Clinical Policy: Factor IX (Human, Recombinant)

Reference Number: CP.PHAR.218
Effective Date: 05.01.16
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The following are factor IX products requiring prior authorization: human – AlphaNine® SD, Mononine®; recombinant – Alprolix®, BeneFIX®, Idelvion®, Ixinity®, Rebinyn®, and Rixubis®.

FDA Approved Indication(s)

Factor IX products are indicated for patients with hemophilia B (congenital factor IX deficiency or Christmas disease) for the following uses:

- On-demand treatment and control of bleeding episodes
  - Adults and children: AlphaNine SD, Alprolix, BeneFIX, Idelvion, Ixinity, Mononine, Rebinyn, and Rixubis
- Perioperative management of bleeding
  - Adults and children: Alprolix, BeneFIX, Idelvion, Ixinity, Rebinyn, and Rixubis
- Routine prophylaxis to reduce the frequency of bleeding episodes
  - Adults and children: Alprolix, BeneFIX, Idelvion, Ixinity, Rebinyn, and Rixubis

Limitation(s) of use:

- AlphaNine SD, and Mononine contain low, non-therapeutic levels of factors II, VII, and X, and, therefore, are not indicated for the treatment of factor II, VII or X deficiencies. They are also not indicated for the reversal of coumarin anticoagulant-induced hemorrhage, nor in the treatment of hemophilia A patients with inhibitors to factor VIII.
- Mononine is also not indicated in a hemorrhagic state caused by hepatitis-induced lack of production of liver dependent coagulation factors.
- Alprolix, BeneFIX, Idelvion, Ixinity, Rebinyn, and Rixubis are not indicated for induction of immune tolerance in patients with hemophilia B.

Policy/Criteria

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

It is the policy of health plans affiliated with Centene Corporation® that AlphaNine SD, Alprolix, BeneFIX, Idelvion, Ixinity, Mononine, Rebinyn, and Rixubis are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Congenital Hemophilia B (must meet all)**:**

1. Diagnosis of congenital hemophilia B (factor IX deficiency);
2. Prescribed by or in consultation with a hematologist;

3. For AlphaNine requests only: Age ≥ 17 years;
4. Request is for one of the following uses (a, b, or c):
   a. Control and prevention of bleeding episodes;
   b. Perioperative management;
   c. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes;
5. For routine prophylaxis requests: Request is for Alprolix, Benefix, Idelvion, Ixinity, Rebinyn, or Rixubis;
6. Documentation of member's current body weight (in kg);
7. Dose does not exceed the FDA approved maximum recommended dose for the relevant indication.

Approval duration:
Surgical/acute bleeding: 3 months
Prophylaxis:
Medicaid/HIM – 6 months (*12 months for HIM Texas*)
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Congenital Hemophilia B (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;

3. If request is for a dose increase, both (a and b):
   a. Documentation of member's current body weight in kg (if requesting a higher dose than previously requested);
   b. New dose does not exceed the FDA approved maximum recommended dose for the relevant indication.

Approval duration:
Surgical/acute bleeding: 3 months
Prophylaxis:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - All products except AlphaNine SD: known history of hypersensitivity reactions, including anaphylaxis, to the product or its excipients*
    **Including mouse or hamster protein for BeneFix, Idelvion, Ixinity, Mononine, Rebinyn, and Rixubis*
  - Rixubis: disseminated intravascular coagulation, signs of fibrinolysis
- Boxed warning(s): none reported

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Factor IX, human (AlphaNine SD)	Control and prevention of bleeding episodes	Minor episodes: 20-30 IU/kg IV twice daily Moderate episodes: 25-50 IU/kg IV twice daily Major episodes: 30-50 IU/kg IV twice daily for at least 3-5 days, followed by 20 IU/kg IV twice daily Surgery: 50-100 IU/kg IV twice daily before surgery, followed by the same regimen for 7-10 days thereafter	Bleeding episodes: 100 IU/kg/day Surgery: 200 IU/kg/day
Factor IX, human (Mononine)	Control and prevention of bleeding episodes	Minor episodes: 20-30 IU/kg IV every 24 hours Major trauma or surgery: 75 IU/kg IV every 18-30 hours	Minor episodes: 30 IU/kg/day Major trauma or surgery: 750 IU/kg/18 hours
Factor IX, recombinant (Alprolix)	Control and prevention of bleeding episodes, perioperative management	Minor and moderate episodes: 30-60 IU/dL/kg IV every 48 hours if there is further evidence of bleeding after the first dose Major episodes: 80-100 IU/dL/kg IV initially; consider a repeat dose after 6-10 hours and then every 24 hours for the first 3 days. May extend to	Bleeding episodes: 100 IU/dL/kg/dose Surgery: 100 IU/dL/kg/dose

Drug Name	Indication	Dosing Regimen	Maximum Dose
		dosing every 48 hours or longer after the first 3 days Minor surgery: 50-80 IU/dL/kg IV initially followed by every 24-48 hours until bleeding stops and healing is achieved Major surgery: 60-100 IU/dL/kg IV initially; consider a repeat dose after 6-10 hours and then every 24 hours for the first 3 days. May extend to dosing every 48 hours or longer after the first 3 days	
	Routine prophylaxis	50 IU/dL/kg IV once weekly or 100 IU/dL/kg IV once every 10 days (start with 60 IU/kg once weekly for < 12 years)	100 IU/dL/kg/dose
Factor IX, recombinant (BeneFIX)	Control and prevention of bleeding episodes, perioperative management	Minor episodes: 20-30 IU/dL/kg IV every 12-24 hours Moderate episodes: 25-50 IU/dL/kg IV every 12-24 hours Major episodes: 50-100 IU/dL/kg IV every 12-24 hours Surgery: 50-100 IU/dL/kg IV every 12-24 hours	200 IU/dL/kg/day
	Routine prophylaxis	100 IU/kg once weekly	100 IU/kg/dose
Factor IX, recombinant (Idelvion)	Control and prevention of bleeding episodes, perioperative management	Minor and moderate episodes: 30-60 IU/dL/kg IV every 48-72 hours Major episodes: 60-100 IU/dL/kg IV every 48-72 hours until bleeding stops and healing is achieved; maintenance dose is weekly	Bleeding episodes: 100 IU/dL/kg/48 hours Surgery: 80 IU/dL/kg/48 hours

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Minor surgery: 50-80 IU/dL/kg IV every 48-72 hours until healing is achieved Major surgery: 60-100 IU/dL/kg IV every 48-72 hours until bleeding stops and healing is achieved; maintenance dose is 1-2 times per week	
	Routine prophylaxis	≥ 12 years of age: 25-40 IU/kg IV every 7 days followed by 50-75 IU/kg IV every 14 days once well-controlled < 12 years of age: 40-55 IU/kg IV every 7 days	55 IU/kg/week
Factor IX, recombinant (Ixinity)	Control and prevention of bleeding episodes, perioperative management	Minor episodes: 30-60 IU/dL/kg IV every 24 hours Moderate episodes: 40-60 IU/dL/kg IV every 24 hours Major episodes: 60-100 IU/dL/kg IV every 12-24 hours Minor surgery: 50-80 IU/dL/kg IV pre-operatively followed by 30-80 IU/dL/kg every 24 hours Major surgery: 60-80 IU/dL/kg IV pre-operatively followed by 40-60 IU/dL/kg IV every 8-24 hours for 1-3 days or 30-50 IU/dL/kg IV every 8-24 hours for 4-6 days or 20-40 IU/dL/kg IV every 8-24 hours for 7-14 days	Bleeding episodes: 127 IU/dL/kg/dose Surgery: 101.6 IU/dL/kg/dose
	Routine prophylaxis	≥ 12 years of age: 40-70 IU/kg IV twice weekly < 12 years of age: 35-75 IU/kg IV twice weekly	150 IU/kg/week
Factor IX, recombinant (Rixubis)	Control and prevention of bleeding episodes,	Minor episodes: 20-30 IU/dL/kg IV every 12-24 hours until healing is achieved	100 IU/dL/kg/dose

Drug Name	Indication	Dosing Regimen	Maximum Dose
	perioperative management	Moderate episodes: 25-50 IU/dL/kg IV every 12-24 hours until bleeding stops and healing is achieved Major episodes: 50-100 IU/dL/kg IV every 12-24 hours until bleeding stops and healing is achieved Minor surgery: 30-60 IU/dL/kg IV every 24 hours until healing is achieved Major surgery: 80-100 IU/dL/kg IV every 8-24 hours until bleeding stops and healing is achieved	
	Routine prophylaxis	≥ 12 years of age: 40-60 IU/kg IV twice weekly < 12 years of age: 60-80 IU/kg IV twice weekly	80 IU/kg/dose
Factor IX, recombinant, glycopegylated (Rebinyn)	On-demand treatment and control of bleeding episodes	40 IU/kg body weight for minor and moderate bleeds, and 80 IU/kg body weight for major bleeds. Additional doses of 40 IU/kg can be given	80 IU/kg/dose
	Perioperative management of bleeding	Pre-operative dose of 40 IU/kg body weight for minor surgery, and 80 IU/kg body weight for major surgery. As clinically needed for the perioperative management of bleeding, repeated doses of 40 IU/kg (in 1-3 day intervals) within the first week after major surgery may be administered. Frequency may be extended to once weekly after the first week until bleeding stops and healing is achieved.	80 IU/kg pre-operatively; 40 IU/kg/dose after surgery

Drug Name	Indication	Dosing Regimen	Maximum Dose
	Routine prophylaxis	40 IU/kg body weight once weekly	40 IU/kg/week

VI. Product Availability

Drug Name	Availability
Factor IX, human (AlphaNine SD)	Vials: 500, 1,000, 1,500 IU
Factor IX, human (Mononine)	Vials: 500, 1,000 IU
Factor IX, recombinant (Alprolix)	Vials: 250, 500, 1,000, 2,000, 3,000, 4,000 IU
Factor IX, recombinant (BeneFIX)	Vials: 250, 500, 1,000, 2,000, 3,000 IU
Factor IX, recombinant (Idelvion)	Vials: 250, 500, 1,000, 2,000, 3500 IU
Factor IX, recombinant (Ixinity)	Vials: 250, 500, 1,000, 1,500, 2,000, 3,000 IU
Factor IX, recombinant (Rixubis)	Vials: 250, 500, 1,000, 2,000, 3,000 IU
Factor IX, recombinant, glycopegylated (Rebinyn)	Vials: 500, 1,000, 2,000, 3,000 IU

VII. References

1. AlphaNine SD Prescribing Information. Los Angeles, CA: Grifols Biologicals, Inc.; January 2024. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=3e99052d-4442-4283-8915-c9a796c77008. Accessed November 1, 2024.
2. Alprolix Prescribing Information. Cambridge, MA: Biogen Idec, Inc.; May 2023. Available at: www.alprolix.com. Accessed November 1, 2024.
3. BeneFix Prescribing Information. Philadelphia, PA: Wyeth Pharmaceuticals, Inc.; November 2022. Available at: www.benefix.com. Accessed November 1, 2024.
4. Idelvion Prescribing Information. Kankakee, IL: CSL Behring LLC; June 2023. Available at: www.idelvion.com. Accessed November 1, 2024.
5. Ixinity Prescribing Information. Berwyn, PA: Aptevo BioTherapeutics LLC; March 2024. Available at: www.ixinity.com. Accessed November 1, 2024.
6. Mononine Prescribing Information. Kankakee, IL: CSL Behring, LLC; December 2018. Available at: www. http://labeling.cslbehring.com/PI/US/Mononine/EN/Mononine-Prescribing-Information.pdf. Accessed November 1, 2024.
7. Rebinyn Prescribing Information. Plainsboro, NJ: Novo Nordisk; August 2022. Available at: https://www.novo-pi.com/rebinyn.pdf. Accessed November 1, 2024.
8. Rixubis Prescribing Information. Westlake Village, CA: Baxalta US Inc.; March 2023. Available at: http://www.rixubis.com. Accessed November 1, 2024.
9. Srivastava A, Santagostino E, Dougall A, et al. WFH guidelines for the management of hemophilia. *Haemophilia.* 2020;26(suppl 6):1-158.
10. Medical and Scientific Advisory Council (MASAC) of the National Bleeding Disorders Foundation (formerly National Hemophilia Foundation): Database of treatment guidelines. Available at https://www.hemophilia.org/healthcare-professionals/guidelines-on-care/masac-documents. Accessed November 18, 2024.

11. Rezende SM, Neumann I, Angchaisuksiri P, et al. International Society on Thrombosis and Haemostasis clinical practice guideline for treatment of congenital hemophilia A and B based on the Grading of Recommendations Assessment, Development, and Evaluation methodology. J Thromb Haemost. 2024;22(9):2629-2652.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J7193	Factor IX (antihemophilic factor, purified, non-recombinant) 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 i.u.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: added Commercial line of business; added requirement for documentation of body weight for calculation of appropriate dosage; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated. RT4: added newly approved indication for Ixinity for routine prophylaxis.	11.30.20	02.21
RT4: revised routine prophylaxis indications for Benefix and Ixinity to limit use to patients aged 16 and older or 18 and older, respectively, in accordance with FDA removal of use for younger patients from the Benefix and Ixinity labels.	05.12.21	
1Q 2022 annual review: no significant changes; lower age limit on BeneFIX for routine prophylaxis was removed to reflect the FDA's reversal on the age limit that had previously been applied for patients 16 years and older; references reviewed and updated.	11.23.21	02.22
Clarified requirement for coverage of factor IX for routine prophylaxis: the requirement for factor IX activity level or documentation of bleed history only applies to requests for new starts to routine prophylactic therapy.	03.03.22	05.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
RT4: for Rebinyn, added newly approved indication for routine prophylaxis and added new 3,000 IU dosage form. Template changes applied to other diagnoses/indications and continued therapy section.	08.24.22	
1Q 2023 annual review: Removed "life-threatening" from "life-threatening or serious bleed" criterion as definition of what is serious vs life-threatening may not be mutually exclusive and there exists potential for misinterpretation; clarified that for Ixinity use as routine prophylaxis, age should be ≥ 12 years per updated PI; references reviewed and updated.	11.09.22	02.23
Added HCPCS code [J7213]	05.24.23	
Extended initial and continued authorization durations for hemophilia prophylaxis from 6 months to 12 months for HIM Texas.	08.28.23	
1Q 2024 annual review: no significant changes; updated sites of serious bleeds per WFH guideline in Appendix D; references reviewed and updated.	10.30.23	02.24
Per March SDC, removed criteria for routine prophylaxis regarding severity of hemophilia, prior use of factor IX, and Appendix D. For continued therapy clarified that member's current weight is only needed if a higher dose is being requested. RT4: updated new Ixinity pediatric age expansion to include children < 12 years of age.	04.10.24	05.24
1Q 2025 annual review: for Medicaid and HIM lines of business, continued approval duration revised from 6 months to 12 months for prophylaxis; for Commercial line of business, all prophylaxis approval durations revised to "6 months or to the member's renewal date, whichever is longer;" references reviewed and updated.	11.01.24	02.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage

decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.