Standard Half-life Factor IX Products: AlphaNine SD, BeneFIX, Ixinity, MonoNine, Profilnine SD, and Rixubis

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 (prophylaxis); 12 months (on-demand)

II. Dosing Limits

Product Name	Dosage Form	Indication/ FDA Labeled Dosing	Quantity Limit‡
AlphaNine SD, coagulation factor IX (human)	500, 1000, 1500 IU	**Control and prevention of bleeding episodes:** Up to 100 IU/kg; Repeat dose after 12 hours as needed for three to five days. Major hemorrhages may require treatment for up to ten days	**Control and prevention of bleeding episodes:** Up to the number of doses requested every 28 days
BeneFIX, coagulation factor IX (recombinant)	250, 500, 1000, 2000, 3000 IU	**Control and prevention of bleeding episodes and perioperative management*:** Up to 100 IU/dL; Consider repeat dose after 12 to 24 hours as needed for seven to ten days	**Control and prevention of bleeding episodes and perioperative management:** Up to the number of doses requested every 28 days
Ixinity, coagulation factor IX (recombinant)	250, 500, 1000 IU	**Control and prevention of bleeding episodes δ:** Up to 100 IU/dL, doses every 12 to 24 hours on days two through 14 until healing is achieved **Perioperative Management δ:** • *Minor*: Up to 80 IU/dL pre- and post-operative; Repeat every 24 hours on days one through five, depending on type of procedure • *Major*: Up to 80 IU/dL pre-op; Post-op: Up to 60 IU, dosed every 8 to 24 hours on days one through three, or up to 50 IU/dL dosed every 8 to 24 hours on days four through six, or up to 40 IU/dL	**Control and prevention of bleeding episodes:** Up to the number of doses requested every 28 days **Perioperative Management:** Up to the number of doses requested for 28 days

		dosed every 8 to 24 hours on days seven through 14	
MonoNine, coagulation factor IX (human)	500, 1000 IU	**Control and prevention of bleeding episodes and perioperative management:** • Minor spontaneous hemorrhage prophylaxis: Up to 30 IU/kg for one dose. Repeat in 24 hours if necessary • Major trauma or surgery: Up to 75 IU/kg, dosed every 18 to 30 hours depending on T ½ and measured factor IX levels. Continue for up to ten days depending on nature of insult	**Control and prevention of bleeding episodes and perioperative management:** Up to the number of doses requested every 28 days
Profilnine SD, factor IX complex	500, 1000, 1500 IU	**Control and prevention of bleeding episodes[€]:** Up to 50 IU/dL for a single dose. Daily infusions are generally required **Perioperative Management:** Up to 50 IU/kg every 16 to 24 hours for seven to ten days until healing is achieved.	**Control and prevention of bleeding episodes:** Up to the number of doses requested every 28 days **Perioperative Management:** Up to the number of doses requested every 28 days
Rixubis, coagulation factor IX (recombinant)	250, 500, 1000, 2000, 3000 IU	**Control and prevention of bleeding episodes[γ]:** Up to 100 IU/dL every 12 to 24 hours for seven to ten days, until bleeding stops and healing is achieved **Routine Prophylaxis:** • < 12 years: Up to 80 IU/kg twice weekly • ≥ 12 years: Up to 60 IU/kg twice weekly **Perioperative Management[γ]:** Up to 100 IU/dL every 8 to 24 hours for seven to ten days, until bleeding stops and healing is achieved	**Control and prevention of bleeding episodes:** Up to the number of doses requested every 28 days **Routine Prophylaxis:** • < 12 years: Up to 672 IU/kg every 28 days • ≥ 12 years: Up to 504 IU/kg every 28 days **Perioperative Management:** Up to the number of doses requested every 28 days

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

* One unit per kilogram body weight increases the circulating Factor IX level by 1% (IU/dL). Adult: Number of Factor IX IU required = body wt (kg) x Desired increase in Plasma Factor IX (%) x 1.3 IU/kg; Pediatric (<15 years): Number of Factor IX IU required = body wt (kg) x Desired increase in Plasma Factor IX (%) x 1.4 IU/kg

[δ] One IU per kg body weight increases the circulating activity of factor IX by 0.98 IU/dL

- Initial dose: required factor IX units (IU) = body weight (kg) x desired factor IX increase (% of normal IU/dL) x reciprocal of observed recovery (IU/kg per IU/dL)
- Maintenance dose: Depends upon the type of bleed or surgery, clinical response, and the severity of the underlying factor IX deficiency

[€] One unit per kilogram body weight increases the circulating Factor IX level by 1% (IU/dL). Number of Factor IX IU required = body wt (kg) x Desired increase in Plasma Factor IX(percent) x 1.0 IU/kg

[γ] One IU per kilogram body weight increases the circulating activity of factor IX by 0.7 IU/dL for patients < 12 years of age and 0.9 IU/dL for patients ≥ 12 years of age. Initial dose = body wt (kg) x desired factor IX increase (percent of normal or IU/dL) x reciprocal of observed recovery (IU/kg per IU/dL)

III. Initial Approval Criteria

I. Standard half-life factor IX products may be considered medically necessary when the following criteria below are met:
   A. Member has a confirmed diagnosis of **hemophilia B (congenital factor IX deficiency)** the following are met:
      1. Treatment is prescribed by or in consultation with a hematologist; **AND**
      2. Use of standard half-life factor IX is planned for one of the following indications:
         i. On-demand treatment and control of bleeding episodes **AND** the number of factor IX 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 B (defined as factor IX 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 IX 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

VI. Billing Code/Availability Information

Drug	Manufacturer	J-Code	1 Billable Unit Equiv.	Vial Size	NDC
AlphaNine SD	Grifols Biologicals Inc	J7193	1 IU	500 units	68516-3600 68516-3602 68516-3605
				1000 units	68516-3600 68516-3603 68516-3606
				1500 units	68516-3600 68516-3601 68516-3604
BeneFIX	Wyeth Biopharma	J7195	1 IU	250 units	58394-0633
				500 units	58394-0634
				1000 units	58394-0635
				2000 units	58394-0636
				3000 units	58394-0637
Ixinity	Cangene Corp	J7195	1 IU	250 units	70504-0287
				500 units	70504-0270 70504-0282
				1000 units	53270-0271 53270-0283 53270-0285
				1500 units	53270-0272 53270-0284 53270-0286
				2000 units	70504-0288
				3000 units	70504-0289
Mononine	CSL Behring LLC	J7193	1 IU	1000 units	00053-6233
Profilnine SD	Grifols Biologicals Inc	J7194	1 IU	500 units	68516-3200 68516-3201 68516-3204
				1000 units	68516-3200 68516-3202 68516-3205

				1500 units	68516-3200 68516-3203 68516-3206
Rixubis	Baxalta US Inc	J7200	1 IU	250 units	00944-3026
				500 units	00944-3028
				1000 units	00944-3030
				2000 units	00944-3032
				3000 units	00944-3034

VII. References

1. AlphaNine SD [package insert]. Los Angeles, CA; Grifols Biologicals Inc.; January 2013.
2. BeneFIX [package insert]. Philadelphia, PA; Wyeth Biopharma; June 2017.
3. Ixinity [package insert]. Winnipeg, Manitoba, Canada. Cangene Corporation; December 2018.
4. Mononine [package insert]. Kankakee, IL; CSL Behring LLC; April 2016.
5. Rixubis [package insert]. Westlake Village, CA; Baxalta US Inc.; May 2018
1. National Hemophilia Foundation. Hemophilia A. Available from: https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Hemophilia-A. Accessed July 5, 2019.
2. 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.
3. 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

ICD-10	ICD-10 Description
D67	Hereditary factor IX 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