Standard Half-life Factor IX Products – Hemophilia B

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO061

Description

AlphaNine SD, BeneFix, Ixinity, Mononine, and Rixubis are standard half-life factor IX products for the treatment and prevention of bleeding in patients with hemophilia B.

Length of Authorization

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

Quantity 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 dosed every 8 to 24 hours on days seven through 14	**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

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Product Name	Dosage Form	Indication/ FDA Labeled Dosing	Quantity Limit‡
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 ѵ:** 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 ѵ:** 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

[¥] 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)

Initial Evaluation

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.

Renewal Evaluation

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

Supporting Evidence

I. Hemophilia B (factor IX deficiency) is an X-linked inherited coagulation factor deficiency that results in a lifelong bleeding disorder. The availability of factor replacement products has dramatically improved care for those with hemophilia B.
II. There are varying severities of hemophilia B depending on the level of factor produced by the patient. Hemophilia B is divided into the following categories based on severity:
    i. **Severe**: <1% factor activity (<0.01 IU/mL)
    ii. **Moderate**: Factor activity level ≥ 1% of normal and ≤ 5% of normal (≥ 0.01 and ≤ 0.05 IU/mL)
    iii. **Mild**: Factor activity level >5% of normal and < 40% of normal (> 0.05 and < 0.40 IU/mL
III. There are three general approaches to bleeding management in those with hemophilia B:
    - Episodic ("on demand") treatment that is given at the time of clinically evident bleeding
    - Perioperative management of bleeding for those undergoing elective surgery/procedures
    - Routine prophylaxis is administered in the absence of bleeding to reduce bleeding and long-term complications of bleeding (e.g. arthropathy)
II. The current standard of care for hemophilia B is to replace the deficient coagulation factor either through episodic ("on demand") treatment given at the time of bleeding, or through continuous prophylaxis to prevent bleeding. Recombinant factor IX products are the treatment of choice for hemophilia B as recommended by The National Hemophilia Foundation's Medical and Scientific Advisory Council (MASAC).
III. MASAC recommends that prophylaxis be considered optimal therapy for individuals age one and older with severe hemophilia B. Therapy should be initiated early with the goal of keeping the trough factor IX level above 1% between doses.
IV. For individuals who have had more than one bleeding episode (e.g. two or more bleeds into a target joint, evidence of joint disease by physical exam or radiography), prophylaxis may be appropriate to prevent further morbidity, regardless of factor activity level.
V. The safety and efficacy of the standard half-life products were established based on open-label, non-randomized trails. All replacement products can produce satisfactory hemostasis.

Investigational or Not Medically Necessary Uses

There is no evidence to support the use of standard half-life factor IX products in any other condition.

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 prophylaxis. UpToDate [database online]. Last updated February 11, 2019.

Policy Implementation/Update:

Date Created	August 2019
Date Effective	August 2019
Last Updated	August 2019
Last Reviewed	08/2019

Action and Summary of Changes	Date
New policy created for standard half-life factor products	08/2019