeding episodes when the following criteria are also met
  - Used as primary prophylaxis in patient with severe factor VIII deficiency (factor VIII level < 1%); **OR**
  - Used as secondary prophylaxis in patients with at least two documented episodes of spontaneous bleeding into joints; **OR**
  - Patient has documented trial and failure of Immune Tolerance Induction (ITI)

Congenital Factor VII Deficiency † Φ

- Diagnosis of congenital factor VII deficiency has been confirmed by blood coagulation testing; **AND**
- Used as treatment for one of the following:
  - Treatment and control of acute bleeding episodes (episodic treatment of acute hemorrhage); **OR**
  - Perioperative management *(*Authorizations valid for 1 month)*

Glanzmann's Thrombasthenia † Φ

- Diagnosis of Glanzmann Thrombasthenia has been confirmed by blood coagulation testing; **AND**
- Used as treatment for one of the following:
  - Treatment and control of acute bleeding episodes (episodic treatment of acute hemorrhage); **OR**
  - Perioperative management *(*Authorizations valid for 1 month)*; **AND**
- The use of platelet transfusions is known or suspected to be ineffective or contraindicated

Sevenfact ONLY [2]

Hemophilia A (Congenital Factor VIII Deficiency)/Hemophilia B (Congenital Factor IX Deficiency) † Φ

- Patient is at least 12 years of age; **AND**
- Diagnosis of congenital factor VIII or IX deficiency has been confirmed by blood coagulation testing; **AND**
- Patient has Hemophilia A (Factor VIII) inhibitors or Hemophilia B (Factor IX) inhibitors with a current or historical titer of ≥ 5 Bethesda Units (BU)**; **AND**
- Used as treatment and control of acute bleeding episodes (episodic treatment of acute hemorrhage); **AND**
- Will not be used for the treatment of Congenital Factor VII Deficiency

***Note: Patients with inhibitor titer levels >0.6 BU to <5 BU who are not responding to or are not a candidate for standard factor replacement, will be evaluated on a case-by-case basis.*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

V. Dispensing Requirements for Rendering Providers (Hemophilia Management Program)

- Prescriptions cannot be filled without an expressed need from the patient, caregiver or prescribing practitioner. Auto-filling is not allowed.
- Monthly, rendering provider must submit for authorization of dispensing quantity before delivering factor product. Information submitted must include:
  - Original prescription information, requested amount to be dispensed, vial sizes available to be ordered from the manufacturer, and patient clinical history (including patient product inventory and bleed history)
  - Factor dose should not exceed +1% of the prescribed dose and a maximum of three vials may be dispensed per dose. If unable to provide factor dosing within the required threshold, below the required threshold, the lowest possible dose able to be achieved above +1% should be dispensed. Prescribed dose should not be increased to meet assay management requirements.
- The cumulative amount of medication(s) the patient has on-hand should be taken into account when dispensing factor product. Patients should not have more than 5 extra doses on-hand for the treatment of acute bleeding episodes.
- Dispensing requirements for renderings providers are a part of the hemophilia management program. This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide.

VI. Renewal Criteria [1,2,3,4,9]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet indication-specific relevant criteria identified in section IV; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: hypersensitivity reactions including anaphylaxis (e.g., hives, itching, rash, difficulty breathing, swelling around the mouth/throat, chest tightness, wheezing, dizziness/fainting, low blood pressure, etc.), serious arterial and venous thrombotic events, development of neutralizing antibodies (inhibitors), etc.; .**AND**
- Any increases in dose must be supported by an acceptable clinical rationale (i.e., weight gain, half-life study results, increase in breakthrough bleeding when patient is fully adherent to therapy, etc.); **AND**
- The cumulative amount of medication(s) the patient has on-hand will be taken into account when authorizing. The authorization will allow up to 5 doses on-hand for the treatment of acute bleeding episodes as needed for the duration of the authorization; **AND**

Treatment and control of acute bleeding episodes

Renewals will be approved for a 6-month authorization period

Perioperative management of bleeding (NovoSeven RT Only)

- Coverage may NOT be renewed

Routine prophylaxis to prevent or reduce the frequency of bleeding episode (NovoSeven RT Only)

- Renewals will be approved for a 12-month authorization period; **AND**
- Patient has demonstrated a beneficial response to therapy (i.e., the frequency of bleeding episodes has decreased from pre-treatment baseline)

VII. Dosage/Administration[1,2,3,4]

Indication	Dose
NovoSeven RT	
Control and prevention of bleeding: Congenital Hemophilia A or B with inhibitors	Hemostatic Administer 90 mcg/kg intravenously every 2 hours, adjustable based on severity of bleeding until hemostasis is achieved, or until the treatment has been judged to be inadequate. Post-Hemostatic Administer 90 mcg/kg intravenously every 3-6 hours after hemostasis is achieved for severe bleeds
Control and prevention of bleeding: Acquired Hemophilia	Administer 70-90 mcg/kg intravenously every 2-3 hours until hemostasis is achieved
Control and prevention of bleeding: Congenital Factor VII deficiency	Administer 15-30 mcg/kg intravenously every 4-6 hours until hemostasis is achieved
Control and prevention of bleeding: Glanzmann's Thrombasthenia	Administer 90 mcg/kg intravenously every 2-6 hours in severe bleeding episodes requiring systemic hemostatic therapy until hemostasis is achieved
Perioperative management Congenital Hemophilia A or B with inhibitors	Minor Initial: Administer 90 mcg/kg intravenously immediately before surgery, repeat every 2 hours during surgery. Post-Op: Administer 90 mcg/kg intravenously every 2 hours after surgery for 48 hours, then every 2-6 hours until healing has occurred. Major Initial: Administer 90 mcg/kg intravenously immediately before surgery, repeat every 2 hours during surgery. Post-Op: Administer 90 mcg/kg intravenously every 2 hours after surgery for 5 days, then every 4 hours or by continuous infusion, via pump, at 50 mcg/kg/hr until healing occurs.
Perioperative management Acquired Hemophilia	Administer 70-90 mcg/kg intravenously immediately before surgery and every 2-3 hours for the duration of surgery and until hemostasis is achieved

Indication	Dose
Perioperative management Congenital Factor VII deficiency	Administer 15-30 mcg/kg intravenously immediately before surgery and every 4-6 hours for the duration of surgery and until hemostasis is achieved
Perioperative management Glanzmann's Thrombasthenia	Initial: Administer 90 mcg/kg intravenously immediately before surgery and repeat every 2 hours for the duration of the procedure. Post-Op: Administer 90 mcg/kg intravenously every 2-6 hours to prevent post-operative bleeding
Sevenfact	
Control and treatment of bleeding: Congenital Hemophilia A or B with inhibitors	<u>For Mild or Moderate Bleeds:</u> – Administer 75 mcg/kg intravenously 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 <u>For Severe Bleeds:</u> – Administer 225 mcg/kg intravenously initially, followed if necessary 6 hours later with 75 mcg/kg every 2 hours until hemostasis is achieved.

VIII. Billing Code/Availability Information

<u>HCPCS Code & NDC:</u>

Drug	Manufacturer	J-Code	1 Billable Unit Equiv.	Vial Size	NDC
Novoseven RT	Novo Nordisk	J7189	1 mcg	1 mg	00169-7010
				2 mg	00169-7020
				5 mg	00169-7050
				8 mg	00169-7040
Novoseven RT with MixPro package				1 mg	00169-7201
				2 mg	00169-7202
				5 mg	00169-7205
				8 mg	00169-7208
Sevenfact	LFB S.A.	J7212	1 mcg	1 mg	71127-1000
				5 mg	71127-5000

IX. References

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9. MASAC Recommendation Concerning Prophylaxis for Hemophilia A and B with and without Inhibitors. Revised April 27, 2022. National Hemophilia Foundation. MASAC Document #267; April 2022. Available at: http://www.bleeding.org/. Accessed May 2024.
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13. Novitas Solutions, Inc. Local Coverage Article: Billing and Coding: Hemophilia Factor Products (A56433). Centers for Medicare & Medicaid Services Inc. Updated on 11/08/2019 with effective date 11/14/2019. Accessed May 2024.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D66	Hereditary factor VIII deficiency
D67	Hereditary factor IX deficiency
D68.0	Von Willebrand's disease
D68.2	Hereditary deficiency of other clotting factors
D68.311	Acquired hemophilia
D69.1	Qualitative platelet defects

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications

Medicare Part B Covered Diagnosis Codes		
Jurisdiction	**NCD/LCA/LCD Document (s)**	**Contractor**
J,M	A56065	Palmetto GBA
H,L	A56433	Novitas Solutions, Inc.
N	A56482	First Coast Service Options, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:
Novoseven and Sevenfact were reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Novoseven and Sevenfact according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.