Drug Coverage Policy

Effective Date.....6/15/2024
Coverage Policy Number.....IP0623
Policy Title.....Factor IX Products

Hemophilia – Factor IX Products

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)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not

recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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 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.[10-12] 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 Bleeding Disorders Foundation (2023)[13] and the World Federation of Hemophilia (2020)[14] recognize the important role of Factor IX products in the management of hemophilia B patients.

Medical Necessity Criteria

I. Alprolix, Idelvion, Rebinyn, BeneFIX, Ixinity, and Rixubis are considered medically necessary when the following criteria are met:

FDA-Approved Indication

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. AlphaNine SD and Profilnine are considered medically necessary when the following criteria are met:

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. Profilnine is also considered medically necessary when the following criteria are met:

Other Uses with Supportive Evidence

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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.

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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.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven (criteria will be updated as new published data are available).

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J7193	Factor IX (antihemophilic factor, purified, nonrecombinant), per IU
J7194	Factor IX, complex, per IU
J7195	Injection, factor IX (antihemophilic factor, recombinant), per IU, not otherwise specified
J7200	Injection, factor, IX, (antihemophilic factor, recombinant), rixubis, per IU
J7201	Injection, factor IX, fc fusion protein (recombinant), Alprolix, 1 IU
J7202	Injection, Factor IX, albumin fusion protein, (recombinant), idelvion, 1 IU
J7203	Injection Factor IX, (antihemophilic factor, recombinant), glycopegylated, (rebinyn), 1 iu
J7213	Injection, coagulation Factor IX (recombinant), ixinity, 1 IU

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; November 2022.
6. Rixubis® intravenous infusion [prescribing information]. Lexington, MA: Baxalta/Takeda; March 2023.
7. AlphaNine® SD intravenous infusion [prescribing information]. Los Angeles, CA: Grifols; November 2022.
8. Profilnine® intravenous infusion [prescribing information]. Los Angeles, CA: Grifols; March 2021.
9. Menegatti M, Peyvandi F. Treatment of rare factor deficiencies other than hemophilia. *Blood*. 2019;133(5):415-424.

10. Sidonio RF, Malec L. Hemophilia B (Factor IX Deficiency). *Hematol Oncol Clin North Am*. 2021;35(6):1143-1155.
11. 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.
12. Croteau SE. Hemophilia A/B. *Hematol Oncol Clin N Am*. 2022;36:797-812.
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 (Revised August 19, 2023 and endorsed on August 20, 2023). MASAC document #280. Available at: https://www.hemophilia.org/sites/default/files/document/files/MASAC-Products-Licensed.pdf. Accessed on February 22, 2024.
14. 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.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy • New stand-alone policy created, criteria previously housed in Clotting Factors and Antithrombin class policy. • Added dosing to the policy for all products • Mononine was removed as it is obsolete.	6/1/2024

The policy effective date is in force until updated or retired.