Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Agents for Hemophilia B	MP-RX-FP-03-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Factor IX Human, Purified [Alphanine], Factor IX Complex Human [Profilnine], Coagulation Factor IX Recombinant [Rixubis], Factor IX Fc Fusion Protein Recombinant [Alprolix], Factor IX Albumin Fusion Protein Recombinant [Idelvion], Coagulation Factor IX Recombinant, GlycoPEGylated [Rebinyn], drugs approved by the Food and Drug Administration (FDA) for the treatment of Hemophilia B.

Background Information

Factor replacement treatments can be created from blood products (human plasma-derived) and others that are manufactured (recombinant). Replacement therapy may be given on a routine, preventive basis which is also called prophylactic therapy. The infusion of factor replacements given to stop a bleeding episode is called on-demand or episodic therapy.

Products in this document include:

- Coagulation Factor IX, Human plasma-derived: Alphanine SD
- Factor IX Complex, human plasma-derived: Profilnine SD
- Factor IX Recombinant: Rixubis, Benefix, Ixinity
- Coagulation Factor IX-Long-Acting
  - Recombinant, Albumin Fusion Protein: Idelvion
  - Recombinant coagulation factor IX, Fc Fusion Protein: Alprolix
  - Recombinant coagulation factor IX, GlycoPEGylated: Rebinyn

Hereditary hemophilia B is the second most common type of hemophilia after hemophilia A (four times less common than hemophilia A). Although it is usually inherited, about one third of cases are caused by spontaneous mutations. Hemophilia A and B are clinically indistinguishable from one another, except by factor analysis. Hemophilia B is related to mutations in the gene coding for coagulation Factor IX (CDC 2014).

The U.S. National Hemophilia Foundation (NHF) and the World Federation of Hemophilia (Srivastava, 2020) both note there is a relationship of bleeding severity to the clotting factor level. Both entities list “severe” hemophilia as a clotting factor level < 1 IU/dl or < 1% of normal. A “mild” bleeding severity is identified as a clotting factor level of 5-40 IU/dl or 5 to < 40% of normal. A bleeding episode for individuals with mild risk includes severe bleeding with major trauma or surgery. Individuals with 1-5 IU/dl or 1-5% of normal are

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considered "moderate" risk for occasional spontaneous bleeding and prolonged bleeding with minor trauma or surgery (Srivastava, 2013).

Hemophilia severity:

- Severe hemophilia – Severe hemophilia is defined as < 1 percent factor activity, which corresponds to < 1 IU/dL.
- Moderate hemophilia – Moderate hemophilia is defined as a factor activity level ≥ 1 percent of normal and < 5 percent of normal, corresponding to ≥ 1 and < 5 IU/dL.
- Mild hemophilia – Mild hemophilia is defined as a factor activity level ≥ 5 percent of normal and < 40 percent of normal (≥ 5 and < 40 IU/dL).

World Federation of Hemophilia 2020 Guidelines for treatment of hemophilia state that prophylaxis prevents bleeding and joint destruction, and that prophylaxis should enable those with hemophilia to lead healthy and active lives. Moreover, the updated 2020 guidelines proposes that the definition of prophylaxis be based on outcomes rather than doses or timing of initiation, and treatment 2 regimens that take into account the hemophilic phenotype of the individual in addition to factor levels. However, more studies are needed to determine if all individuals should remain on therapy as adults (that is, those with severe hemophilia vs. moderate or mild). The WFH 2020 guidelines have been endorsed by several societies worldwide, including the U.S. NHF. Short-term prophylaxis (of 4 to 8 weeks) may interrupt the bleeding cycle and benefit individuals with repeated bleeding into target joints. Prophylaxis does not reverse existing joint damage but reduces bleeding and may slow progression of joint damage. Prophylactic clotting factor administration is recommended prior to the individual engaging in activities with higher risk of injury. Randomized trials of prophylactic therapy of hemophilia have demonstrated a decreased incidence of arthropathy (Gringeri, 2011; Manco-Johnson, 2007).

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

Coagulation Factor IX, Human plasma-derived (Alphanine SD)

HCPCS	Description
J7193	Factor IX (Anti-hemophilic factor, purified, non-recombinant) per IU [AlphaNine SD]

ICD-10	Description
D67	Hereditary factor IX deficiency [hemophilia B]
D68.311	Acquired hemophilia
Z29.8	Encounter for other specified prophylactic measure

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Z79.899	Other long term (current) drug therapy [prophylactic]

Factor IX Complex Human (Profilnine SD)

HCPCS	Description
J7194	Factor IX complex, per IU [Profilnine SD]

ICD-10	Description
D67	Hereditary factor IX deficiency [hemophilia B]
Z29.8	Encounter for other specified prophylactic measure
Z79.899	Other long term (current) drug therapy [prophylactic]

Factor IX Recombinant (Benefi, Ixinity, Rixubis)

HCPCS	Description
J7200	Injection, factor IX, (Anti-hemophilic factor, recombinant), Rixubis, per IU
J7195	Injection, factor IX (Anti-hemophilic factor, recombinant) per IU, not otherwise specified [Benefix, Ixinity]
J7213	Injection, coagulation factor ix (recombinant) [Ixinity], 1 IU

ICD-10	Description
D67	Hereditary factor IX deficiency [hemophilia B]
D68.311	Acquired hemophilia
Z29.8	Encounter for other specified prophylactic measure
Z79.899	Other long term (current) drug therapy [prophylactic]

Coagulation Factor IX—Long Acting Recombinant, Albumin Fusion Protein (Idelvion); Recombinant Coagulation Factor IX, Fc Fusion Protein (Alprolix); Recombinant Coagulation Factor IX, GlycoPEGylated (Rebinyn)

HCPCS	Description
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, 1IU

ICD-10	Description
D67	Hereditary factor IX deficiency [hemophilia B]
D68.311	Acquired hemophilia
Z29.8	Encounter for other specified prophylactic measure
Z79.899	Other long term (current) drug therapy [prophylactic]

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Alphanine SD (Human plasma-derived, Coagulation Factor IX)

A. Criteria for Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

I. Individual has a diagnosis of hemophilia B (also called factor IX deficiency or Christmas disease); **AND**

II. Individual is using for the treatment of bleeding episodes;

OR

III. Individual has a diagnosis of severe hemophilia B (defined as less than 1 IU/dL or 1% endogenous Factor IX) (NHF,Srivastava 2020); **AND**

IV. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes;

OR

V. Individual has a diagnosis of mild to moderate hemophilia B (defined as endogenous Factor IX less than 40 IU/dL [less than 40%], but greater than or equal to 1 IU/dL) (NHF, Srivastava 2020); **AND**

VI. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**

VII. Individual has one of the following:

a. One or more episodes of spontaneous bleeding into joint; **OR**

b. One or more episodes severe, life-threatening, or spontaneous bleeding as determined by prescriber; **OR**

c. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

B. Criteria For Continuation of Therapy

I. MMM considers continuation Alphanine SD therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when all of the following criteria is met:

a. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

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C. Authorization Duration

I. Initial Approval Duration: 1 year
II. Reauthorization Approval Duration: 1 year

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

I. Treatment or reversal of coumarin-induced anticoagulation; **OR**
II. Hemorrhagic state or coagulopathy associated with liver dysfunction; **OR**
III. Treatment of individuals with hemophilia A with inhibitors to factor VIII; **OR**
IV. Replacement therapy of other clotting factors which include factors II, VII, and X; **OR**
V. When the above criteria are not met and for all other indications

Profilnine SD (Human plasma-derived, Factor IX Complex)

A. Criteria for Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

I. Individual has a diagnosis of hemophilia B (also called factor IX deficiency or Christmas disease); **AND**
II. Individual is using for the treatment of bleeding episodes,

OR

III. Individual has a diagnosis of severe hemophilia B (defined as less than 1 IU/dL or 1% endogenous Factor IX) (NHF, Srivastava 2020); **AND**
IV. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes;

OR

V. Individual has a diagnosis of mild to moderate hemophilia B (defined as endogenous Factor IX less than 40 IU/dL [less than 40%], but greater than or equal to 1 IU/dL) (NHF, Srivastava 2020); **AND**
VI. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
VII. Individual has one of the following:
    a. One or more episodes of spontaneous bleeding into joint; **OR**
    b. One or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
    c. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid

conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

B. Criteria for Continuation of Therapy

I. MMM considers continuation Profilnine SD (Human plasma-derived, Factor IX Complex) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when all of the following criteria is met:
   a. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

C. Authorization Duration

I. Initial Approval Duration: 1 year
II. Reauthorization Approval Duration: 1 year

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

I. Individual has a diagnosis of Factor VII deficiency; **OR**
II. When the above criteria are not met and for all other indications.

Benefix, Ixinity, Rixubis (Recombinant Factor IX)

A. Criteria for Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

I. Individual has a diagnosis of hemophilia B, (also called factor IX deficiency or Christmas disease); **AND**
II. Individual is using for one of the following:
   a. The treatment of bleeding episodes; **OR**
   b. Peri-procedural management for surgical, invasive or interventional radiology procedures;

OR

III. Individual has a diagnosis of severe hemophilia B (defined as less than 1 IU/dL or 1% endogenous Factor IX) (NHF,Srivastava 2020); **AND**
IV. Individual is using as routine prophylaxis to prevent or reduce the frequency of bleeding episodes;

OR

V. Individual has a diagnosis of mild to moderate hemophilia B (defined as endogenous Factor IX less than 40 IU/dL [less than 40%], but greater than or equal to 1 IU/dL) (NHF, Srivastava 2020); **AND**
VI. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**

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VII. Individual has one of the following:
   a. One or more episodes of spontaneous bleeding into joint; **OR**
   b. One or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
   c. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

B. Criteria for Continuation of Therapy

MMM considers continuation Benefix, Ixinity, Rixubis (Recombinant Factor IX therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when all of the following criteria is met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

C. Authorization Duration

I. Initial Approval Duration: 1 year
II. Reauthorization Approval Duration: 1 year

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

I. Treatment of other factor deficiencies (for example factors II, VII, VIII and X); **OR**
II. Treatment of individuals with hemophilia A with inhibitors to factor VIII; **OR**
III. To reverse coumarin-induced anticoagulation; **OR**
IV. Treatment of bleeding due to low levels of liver-dependent coagulation factors; **OR**
V. Using for the induction of immune tolerance in individuals with hemophilia B; **OR**
VI. When the above criteria are not met and for all other indications.

Idelvion (Recombinant Long-Acting, Albumin Fusion Protein Coagulation Factor IX), Alprolix (Recombinant, Fc Fusion Protein Coagulation Factor IX), or Rebinyn (Recombinant, glycoPEGylated Coagulation Factor IX)

A. Criteria for Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

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I. Individual has a diagnosis of severe hemophilia B (also called factor IX deficiency or Christmas disease); **AND**
II. Individual has less than 1 IU/dL (less than 1%) endogenous Factor IX (NHF, Srivastava 2020); **AND**
III. Individual is using for one of the following:
    a. The treatment of bleeding episodes; **OR**
    b. Peri-procedural management for surgical, invasive or interventional radiology procedures; **OR**
    c. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes;

OR

IV. Individual has a diagnosis of mild to moderate hemophilia B; **AND**
V. Individual has endogenous Factor IX level less than 40 IU/dL (less than 40%) but greater than or equal to 1 IU/dL (NHF,Srivastava 2020); **AND**
VI. Individual is using for one of the following:
    a. Individual is using for the treatment of bleeding episodes; **OR**
    b. Individual is using for peri-procedural management for surgical, invasive or interventional radiology procedures; **OR**
    c. Individual is using for routine prophylaxis to prevent or reduce the frequency of bleeding episodes for one of the following:
        1. Individual has had one or more episodes of spontaneous bleeding into joint; **OR**
        2. Individual has had one or more episodes of severe, life-threatening, or spontaneous bleeding as determined by the prescriber; **OR**
        3. Severe phenotype hemophilia determined by the individual's risk factors that increase the risk of a clinically significant bleed, including but not limited to, participation in activities likely to cause injury/trauma, procoagulant and anticoagulant protein levels, comorbid conditions affecting functional ability and physical coordination, or history of a clinically significant bleed.

B. Criteria for Continuation of Therapy

MMM considers continuation Idelvion (Recombinant Long-Acting, Albumin Fusion Protein Coagulation Factor IX), Alprolix (Recombinant, Fc Fusion Protein Coagulation Factor IX), or Rebinyn (Recombinant, glycoPEGylated Coagulation Factor IX) necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when all of the following criteria is met:

I. Individual has had a positive therapeutic response to treatment (for example, reduction in frequency and/or severity of bleeding episodes).

C. Authorization Duration

I. Initial Approval Duration: 1 year
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D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

I. Using for the induction of immune tolerance in individuals with hemophilia B; **OR**
II. When the above criteria are not met and for all other indication.

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

For the most up-to-date FDA-approved prescribing information, visit the DailyMed website at https://dailymed.nlm.nih.gov/dailymed/ or the respective product websites:

- Coagulation Factor IX, Human plasma-derived: Alphanine SD (https://www.alphaninesd.com/en/product-information)
- Factor IX Complex, human plasma-derived: Profilnine SD
- Factor IX Recombinant: Rixubis (https://www.rixubis.com), Benefix (https://www.benefix.com), Ixinity (https://www.ixinity.com)
- Coagulation Factor IX-Long-Acting
  - Recombinant, Albumin Fusion Protein: Idelvion (https://www.idelvion.com)
  - Recombinant coagulation factor IX, Fc Fusion Protein: Alprolix (https://www.alprolix.com)
  - Recombinant coagulation factor IX, GlycoPEGylated: Rebinyn (https://www.rebinyn.com)

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Reference Information

1. Centers for Disease Control and Prevention. Hemophilia Facts. Available at: http://www.cdc.gov/ncbddd/hemophilia/facts.html.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2022. URL: http://www.clinicalpharmacology.com. Updated periodically. 6
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: September 29, 2022.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
6. National Hemophilia Foundation (NHF). Available at: http://www.hemophilia.org/. Accessed on September 29, 2022.
7. National Hemophilia Foundation (NHF). Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders. September 2020. Available at https://www.hemophilia.org/Researchers-Healthcare-Providers/Medicaland-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/MASAC-Recommendations-Concerning-Products-Licensedfor-the-Treatment-of-Hemophilia-and-Other-Bleeding-Disorders. Accessed: September 29, 2022.
8. Srivastava A, Santagostino E, Dougall A, et al. World Federation of Hemophilia. Guidelines for the management of hemophilia. Haemophilia. 3rd edition. August 2020. Available at https://onlinelibrary.wiley.com/doi/epdf/10.1111/hae.14046. Accessed: September 29, 2022.
9. CMS IOM Publication 100-04, Medicare Claims Processing Manual, Chapter 17, Section 80.4 Billing for Hemophilia Clotting Factors, Section 80.4.1 Clotting Factor Furnishing Fee. Local Coverage Article, A56482, Billing and Coding: Hemophilia Factor Products (Revision Effective Date: 10/01/2023). Available at: Article - Billing and Coding: Hemophilia Factor Products (A56482) (cms.gov)

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Annual Review 11/15/2024	Added Duration of Therapy and Quantity Limits section; Wording, and formatting changes; Coding Reviewed: No changes.	2/18/2025	3/6/2025
Policy Inception 11/18/2022	Elevance Health's Medical Policy adoption.	N/A	11/30/2023