POLICY: Hemophilia – Factor IX Products

Extended Half-Life Recombinant Products

- Alprolix® (Coagulation Factor IX [recombinant] Fc fusion protein injection – Bioverativ)
- Idelvion (Coagulation Factor IX [recombinant] albumin fusion protein injection – CSL Behring)
- Rebinyn® (Coagulation Factor IX [recombinant] glycoPEGylated injection – NovoNordisk)

Standard Half-Life Recombinant Products

- BeneFIX® (Coagulation Factor IX [recombinant] injection – Wyeth/Pfizer)
- Ixinity® (Coagulation Factor IX [recombinant] injection – Aptevo BioTherapeutics)
- Rixubis® (Coagulation Factor IX [recombinant] injection – Baxalta)

Plasma-Derived Standard Half-Life Products

- AlphaNine® SD (Coagulation Factor IX [plasma-derived] injection – Grifols)
- Mononine® (Coagulation Factor IX [plasma-derived] injection – CSL Behring)
- Profilnine® (Factor IX Complex [plasma-derived] injection – Grifols)

APPROVAL DATE: 02/27/2019

OVERVIEW

Alprolix, Idelvion, and Rebinyn are extended half-life recombinant Factor IX products indicated in adults and children with hemophilia B for on-demand treatment and control of bleeding episodes and perioperative management of bleeding.[1-3] Alprolix and Idelvion are also indicated for routine prophylaxis to reduce the frequency of bleeding episodes. BeneFIX, Ixinity, and Rixubis are standard half-life recombinant Factor IX products that are indicated for the control and prevention of bleeding episodes in adult and pediatric patients with hemophilia B.[4-6] BeneFIX and Ixinity are also indicated for the perioperative management in adult and pediatric patients with hemophilia B. AlphaNine SD, Mononine, and Profilnine plasma-derived Factor IX products that are indicated for the prevention and control of bleeding in patients with Factor IX deficiency due to hemophilia B.[7-9]

Disease Overview

Hemophilia B is a recessive X-linked bleeding disorder caused by mutations in the factor IX gene that leads to the deficiency or absence of the coagulation factor IX.[10,11] It occurs in 1 out of 30,000 male births and affects about 5,000 people in the US. Hemophilia B predominantly occurs in males; however, approximately 10% of females are carriers and are at risk of usually mild bleeding. The severity of bleeding depends on the degree of the factor IX defect and the phenotypic expression. Factor levels of <1%, 1% to 5%, and > 5% to < 40% are categorized as severe, moderate, and mild hemophilia B, respectively. Patients with mild hemophilia B may only experience abnormal bleeding during surgery, during tooth extractions, or when injured. Patients with moderate hemophilia B generally have prolonged bleeding responses to minor trauma. Severe hemophilia B is marked by spontaneous bleeding such as spontaneous hemarthrosis, soft-tissue hematomas, retroperitoneal bleeding, intracerebral hemorrhage, and delayed bleeding post-surgery. Complications from recurrent bleeding and soft-tissue hematomas include severe arthropathy, and joint contractures, which may lead to pain and disability. The main treatment of hemophilia B is replacement of missing blood coagulation with Factor IX products. Factor IX replacement therapy may be used on-demand when bleeding occurs or given as routine prophylaxis with scheduled infusions. Both plasma-derived and recombinant Factor IX products are available. In general, prophylactic therapy has been associated with a reduction in

bleeds and improved outcomes for selected patients (e.g., patients with moderate or severe factor IX deficiency). The goal of therapy is to prevent uncontrolled internal hemorrhage and severe joint damage and to properly manage bleeding episodes. The development of inhibitors occurs at a lower frequency in patients with severe hemophilia B compared with severe hemophilia A but can occur in up to 5% of patients. Higher doses than that typically used for these uses of standard half-life products can be given if the patient develops an inhibitor.

Guidelines

In April 2018, the Medical and Scientific Council (MASAC) from the National Hemophilia Foundation (NHF) updated recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders.[12] The guidelines discuss Factor IX products. Due to safety issues, recombinant Factor IX is the treatment of choice for patients in the management of hemophilia B. Regarding plasma-derived Factor IX concentrates, improved viral-depleting processes and donor screening practices have led to plasma-derived Factor IX products that have a greatly reduced risk for transmission of human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV). Due to higher purity and only limited amounts of other factors contained in the products, AlphaNine SD and Mononine are the human plasma-derived products that are considered to be of high purity and are recognized options by MASAC in the management of hemophilia B. Profilnine is used in patients with Factor II or X deficiency.[12] Some data are available, albeit limited.[13]

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of the following Factor IX products: Alprolix, Idelvion, Rebinyn, BeneFIX, Ixinity, Rixubis, AlphaNine, Mononine, and Profilnine. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the criteria and dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). Because of the specialized skills required for evaluation and diagnosis of patients treated with recombinant Factor IX products, as well as the monitoring required for adverse events and long-term efficacy, the agent is required to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of the following Factor IX products is recommended for patients who meet criteria: Alprolix, Idelvion, Rebinyn, BeneFIX, Ixinity, Rixubis, AlphaNine, Mononine, and Profilnine.

I. Coverage of Alprolix, Idelvion, Rebinyn, BeneFIX, Ixinity, and Rixubis is recommended for patients who meet the following criteria:

FDA-Approved Indications

1. Hemophilia B. Approve for 1 year if the agent is prescribed by or in consultation with a hemophilia specialist.

Dosing. Approve one of the following dosing regimens (A or B):

A) For Alprolix, Idelvion, and Rebinyn approve the following dosing regimens (i, ii, and/or iii):

i. Routine prophylaxis: approve up to 100 IU per kg intravenously at an interval no more frequently than once weekly; AND/OR;

ii. On-demand treatment and control of bleeding episodes: approve up to 100 IU per kg intravenously no more frequently than once every 6 hours for up to 10 days per episode; AND/OR

iii. Perioperative management: approve up to 100 IU per kg intravenously no more frequently than once every 24 hours for up to 10 days per procedure; OR

B) For BeneFIX, Ixinity, and Rixubis approve the following dosing regimens (i, ii, iii, and/or iv):

i. Routine prophylaxis: approve up to 100 IU per kg intravenously no more frequently than twice weekly; AND/OR

ii. On-demand treatment and control of bleeding episodes: approve up to 100 IU per kg intravenously no more frequently than once every 12 hours for up to 10 days per episode; AND/OR

iii. Perioperative management: approve up to 100 IU per kg intravenously no more frequently than once every 8 hours for up to 10 days per procedure; AND/OR

iv. Immune tolerance therapy (also known as immune tolerance induction): approve up to 200 IU per kg intravenously no more frequently than once daily.

II. Coverage of AlphaNine SD, Mononine, and Profilnine is recommended for patients who meet the following criteria:

FDA-Approved Indications

1. Hemophilia B. Approve AlphaNine SD, Mononine, and Profilnine for 1 year if the agent is prescribed by or in consultation with a hemophilia specialist.

Dosing. Approve the following dosing regimens:

A) Routine prophylaxis: approve up to 50 IU per kg intravenously up to no more frequently than twice weekly; AND/OR

B) On-demand treatment of and control of bleeding episodes and perioperative management: approve up to 100 IU per kg intravenously no more frequently than twice daily for up to 10 days; AND/OR

C) Immune tolerance therapy (also known as immune tolerance induction): approve up to 200 IU per kg intravenously no more frequently than once daily.

III. Coverage of Profilnine is recommended for patients who meet the following criteria:

Other Uses with Supportive Evidence

2. Factor II Deficiency. Approve Profilnine for 1 year if the agent is prescribed by or in consultation with a hemophilia specialist.

Dosing. Limited dosing is available. Recommended dosing in hemophilia B (an FDA-approved use) is cited below.

A) Routine prophylaxis: approve up to 50 IU per kg intravenously no more frequently than twice weekly; AND/OR

B) On-demand treatment of and control of bleeding episodes and perioperative management: approve up to 100 IU per kg intravenously no more frequently than twice daily for up to 10 days.

3. Factor X Deficiency. Approve Profilnine for 1 year if the agent is prescribed by or in consultation with a hemophilia specialist.

Dosing. Limited dosing is available. Recommended dosing in hemophilia B (an FDA-approved use) is cited below.

A) Routine prophylaxis: approve up to 50 IU per kg intravenously no more frequently than twice weekly; AND/OR

B) On-demand treatment of and control of bleeding episodes and perioperative management: approve up to 100 IU per kg intravenously no more frequently than twice daily for up to 10 days.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

1. Other Indications. Coverage is not recommended for circumstances not listed in the Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Alprolix® lyophilized powder for intravenous injection [prescribing information]. Waltham, MA: Bioverativ; June 2018.
2. Idelvion® lyophilized powder for solution for intravenous injection [prescribing information]. Kankakee, IL: CSL Behring; May 2018.
3. Rebinyn® lyophilized powder for solution for intravenous injection [prescribing information]. Plainsboro, NJ: Novo Nordisk; May 2017.
4. BeneFIX® injection for intravenous use [prescribing information]. Philadelphia, PA: Wyeth Pharmaceuticals, Inc. (a subsidiary of Pfizer); June 2017.
5. Ixinity® solution for intravenous injection [prescribing information]. Seattle, WA: Aptevo BioTherapeutics; December 2018.
6. Rixubis® for intravenous injection [prescribing information]. Lexington, MA: Baxalta; May 2018.
7. AlphaNine® SD injection [prescribing information]. Los Angeles, CA: Grifols; March 2017.
8. Mononine® injection [prescribing information]. Kankakee, IL: CSL Behring; April 2016.
9. Profilnine® injection [prescribing information]. Los Angeles, CA: Grifols; May 2014.
10. Franchini M. Current management of hemophilia B: recommendations, complications and emerging issues. *Expert Rev Hematol.* 2014;7(5):573-581.
11. Peyvandi F, Garagiola I, Young G. The past and future of haemophilia: diagnosis, treatments, and its complications. *Lancet*. 2016;388(10040):187-197.
12. National Hemophilia Foundation. Medical and Scientific Advisory Council (MASAC) recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders (Revised April 2018). MASAC document #253. Available at: https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/MASAC-Recommendations-Concerning-Products-Licensed-for-the-Treatment-of-Hemophilia-and-Other-Bleeding-Disorders Accessed on February 15, 2019.
13. Menegatti M, Peyvandi F. Treatment of rare factor deficiencies other than hemophilia. *Blood*. 2019;133(5):415-424.

HISTORY

Type of Revision	Summary of Changes*	Approval Date
New policy	--	02/27/2019