Extended Half-life Factor IX Products: Alprolix, Idelvion, and Rebinyn

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‡
Alprolix, coagulation factor IX (recombinant, Fc fusion protein	250, 500, 1000, 2000, 3000, 4000 IU	**On-demand Treatment**[6]**:** Up to 100 IU/dL for the first dose, then again every 6 to 10 hours for another dose. Dosing is then every 24 hours for three days, then every 48 hours until healing is achieved **Routine Prophylaxis:** • ≥12 years: Up to 50 IU/kg once weekly or 100 IU/kg once every ten days • <12 years: Up to 60 IU/kg once weekly. More frequent or higher doses may be required **Perioperative Management**[6]**:** • *Minor surgery*: Up to 80 IU/dL as a single infusion, then every 24 to 48 hours if needed until bleeding stops • *Major surgery*: Up to 100 IU/dL as the initial dose, then repeat dose after 6 to 10 hours and then every 24 hours for the first three days. After day three, the dosing may be extended to	**On-demand Treatment:** Up to the number of doses requested every 28 days **Routine Prophylaxis:** • ≥12 years: Up to 315 IU/kg every 28 days • <12 years: Up to 255 IU/kg every 28 days **Perioperative Management:** Up to the number of doses requested for 28 days

		every 48 hours until healing is achieved	
Idelvion, coagulation factor IX (recombinant, albumin fusion protein	250, 500, 1000, 2000, 3500 IU	**On-demand Treatment*:** Up to 100 IU/dL every 48-72 hours for seven to 14 days until bleeding stops **Routine Prophylaxis:** • ≥12 years: Up to 40 IU/kg once weekly. Patients who are well controlled may be changed to 50-75 IU/kg every 14 days • <12 years: Up to 55 IU/kg every seven days **Perioperative Management*:** • *Minor*: Up to 80 IU/dL every 48 to 72 hours for at least one day until healing is achieved • *Major*: Up to 100 IU/dL every 48 to 72 hours for 7 to 14 days, or until bleeding stops and healing is achieved	**On-demand Treatment:** Up to the number of doses requested every 28 days **Routine Prophylaxis:** • ≥12 years: Up to 170 IU/kg every 28 days • <12 years: Up to 230 IU/kg every 28 days **Perioperative Management:** Up to the number of doses requested for 28 days
Rebinyn, coagulation factor IX (recombinant, GlycoPEGylated	500, 1000, 2000 IU	**On-demand Treatment:** Up to 80 IU/kg for the initial dose. Additional doses of 40 IU/kg can be given. **Perioperative Management:** • *Minor*: Preoperative dose of up to 40 IU/kg. Additional doses can be given if needed. • *Major*: Preoperative dose of up to 80 IU/kg. Repeated doses of 40 IU/kg (in one to three day intervals) within the first week after surgery may be administered.	**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

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

δ One unit per kilogram body weight increases the circulating Factor IX level by 1% (IU/dL). Estimate the required dose or the expected in vivo peak increase in Factor IX level expressed as IU/dL (or % of normal) using the following: IU/dL (or % of normal) = [Total dose (IU)/Body Weight (kg)] x Recovery (IU/dL per IU/kg)

* One IU of Idelvion per kg body weight is expected to increase the circulating activity of factor IX as follows: adolescents and adults: 1.3 IU/dL per IU/kg; pediatrics (<12 years): 1 IU/dL per IU/kg. Determine the initial dose using the following: Required dose (IU) = body weight (kg) x desired factor IX rise (%of normal or IU/dL) x (reciprocal of recovery (IU/kg per IU/dL))

III. Initial Approval Criteria

I. Extended 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)** and the following are met:
      1. Treatment is prescribed by or in consultation with a hematologist; **AND**
      2. Use of extended 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. ***Alprolix and Idelvion only****:* 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. Prior treatment with a standard half-life factor IX product administered at the FDA approved dose for at least 50 exposure days was ineffective for the treatment or prevention of bleeding episodes; **OR**
      4. There is clinical documentation that all available standard half-life factor IX products are inappropriate; **AND**
      5. 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**
      6. 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. Extended half-life factor IX products are considered investigational when used for all other conditions.

III. 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
Alprolix	Biogen Idec, Inc	J7201	1 IU	250 units	64406-0966
				500 units	64406-0911
				1000 units	64406-0922
				2000 units	64406-0933
				3000 units	64406-0944
				4000 units	64406-0977
Idelvion	Novozymes Biopharma A/S	J7202	1 IU	500 units	69911-0865
				1000 units	69911-0866
				2000 units	69911-0867
Rebinyn	Novo Nordisk Inc	J7203	1 IU	500 units	00169-7905
				1000 units	00169-7901
			N/A	2000 units	00169-7902

VII. References

1. Alprolix® [Prescribing Information]. Waltham, MA: Bioverativ; July 2019
2. Idelvion® [Prescribing Information]. Kankakee, IL: CSL Behring; May 2018
3. Rebinyn® [Prescribing Information]. Plainsboro, NJ: Novo Nordisk; May 2017
4. National Hemophilia Foundation. Hemophilia B. Available from: https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Hemophilia-B. Accessed July 8, 2019.
5. 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.
6. 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