CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hemophilia – Factor IX Products Utilization Management Medical Policy

Extended Half-Life Recombinant Products

- Alprolix® (Coagulation Factor IX [recombinant] Fc fusion protein intravenous infusion – Bioverativ/Sanofi)
- 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/Takeda)

Plasma-Derived Standard Half-Life Products

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

REVIEW DATE: 02/11/2026

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 and Profilnine are plasma-derived Factor IX products.[1-8] 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.[9] Some data are available, albeit limited.

Disease Overview

Hemophilia B is a genetic bleeding disorder caused by missing or insufficient levels of blood Factor IX, a protein required to produce blood clots to halt bleeding.[10-12] The condition is a rare X-linked bleeding disorder that mainly impacts males. The prevalence of hemophilia B in males is one in 30,000 live births.[12] Symptoms include heavy or prolonged bleeding following an injury or trauma, after a medical or dental procedure, or post-surgery.[10-12] Bleeding can also occur internally into joints, muscles, or internal organs. Spontaneous bleeding events may also occur. Complications in patients with hemophilia B include joint disease and hemarthrosis.[10-12] For a patient with hemophilia B, bleeding episodes may be more common in childhood and adolescence than in adulthood.[10] There is a strong correlation between Factor IX levels and phenotypic expression of bleeding. Normal plasma levels of Factor IX range from 50% to 150%.[11] The disease is classified based on reduced levels. Mild, moderate, and severe hemophilia B is characterized by Factor IX levels ranging from 6% up to 49%, 1% up to 5%, and < 1%, respectively.[11] In general, a patient with factor IX clotting activity > 40% usually had normal coagulation.[10] Other therapies used in the management of hemophilia B involve Factor IX products administered intravenously (both recombinant and plasma-derived), are used routinely to prevent bleeding or are given on-demand to treat bleeding episodes associated with hemophilia B.[10] Also, non-factor prophylactic agents given by subcutaneous (SC)

injection are also available for use in patients ≥ 12 years of age (i.e., Qfitlia™ [fitusiran SC injection], Hympavzi® [marstacimab SC injection], and Alhemo® [concizumab SC injection]).

Guidelines

Guidelines for hemophilia from the National Bleeding Disorders Foundation (2024)[13] and the International Society on Thrombosis and Haemostasis (2024)[14] recognize the important role of Factor IX products in the management of hemophilia B patients.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of the following Factor IX products: Alprolix, Idelvion, Rebinyn, BeneFIX, Ixinity, Rixubis, AlphaNine, and Profilnine. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. 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). 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

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

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 the requested agent 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 and Profilnine is recommended for patients who meet the following criteria:

FDA-Approved Indication

1. Hemophilia B. Approve AlphaNine SD 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 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 also recommended for patients who meet the following criteria:

Other Uses with Supportive Evidence

1. 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.

2. 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

Coverage of the cited Factor IX products are 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/Sanofi; May 2023.
2. Idelvion® intravenous infusion [prescribing information]. Kankakee, IL: CSL Behring; June 2023.
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; March 2024.
6. Rixubis® intravenous infusion [prescribing information]. Cambridge, MA: Baxalta/Takeda; March 2025.
7. AlphaNine® SD intravenous infusion [prescribing information]. Los Angeles, CA: Grifols; November 2022.
8. Profilnine® intravenous infusion [prescribing information]. Los Angeles, CA: Grifols; November 2022.
9. Menegatti M, Peyvandi F. Treatment of rare factor deficiencies other than hemophilia. *Blood*. 2019;133(5):415-424.
10. Konkle BA, Nakaya Fletcher S. Hemophilia B. 2000 Oct 2 [Updated 2025 Aug 7]. In: Adam MP, Bick S, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2026.
11. National Bleeding Disorders Foundation. Hemophilia B. An overview of symptoms, genetics, and treatments to help you understand hemophilia B. Available at: https://www.hemophilia.org/bleeding-disorders-a-z/types/hemophilia-b. Accessed on February 8, 2026.
12. Chowdary P, Carcao M, Kenet G, Pipe SW. *Haemophilia*. 2025;405:736-750.
13. National Bleeding Disorders Foundation. Medical and Scientific Advisory Council (MASAC) recommendations concerning products licensed for the treatment of hemophilia selected disorders of the coagulation system (endorsed on October 2, 2024). MASAC document #290. Available at: https://www.hemophilia.org/sites/default/files/document/files/MASAC-Products-Licensed.pdf. Accessed on February 9, 2026.
14. Rezende SM, Neumann I, Angchaisuksiri P, et al. International Society on Thrombosis and Haemostasis clinical practice guideline for the treatment of congenital hemophilia A and B based on the Grading of Recommendations Assessment, Development, and Evaluation methodology. *J Thromb Haemost*. 2024;22:2629-2652.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	Mononine was removed from the policy as it is obsolete.	02/28/2024
Annual Revision	No criteria changes.	02/19/2025
Annual Revision	No criteria changes.	02/11/2026