

## PHARMACY COVERAGE GUIDELINE

### HEMOPHILIA B FACTOR IX PRODUCTS:

ALPHANINE SD®

ALPROLIX®

BENEFIX®

IDELVION®

IXINITY®

PROFILNINE®

REBINYN®

RIXUBIS®

Generic Equivalent (if available)

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#### **This Pharmacy Coverage Guideline (PCG):**

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

#### **Scope**

- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

#### **Instructions & Guidance**

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
- The “Description” section describes the Service.
- The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
- The “Resources” section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy). You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to [Pharmacyprecert@azblue.com](mailto:Pharmacyprecert@azblue.com).

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#### **Criteria:**

- **Criteria for initial therapy:** AlphaNine, Alprolix, BeneFIX, Idelvion, Ixinity, Profilnine, Rebinyn, Rixubis and/or generic equivalent (if available) is considered **medically necessary** and will be approved when **ALL** the following criteria are met:

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1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Hematologist
2. Individual's age is consistent with FDA label
3. Individual has a confirmed diagnosis of Hemophilia B (congenital Factor IX deficiency)
4. There is documentation that the requested medication is to be used for **ONE** of the following:
  - a. On-demand treatment to control bleeding episodes given at the time of bleeding
  - b. Routine prophylaxis/prevention to reduce the frequency of bleeding episodes and prevent bleeding for at least 45 of 52 weeks (85%) of a year
  - c. Perioperative management of bleeding to prevent bleeding for short periods of time
5. **Additional Criteria for request for long acting Alprolix, Idelvion or Rebinyn for routine prophylaxis:** Individual has failure after 3-month trial, contraindication per FDA label, intolerance, or is not a candidate for **TWO** of the following standard half-life products:
  - a. AlphaNine
  - b. BeneFIX
  - c. Ixinity
  - d. Profilnine
  - e. Rixubis
6. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
7. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation

**Initial approval duration:** 6 months

- **Criteria for continuation of coverage (renewal request):** AlphaNine, Alprolix, BeneFIX, Idelvion, Ixinity, Profilnine, Rebinyn, Rixubis, and/or generic equivalent (if available) is considered **medically necessary** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):
1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Hematologist
  2. Individual's condition has responded while on therapy with response defined as the following:
    - a. Bleeding episodes are controlled
    - b. Frequency of bleeding episodes are reduced
  3. Individual has been adherent with the medication
  4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))

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5. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation

**Renewal duration:** 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
  2. **Off-Label Use of Cancer Medications**
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#### **Description:**

Hemophilia A (factor VIII [factor 8] deficiency) and hemophilia B (factor IX [factor 9] deficiency) are X-linked clotting factor deficiencies associated with bleeding of variable severity, ranging from life-threatening to clinically silent. Hemophilia A and B are X-linked disorders that primarily affect males. Females who are heterozygous carriers can be affected and can have factor levels in the hemophilic range. Hemophilia A may also be referred to as classical hemophilia. Hemophilia B is also known as Christmas disease and as Royal disease. Hemophilia C, also known as Rosenthal syndrome, is an inherited autosomal recessive bleeding disorder caused by a deficiency of factor XI [factor 11].

Hemophilia may be characterized as mild, moderate, or severe, based on residual factor activity level which is expressed either as a percent of normal or in international units (IU)/mL. Factor levels usually correlate with the degree of bleeding symptoms. Severe hemophilia can be defined as <1 percent factor activity, which corresponds to <0.01 IU/mL. Moderate hemophilia can be defined as a factor activity level greater than or equal to 1 percent of normal and less than or equal to 5 percent of normal (corresponding to greater than or equal to 0.01 and less than or equal to 0.05 IU/mL). Mild hemophilia is usually defined as a factor activity level of 6 percent of normal and less than 40 percent of normal (greater than or equal to 0.05 and less than 0.40 IU/mL). Individuals with more severe hemophilia are more likely to have spontaneous bleeding, severe bleeding, and first bleeding episode at an earlier age.

Untreated individual with hemophilia is characterized by spontaneous bleeding including intracranial bleeding, muscle, and joint bleeding (usually in severe disease), immediate or delayed bleeding or prolonged oozing after injuries, tooth extractions, or surgery, or renewed bleeding after initial bleeding has stopped. Intermittent oozing may last for days or weeks after tooth extraction. Prolonged or delayed bleeding or wound hematoma formation after surgery is common. The leading cause of death is intracranial bleeding and the major cause of disability from bleeding is chronic joint disease.

Another complication in severe hemophilia is the development of alloantibodies (inhibitors) that block the factor activity. Inhibitors can also develop in individuals with moderate and mild hemophilia. These inhibitory antibodies develop in response to administration of exogenous factor and occur in approximately 30 percent of patients with severe hemophilia A and 5 to 15 percent with severe hemophilia B. Inhibitors decrease responsiveness to factor infusions and may lead to anaphylactoid reactions.

Treatment of hemophilia involves infusion of the deficient clotting factor to a level that achieves adequate blood clotting in an effort to prevent complications associated with the disorder.

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Individuals with mild or moderate hemophilia may be treated with replacement therapy as needed (episodic infusion therapy) to treat a bleeding episode that has already started. Some individuals with mild or moderate hemophilia may receive prophylaxis (either short or longer term) for prevention of bleeding during activities before a specific activity. Individuals with severe hemophilia may receive regular infusions (prophylactic therapy) to prevent bleeding episodes before they occur.

Referral to a hemophilia treatment center (HTC) for assessment, education, genetic counseling, and treatment is recommended. These specialized centers provide comprehensive care for individuals with hemophilia including the development of specific treatment plans, monitoring and follow-up of affected individuals and state-of-the-art medical care. To locate a hemophilia treatment center, visit the Centers for Disease Control and Prevention website at: <https://www.cdc.gov/ncbddd/hemophilia/HTC.html>. For young children with severe or moderate hemophilia B, assessments every six to 12 months at an HTC is recommended. Older children and adults with severe or moderate hemophilia benefit from at least annual assessment at an HTC. For individuals with mild hemophilia B, assessment at an HTC every one to two years may be sufficient.

#### Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting  
[MedWatch Forms for FDA Safety Reporting | FDA](#)

#### Hemophilia Treatment Centers

Individuals with hemophilia significantly benefit from receiving care from a federally recognized hemophilia treatment center. These specialized centers provide comprehensive care for individuals with hemophilia including the development of specific treatment plans, monitoring and follow-up of affected individuals and state-of-the-art medical care.

To locate a hemophilia treatment center, visit the Centers for Disease Control and Prevention website at: <https://www.cdc.gov/ncbddd/hemophilia/HTC.html>

#### Selected available factor IX products for hemophilia B

Product name	Approximate Half-life (hours)	Characteristics
<b>Standard half-life products</b>		
AlphaNine SD	18	Plasma-derived; solvent/detergent treated
Bebulin	11 to 28	Factor IX Complex (Human) [(Factors II, VII, X)]; plasma-derived
BeneFIX	16 to 19	Recombinant
Ixinity	16 to 24	Recombinant
Profilnine	19 to 25	Factor IX Complex (Human) [(Factors II, IX, X)]; plasma-derived; solvent/detergent treated
Rixubis	23 to 26	Recombinant
<b>Long-lasting products</b>		
Alprolix	54 to 90	Recombinant; Fc fusion
Idelvion	87 to 104	Recombinant; albumin fusion
Rebinyn	103 to 115	Recombinant; glycoPEGylated

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#### Types of prophylaxis for patients with hemophilia A or B

Type of treatment	Definition
Episodic (on demand) treatment	Replacement factor given at the time of bleeding
Continuous (regular) prophylaxis:	Replacement factor given to prevent bleeding for at least 45 of 52 weeks (85%) of a year
Primary prophylaxis	Continuous prophylaxis started before age three years and before the second large joint bleed
Secondary prophylaxis	Continuous prophylaxis started after two or more large joint bleeds but before the onset of chronic arthropathy
Tertiary prophylaxis	Continuous prophylaxis started after the onset of arthropathy to prevent further damage
Intermittent (periodic) prophylaxis	Replacement factor given to prevent bleeding for short periods of time such as during and after surgery

#### Resources:

Alphanine SD (coagulation factor IX- human) product information, revised by Grifols USA, LLC 11-2022. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed June 04, 2024.

Alprolix (coagulation Factor IX (recombinant), Fc fusion protein) product information, revised by Bioverativ Therapeutics Inc. 05-2023. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed June 04, 2024.

Bebulin (Factor IX complex), product information, revised by Baxter Healthcare Corporation 07-2012. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed June 08, 2024. **DISCONTINUED July 30, 2018.**

BeneFIX [coagulation factor IX (recombinant)] product information, revised by Wyeth BioPharma Division of Wyeth Pharmaceuticals LLC 11-2022. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed June 04, 2024.

Idelvion [coagulation Factor IX (recombinant), albumin fusion protein] product information, revised by CSL Behring Lengnau AG 06-2023. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed June 04, 2024.

Ixinity [coagulation Factor IX (recombinant)] product information, revised by Aptevo BioTherapeutics LLC 02-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed June 04, 2024.

Profilnine (Factor IX complex) product information, revised by Grifols USA, LLC 11-2022. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed June 04, 2024.

Rebinyn (coagulation Factor IX (recombinant), glycoPEGylated product information, revised by Novo Nordisk 08-2022. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed June 04, 2024.

Rixubis [coagulation Factor IX (recombinant)] product information, revised by Takeda Pharmaceuticals America, Inc. 03-2023. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed June 04, 2024.

Hoots WK, Malec L. Clinical manifestations and diagnosis of hemophilia. In: UpToDate, Shapiro AD, Tirnauer JS (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through May 2024. Topic last updated June 04, 2024. Accessed June 08, 2024.

Hoots WK, Shapiro AD. Hemophilia A and B: Routine management including prophylaxis. In: UpToDate, Lueng LLK, Tirnauer JS (Ed), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through May 2024. Topic last updated April 16, 2023. Accessed June 08, 2024.

Hoots WK, Lewandowska M. Acute treatment of bleeding and surgery in hemophilia A and B. In: UpToDate, Shapiro AD, Tirnauer JS (Ed), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through May 2024. Topic last updated April 30, 2024. Accessed June 08, 2024.

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Konkle BA, Nakaya Fletcher S. Hemophilia B. 2000 Oct 2 [Updated 2024 Jun 6]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1495/>. Accessed June 08, 2024.

Konkle BA, Nakaya Fletcher S. Hemophilia A. 2000 Sep 21 [Updated 2023 Jul 27]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1404/>. Accessed June 08, 2024.

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