Standard Half-life Factor VIII Products: Advate, Afstyla, Hemofil M, Koate DVI, Kogenate FS, Kovaltry, Novoeight, Nuwiq, Recombinate, and Xyntha

Date of Origin: 01/22/2020 **Last Review Date: 01/22/2020** **Effective Date: 02/01/2020**

Dates Reviewed: 01/22/2020

Developed By: Medical Criteria Committee

I. Length of Authorization

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

II. Dosing Limits

Product Name	Dosage Form	Indication/ FDA Labeled Dosing	Quantity Limit‡
Advate, antihemophilic factor (recombinant)	250, 500, 1000, 1500, 2000, 3000, 4000 IU	**On-demand Treatment:** Up to 50 IU/kg every 8 to 24 hours until bleeding is resolved **Routine Prophylaxis:** • Up to 40 IU/kg every other day (3 to 4 times weekly) or every third day **Perioperative Management:** • *Minor* (e.g. tooth extraction): Up to 50 IU/kg within one hour before surgery; Repeat every 12 to 24 hours as needed until bleeding is resolved • *Major* (e.g. intracranial, intra-abdominal, or intrathoracic, or joint- replacement): Up to 60 IU/kg preoperative to achieve 100% activity; Repeat every 8 to 24 (every 6 to 24 hours for patients under the age of six) hours to keep factor VIII activity in desired range until healing is complete	**On-demand Treatment:** Up to the number of doses requested every 28 days **Routine Prophylaxis:** Up to 672 IU/kg every 28 days **Perioperative Management:** Up to the number of doses requested for 28 days

Afstyla, antihemophilic factor (recombinant), single chain	250, 500, 1000, 1500, 2000, 2500, 3000 IU	**On-demand Treatment:** Up to 50 IU/kg every 8 to 24 hours until bleeding is resolved **Routine Prophylaxis:** • ≥12 years: Up to 50 IU/kg two to three times per week • <12 years: Up to 50 IU/kg two to three times per week. More frequent or higher dosing may be required to account for the higher clearance in this age group. **Perioperative Management:** • *Minor* (e.g. tooth extraction): Up to 30 IU/kg every 24 hours for at least one day until healing is resolved • *Major* (e.g. intracranial, intra-abdominal, or intrathoracic, or joint- replacement): Up to 50 IU/kg every 8 to 24 hours until adequate wound healing, then continue therapy for at least another seven days	**On-demand Treatment:** Up to the number of doses requested every 28 days **Routine Prophylaxis:** • ≥12 years: Up to 630 IU/kg every 28 days • <12 years: Up to 630 IU/kg every 28 days **Perioperative Management:** Up to the number of doses requested for 28 days
Hemofil M, antihemophilic factor (human)	250, 500, 1000, 1700 IU	**On-demand Treatment** [δ]**:** Up to 100 IU/dL; Repeat every 8 to 24 hours until the bleeding threat is resolved **Perioperative Management** [δ]**:** • *Minor* (e.g. tooth extraction): A single infusion of up to 80 IU/dL plus oral antifibrinolytic therapy within one hour is sufficient in approximately 70% of cases • *Major* (e.g. intracranial, intra-abdominal, or intrathoracic, or joint- replacement): Up to 100 IU/dL pre- and post-operative; Repeat dose every 8 to 24 hours depending on state of healing	**On-demand Treatment:** Up to the number of doses requested every 28 days **Perioperative Management:** Up to the number of doses requested for 28 days
Koate DVI, antihemophilic factor (human)	250, 500, 1000 IU	**On-demand Treatment** [δ]**:** Up to 100 IU/dL every 8 to 12 hours until bleeding threat is resolved **Perioperative Management** [δ]**:** For major surgical procedures, the	**On-demand Treatment:** Up to the number of doses requested every 28 days

		factor VIII level should be raised to approximately 100% by giving a preoperative dose of 50 IU/kg. Repeat infusions may be necessary every 6 to 12 hours initially, and for a total of 10 to 14 days until healing is complete. The intensity of factor replacement therapy required depends on the type of surgery and postoperative regimen employed. For minor surgical procedures, less intensive treatment schedules may provide adequate homeostasis.	**Perioperative Management:** Up to the number of doses requested for 28 days
Kogenate FS, antihemophilic factor (recombinant), formulated with sucrose	250, 500, 1000, 2000, 3000 IU	**On-demand Treatment** [δ]**:** Up to 50 IU/kg every 8 to 12 hours until bleeding is resolved **Routine Prophylaxis:** • Adults: Up to 25 IU/kg three times per week • Children: Up to 25 IU/kg every other day **Perioperative Management** [δ]**:** • *Minor* (e.g. tooth extraction): Up to 30 IU/kg every 12 to 24 hours until bleeding is resolved • *Major* (e.g. intracranial, intra-abdominal, or intrathoracic, or joint- replacement): Up to 50 IU/kg preoperative to achieve 100% activity; Repeat every 6 to 12 hours to keep factor VIII activity in desired range until healing is complete	**On-demand Treatment:** Up to the number of doses requested every 28 days **Routine Prophylaxis:** • Adults: Up to 315 IU/kg every 28 days • Children: Up to 368 IU/kg every 28 days **Perioperative Management:** Up to the number of doses requested for 28 days
Kovaltry, antihemophilic factor (recombinant)	250, 500, 1000, 2000, 3000 IU	**On-demand Treatment** [δ]**:** Up to 100 IU/dL every 8 to 24 hours until bleeding is resolved **Routine Prophylaxis:** • ≥12 years: Up to 40 IU/kg two or three times per week • ≤ 12 years: Up to 50 IU/kg twice weekly, three times weekly, or every other day **Perioperative Management** [δ]**:**	**On-demand Treatment:** Up to the number of doses requested every 28 days **Routine Prophylaxis:** • ≥12 years: Up to 504 IU/kg every 28 days • ≤12 years: Up to 735 IU/kg every 28 days

		• *Minor* (e.g. tooth extraction): Up to 60 IU/dL every 24 hours until healing is achieved • *Major* (e.g. intracranial, intra-abdominal, or intrathoracic, or joint- replacement): Up to 100 IU/dL pre- and post-operative; Repeat every 8 to 24 hours until adequate wound healing is complete, then continue therapy for at least another seven days to maintain factor VIII activity of 30-60% (IU/dL)	**Perioperative Management:** Up to the number of doses requested for 28 days
Novoeight, antihemophilic factor (recombinant)	250, 500, 1000, 2000, 3000 IU	**On-demand Treatment** δ**:** Up to 100 IU/dL every 8 to 24 hours until resolution of bleed (approximately seven to ten days) **Routine Prophylaxis:** • ≥12 years: Up to 50 IU/kg three times per week or up to 40 IU/kg every other day • ≤ 12 years: Up to 60 IU/kg three times weekly or up to 50 IU/kg every other day **Perioperative Management** δ**:** • *Minor* (e.g. tooth extraction): Up to 60 IU/dL every 12 to 24 hours until bleeding is resolved • *Major* (e.g. intracranial, intra-abdominal, or intrathoracic, or joint- replacement): Up to 100 IU/dL pre- and post-operative; Repeat every 8 to 24 hours until adequate wound healing is complete, then continue therapy for at least another seven days to maintain factor VIII activity of 30-60% (IU/dL)	**On-demand Treatment:** Up to the number of doses requested every 28 days **Routine Prophylaxis:** • ≥12 years: Up to 630 IU/kg every 28 days • ≤12 years: Up to 756 IU/kg every 28 days **Perioperative Management:** Up to the number of doses requested for 28 days
Nuwiq, antihemophilic factor (recombinant)	250, 500, 1000, 2000, 2500, 3000, 4000 IU	**On-demand Treatment** δ**:** Up to 100 IU/dL every 8 to 24 hours until bleeding risk is resolved **Routine Prophylaxis:** • ≥12 years: Up to 40 IU/kg every other day	**On-demand Treatment:** Up to the number of doses requested every 28 days **Routine Prophylaxis:**

		• ≤ 12 years: Up to 50 IU/kg every other day or three times per week **Perioperative Management** δ**:** • *Minor* (e.g. tooth extraction): Up to 40 IU/dL every 12 to 24 hours until bleeding is resolved • *Major* (e.g. intracranial, intra-abdominal, or intrathoracic, or joint- replacement): Up to 100 IU/dL pre- and post-operative; Repeat every 8 to 24 hours until adequate wound healing, then continue therapy for at least another seven days to maintain factor VIII activity of 30-60% (IU/dL)	• ≥12 years: Up to 588 IU/kg every 28 days • ≤12 years: Up to 735 IU/kg every 28 days **Perioperative Management:** Up to the number of doses requested for 28 days
Recombinate, antihemophilic factor (recombinant)	250, 500, 1000, 1500, 2000 IU	**On-demand Treatment** δ**:** Up to 100 IU/dL every 8 to 24 hours until bleeding threat is resolved **Perioperative Management** δ**:** • *Minor* (e.g. tooth extraction): Up to 80 IU/dL as a single infusion plus oral antifibrinolytic therapy within one hour is sufficient in approximately 70% of cases • *Major* (e.g. intracranial, intra-abdominal, or intrathoracic, or joint- replacement): Up to 100 IU/dL pre- and post-operative; Repeat every 8 to 24 hours depending on state of healing	**On-demand Treatment:** Up to the number of doses requested every 28 days **Perioperative Management:** Up to the number of doses requested for 28 days
Xyntha, antihemophilic factor (recombinant)	250, 500, 1000, 2000 IU	**On-demand Treatment** δ**:** Up to 100 IU/dL every 8 to 24 hours until bleeding threat is resolved **Perioperative Management** δ**:** • *Minor* (e.g. tooth extraction): Up to 60 IU/dL for 3 to 4 days or until adequate hemostasis is achieved. For tooth extraction, a single infusion plus oral antifibrinolytic therapy within 1 hour may be sufficient	**On-demand Treatment:** Up to the number of doses requested every 28 days **Perioperative Management:** Up to the number of doses requested for 28 days

		• *Major* (e.g. intracranial, intra-abdominal, or intrathoracic, or joint- replacement): Up to 100 IU/dL pre- and post-operative; Repeat every 8 to 24 hours until threat is resolved, or in the case of surgery, until adequate local hemostasis and wound healing are achieved	

‡Allows for +5% to account for assay and vial availability

δ Dose (IU/kg) = Desired factor VIII rise (IU/dL or % of normal) x 0.5 (IU/kg per IU/dL); *Expected Factor VIII rise (% of normal) = 2 x administered IU/body weight (kg)*

III. Initial Approval Criteria

I. Standard half-life factor VIII products may be considered medically necessary when the following criteria below are met:
   A. Member has a confirmed diagnosis of **hemophilia A (congenital factor VIII deficiency)** and the following are met:
      1. Treatment is prescribed by or in consultation with a hematologist; **AND**
      2. Use of standard half-life factor VIII is planned for one of the following indications:
         i. On-demand treatment and control of bleeding episodes **AND** the number of factor VIII units requested does not exceed those outlined in the Quantity Limits table above for routine prophylaxis; **OR**
         ii. Perioperative management of bleeding; **OR**
         iii. Routine prophylaxis to reduce the frequency of bleeding episodes when one of the following is met:
            a. Member has severe hemophilia A (defined as factor VIII level of <1%); **OR**
            b. Member has had more than one documented episode of spontaneous bleeding; **AND**
      3. Documentation that inhibitor testing has been performed within the last 12 months AND if inhibitor titers are high (≥5 Bethesda units), there is a documented plan to address inhibitors; **AND**
      4. Dose and frequency does not exceed those outlined in the Quantity Limit Table above, unless documented clinical reasoning for higher dosing and/or frequency is supported by a half-life study to determine the appropriate dose and dosing interval

II. Standard half-life factor VIII products are considered investigational when used for all other conditions.

IV. Renewal Criteria

I. For **on-demand treatment** and **routine prophylaxis**:

i. Documentation of clinical benefit, including decreased incidence of bleeding episodes or stability of bleeding episodes relative to baseline; **AND**

ii. Documentation that inhibitor testing has been performed within the last 12 months AND if inhibitor titers are high (≥5 Bethesda units), there is documented plan to address inhibitors; **AND**

iii. *For **on-demand treatment only***, the dose and frequency is not greater than the routine prophylactic dose outlined in the Quantity Limit Table above

V. Billing Code/Availability Information

Drug	Manufacturer	J-Code	1 Billable Unit Equiv.	Vial Size	NDC
Advate	Baxalta US Inc	J7192	1 IU	250 units	00944-3051-02
				500 units	00944-3052-02
				1000 units	00944-3053-02
				1500 units	00944-3054-02
				2000 units	00944-3045-10
				3000 units	00944-3046-10
				4000 units	0944-3047-10
Afstyla	CSL Behring, LLC	J7210	1 IU	250 units	69911-0474-02
				500 units	69911-0475-02
				1000 units	69911-0476-02
				1500 units	69911-0480-02
				2000 units	69911-0477-02
				2500 units	69911-0481-02
				3000 units	69911-0478-02
Hemofil M	Baxalta US Inc	J7190	1 IU	250 units	00944-3940-02
				500 units	00944-3942-02
				1700 units	00944-3946-02
				1000 units	00944-3944-02
Koate DVI	Grifols Therapeutics Inc	J7190	1 IU	250 units	76125-0250-20 76125-0253-25
				500 units	76125-0667-30 76125-0662-50
				1000 units	76125-0672-50 76125-0674-10
Kogenate FS		J7192	1 IU	250 units	00026-3782-25

	Bayer HealthCare LLC			500 units	00026-3783-35
				1000 units	00026-3785-55
				2000 units	00026-3786-65
				3000 units	00026-3787-75
Kovaltry	Bayer HealthCare LLC	J7211	1 IU	250 units	00026-3821-25
				500 units	00026-3822-25
				1000 units	00026-3824-25
				2000 units	00026-3826-50
				3000 units	00026-3828-50
Novoeight	Novo Nordisk	J7182	1 IU	250 units	00169-7825-01
				500 units	00169-7850-01
				1000 units	00169-7810-01
				1500 units	00169-7815-01
				2000 units	00169-7820-01
				3000 units	00169-7830-01
Nuwiq	Octapharma AB	J7209	1 IU	250 units	68982-0140-01
				500 units	68982-0142-01
				1000 units	68982-0144-01
				2000 units	68982-0146-01
Recombinate	Baxalta US Inc	J7192	1 IU	220-400 units	00944-2841-10
				401-800 units	00944-2842-10
				801-1240 units	00944-2843-10
				1241-1800 units	00944-2844-10
				1801-2400 units	00944-2845-10
Xyntha	Wyeth Biopharma	J7185	1 IU	250 units	58394-0022-03 58394-0012-01
				500 units	58394-0023-03 58394-0013-01
				1000 units	58394-0024-03 58394-0014-01
				2000 units	58394-0025-03 58394-0015-01
				3000 units	58394-0016-03

VII. References

1. Advate [package insert]. Westlake Village, CA; Baxalta US Inc. May 2018.
2. Afstyla [package insert]. Kankakee, IL; CSL Behring, LLC; April 2017.
3. Hemofil M [package insert]. Westlake Village, CA; Baxalta US Inc. June 2018.
4. Koate DVI [package insert]. Research Triangle Park, NC; Grifols Therapeutics Inc.; August 2012.
5. Kogenate FS [package insert]. Whippany, NJ. Bayer HealthCare LLC; May 2016.
6. Novoeight [package insert]. Bagsvaerd, Denmark; Novo Nordisk; November 2018.
7. NUWIQ [package insert]. Elersvagen, Sweden; Octapharma AB; July 2017.
8. Recombinate [package insert]. Westlake Village, CA; Baxalta US Inc. June 2018.
9. Kovaltry [package insert]. Whippany, NJ; Bayer HealthCare LLC; March 2016
10. National Hemophilia Foundation. Hemophilia A. Available from: https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Hemophilia-A. Accessed July 5, 2019.
11. National Hemophilia Foundation. MASAC Recommendations Concerning products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders. Available from: https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations. Accessed July 5, 2019.
12. UpToDate, Inc. Hemophilia A and B: Routine management including prophylaxisHemophilia A and B: Routine management including prophylaxis. UpToDate [database online]. Last updated February 11, 2019.

Appendix 1 – Covered Diagnosis Codes

Advate, Eloctate, Hemofil M, Koate-DVI, Kogenate FS, Monoclate-P, Recombinate, Xyntha, Novoeight, NUWIQ, Adynovate, Kovaltry, Afstyla, and Jivi

ICD-10	ICD-10 Description
D66	Hereditary factor VIII deficiency

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

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 Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

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 Corporation (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 Corporation (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Cahaba Government Benefit Administrators, 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 VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC