PRIOR AUTHORIZATION POLICY

POLICY: Hemophilia Factor IX Products Prior Authorization Policy

Extended Half-Life Recombinant Products

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

Standard Half-Life Recombinant Products

- BeneFIX® (Coagulation Factor IX [recombinant] intravenous infusion – Wyeth/Pfizer)
- Ixinity® (Coagulation Factor IX [recombinant] intravenous infusion – Medexus)
- Rixubis® (Coagulation Factor IX [recombinant] intravenous infusion – Baxalta)

Plasma-Derived Products

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

REVIEW DATE: 03/22/2023

OVERVIEW

Alprolix, Idelvion, and Rebinyn are extended half-life recombinant Factor IX products; BeneFIX, Ixinity and Rixubis are standard half-life recombinant Factor IX products; and AlphaNine SD, Mononine, and Profilnine are plasma-derived Factor IX products.[1-9] All agents are indicated in various clinical scenarios for use in the management of patients with hemophilia B.

Profilnine is also used in patients with Factor II and/or X deficiency.[10] Some data are available, albeit limited.

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.[11-13] 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 factor 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 the uses of standard half-life products can be given if the patient develops an inhibitor.

Guidelines

Guidelines for hemophilia from the National Hemophilia Foundation (2022)[14] and the World Federation of Hemophilia (2020)[15] recognize the important role of Factor IX products in the management of hemophilia B patients.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of the following Factor IX products: Alprolix, Idelvion, Rebinyn, BeneFIX, Ixinity, Rixubis, AlphaNine, Mononine, and Profilnine. All approvals are provided for the duration noted below. 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

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

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

FDA-Approved Indication

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

III. Coverage of Profilnine is also 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.

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

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of the cited Factor IX products is not recommended in the following situations:

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

REFERENCES

1. Alprolix® intravenous infusion [prescribing information]. Waltham, MA: Bioverativ; October 2020.
2. Idelvion® intravenous infusion [prescribing information]. Kankakee, IL: CSL Behring; July 2021.
3. Rebinyn® intravenous infusion [prescribing information]. Plainsboro, NJ: Novo Nordisk; August 2022.
4. BeneFIX® intravenous infusion [prescribing information]. Philadelphia, PA: Wyeth/Pfizer; November 2022.
5. Ixinity® intravenous infusion [prescribing information]. Chicago, IL: Medexus; November 2022.
6. Rixubis® intravenous infusion [prescribing information]. Lexington, MA: Baxalta; June 2020.
7. AlphaNine® SD intravenous infusion [prescribing information]. Los Angeles, CA: Grifols; March 2021.
8. Mononine® intravenous infusion [prescribing information]. Kankakee, IL: CSL Behring; December 2018.
9. Profilnine® intravenous infusion [prescribing information]. Los Angeles, CA: Grifols; March 2021.
10. Menegatti M, Peyvandi F. Treatment of rare factor deficiencies other than hemophilia. *Blood*. 2019;133(5):415-424.
11. Sidonio RF, Malec L. Hemophilia B (Factor IX Deficiency). *Hematol Oncol Clin North Am*. 2021;35(6):1143-1155.
12. Mancuso ME, Mahlangu JN, Pipe SW. The changing treatment landscape in haemophilia: from standard half-life clotting factor concentrates to gene editing. *Lancet*. 2021;397:630-640.
13. Croteau SE. Hemophilia A/B. *Hematol Oncol Clin N Am*. 2022;36:797-812.
14. National Hemophilia Foundation. Medical and Scientific Advisory Council (MASAC) recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders (Revised March 2022). MASAC document #272. Available at: https://www.hemophilia.org/sites/default/files/document/files/272._Treatment.pdfAccessed on March 14, 2023.
15. Srivastava A, Santagostino E, Dougall A, on behalf of the WFH guidelines for the management of hemophilia panelists and co-authors. Guidelines for the management of hemophilia, 3rd edition. *Haemophilia*. 2020;26(Suppl 6):1-158.