Medicare Part B Hemophilia Factor IX Prior Authorization

FDA APPROVED INDICATIONS AND DOSAGE[1-9]

Recombinant Factor IX Concentrates		
Agent(s)	**Indication(s)**	**Dosage**
Alprolix® [Coagulation Factor IX (recombinant), Fc Fusion protein] Powder for solution for intravenous use	Adults and children with hemophilia B for: • On-demand treatment and control of bleeding episodes • Perioperative management of bleeding • Routine prophylaxis to reduce the frequency of bleeding episodes Limitations of Use: Alprolix is not indicated for induction of immune tolerance in patients with hemophilia B	• Dose and duration of treatment depend on the severity of the Factor IX deficiency, the location and extent of bleeding, the individual patient's pharmacokinetic profile, and/or the patient's clinical condition. Base the dose and frequency of Alprolix on the individual clinical response • More frequent or higher doses may be needed in children < 12 years of age, especially in children < 6 years of age • On average, one IU per kg body weight increases the circulating Factor IX level by approximately 1% [IU/dL] in adults and children ≥ 6 years of age and by 0.6% [IU/dL] in children under 6 years of age Estimate the in vivo peak increase in Factor IX level expressed as IU/dL (or % of normal) using the following formulas: IU/dL (or % of normal) = (Total Dose [IU]/Body weight [kg]) X Recovery (IU/dL per IU/kg) OR Dose (IU) = Body weight (kg) X desired Factor IX Rise (IU/dL or % of normal) X Reciprocal of Recovery (IU/kg per IU/dL) = Number of Factor IX IU required • See prescribing information for more specific dosing

BeneFIX® [Coagulation Factor IX (Recombinant)] Powder for reconstitution for intravenous use	Adult and pediatric patient with hemophilia B for: ● On-demand treatment and control of bleeding episodes ● Peri-operative management of bleeding ● Routine prophylaxis to reduce the frequency of bleeding episodes Limitations of Use: BeneFIX is not indicated for induction of immune tolerance in patients with hemophilia B	● Dosage and duration of treatment with BeneFIX depend on the severity of the Factor IX deficiency, the location and extent of bleeding, and the patient's clinical condition, age and recovery of Factor IX ● On average one international unit (IU) of BeneFIX per kilogram of body weight increased the circulating activity of factor IX as follows: ● 12 years of age and older: 0.8 ± 0.2 IU/dL [range 0.4 to 1.2 IU/dL] ● Pediatric (<12 years): 0.7 ± 0.3 IU/dL [range 0.2 to 2.1 IU/dL] ● Determine the initial estimated dose using the following formula: 12 years of age and older Required units = body weight (kg) X desired factor IX increase (IU/dL or % of normal) X 1.3 (IU/kg per IU/dL) Children < 12 years Required units = body weight (kg) X desired factor IX increase (IU/dL or % of normal) X 1.4 (IU/kg per IU/dL) ● See prescribing information for more specific dosing

Idelvion® [Coagulation Factor IX (recombinant), Albumin Fusion Protein (rIX-FP)] Powder for solution for intravenous use	Children and adults with Hemophilia B (congenital Factor IX deficiency) for: ● On-demand treatment and control of bleeding episodes ● Perioperative management of bleeding ● Routine prophylaxis to reduce the frequency of bleeding episodes Limitations of Use: Idelvion is not indicated for immune tolerance induction in patients with Hemophilia B.	● Dosage and duration of treatment with Idelvion depends on the severity of Factor IX deficiency, the location and extent of bleeding, and the patient's clinical condition, age and recovery of Factor IX ● One IU per kg body weight is expected to increase the circulating activity of Factor IX as follows: ● Patients ≥ 12 years of age: 1.3 IU/dL per IU/kg ● Pediatrics (<12 years): 1 IU/dL per IU/kg ● Determine the initial dose using the following formula: Required Dose (IU) = Body Weight (kg) X Desired Factor IX rise (% of normal or IU/dL) X (reciprocal of recovery (IU/kg per IU/dL)) OR Increase in Factor IX IU/dL (or % of normal) = Dose (IU) X Recovery (IU/dL per IU/kg)/body weight (kg) ● See prescribing information for more specific dosing

Ixinity® [Coagulation Factor IX (Recombinant)] Powder for solution for intravenous use	Adults and children ≥ 12 years of age with hemophilia B for: ● On-demand treatment and control of bleeding episodes ● Perioperative management ● Routine prophylaxis to reduce the frequency of bleeding episodes Limitations of Use: Ixinity is not indicated for induction of immune tolerance in patients with hemophilia B.	● Dosage and duration of treatment for Factor IX products depend on the severity of the Factor IX deficiency, the location and extent of bleeding, the patient's clinical condition, age, and pharmacokinetic parameters of Factor IX, such as incremental recovery and half-life ● One international unit (IU) per kg body weight increases the circulating activity of factor IX by 0.98 IU/dL of plasma in adults and children ≥ 12 years of age ● Initial dose: = body weight (kg) X desired Factor IX increase (% of normal or IU/dL) X reciprocal of observed recovery (IU/kg per IU/dL) ● See prescribing information for more specific dosing
Rebinyn® [Coagulation Factor IX (Recombinant), GlycoPEGylated] Powder for solution for intravenous use	Adults and children with hemophilia B for: ● On-demand treatment and control of bleeding episodes ● Perioperative management of bleeding Limitations of Use: Rebinyn is not indicated for routine prophylaxis in the treatment of patients with hemophilia B. Rebinyn is not indicated for immune tolerance induction in patients with hemophilia B	● Dose and duration of treatment depend on the location and extent of bleeding, and the patient's clinical condition ● On-demand Treatment/Control of Bleeding Episodes and Perioperative management: 40 or 80 IU/kg body weight See prescribing information for more specific dosing

Rixubis® [Coagulation Factor IX (Recombinant)] Powder for solution for intravenous use	Adults and children with hemophilia B for: ● On-demand treatment and control of bleeding episodes ● Perioperative management of bleeding ●Routine prophylaxis to reduce the frequency of bleeding episodes Rixubis is not indicated for induction of immune tolerance in patients with Hemophilia B	● Dosage and duration of treatment with Rixubis depend on the severity of Factor IX deficiency, the location and extent of bleeding, the patient's clinical condition, age, and pharmacokinetic parameters of Factor IX, such as incremental recovery and half-life ● One international unit per kg of body weight increases the circulating activity of factor IX by: 0.7 international units/dL for patients <12 years of age and 0.9 international units/dL for patients ≥12 years of age. ● Initial Dose: Patients ≥ 12 years of age Required international units = body weight (kg) X desired factor IX increase (% of normal or IU/dL) X reciprocal of observed recovery (IU/kg per IU/dL) Patients < 12 years of age Dose (international units) = body weight (kg) X desired Factor IX increase (% of normal or IU/dL) X 1.4 dL/kg ● Routine prophylaxis: Patients <12 years of age: 60 to 80 international units per kg twice weekly Patients ≥12 years of age: 40 to 60 international units per kg twice weekly See prescribing information for more specific dosing
Human Plasma-derived Coagulation Factor IX Concentrates		
Agent(s)	**Indication(s)**	**Dosage**

AlphaNine SD® [Coagulation Factor IX (Human)] Powder for reconstitution for intravenous use	• The prevention and control of bleeding in patients with Factor IX deficiency due to hemophilia B. • AlphaNine SD contains low, non-therapeutic levels of Factors II, VII, and X, and, therefore, is *not* indicated for the treatment of Factor II, VII or X deficiencies. This product is also *not* indicated for the reversal of coumarin anticoagulant-induced hemorrhage, nor in the treatment of hemophilia A patients with inhibitors to Factor VIII.	• Guide in determining the number of units to be administered: body weight (kg) x desired increase in plasma factor IX (percent) x 1.0 IU/kg = number of factor IX IU required • See prescribing information for more specific dosing

Mononine® [Coagulation Factor IX (Human)] Lyophilized concentrate for reconstitution for intravenous use	• The prevention and control of bleeding in Factor IX deficiency, also known as Hemophilia B or Christmas disease. Limitations of Use: Mononine is not indicated in the treatment or prophylaxis of Hemophilia A patients with inhibitors to Factor VIII Mononine contains non-detectable levels of Factors II, VII and X (≤ 0.0025 IU per Factor IX unit using standard coagulation assays) and is, therefore, not indicated for replacement therapy of these clotting factors. Mononine is also not indicated in the treatment or reversal of coumarin-induced anticoagulation or in a hemorrhagic state caused by hepatitis-induced lack of production of liver dependent coagulation factors	• As a general rule, 1 IU of Factor IX activity per kg can be expected to increase the circulating level of Factor IX by 1% [IU/dL] of normal. The following formula provides a guide to dosage calculations: number of Factor IX IU required (IU) = Body Weight (kg) x desired Factor IX increase (% or IU/dL normal) x 1.0 IU/kg (per IU/dL) • See prescribing information for more specific dosing
Profilnine® SD (Factor IX complex) Lyophilized concentrate for reconstitution for intravenous use	• The prevention and control of bleeding in patients with factor IX deficiency (hemophilia B) Profilnine SD contains non-therapeutic levels of factor VII and is not indicated for use in the treatment of VII deficiency	One unit administered per kg of body weight can be expected to increase factor IX by 1% • Use the following formula as a guide in determining the number of units to be administered: Body weight (in kg) X Desired increase in Plasma Factor IX (Percent) X 1 units/kg = number of Factor IX Units Required • See prescribing information for more specific dosing

CLINICAL RATIONALE

Hemophilia B, also called Factor IX (FIX) deficiency or Christmas disease, is a genetic disorder caused by missing or defective Factor IX, a clotting protein. Although it is passed down from parents to children, about 1/3 of cases are caused by a spontaneous mutation.[10]

The main goal of any therapy is to completely prevent bleeding. The current World Hemophilia Federation Guidelines for the Management of Hemophilia state:[14]

- Both virus-inactivated plasma-derived and recombinant clotting factor concentrates (CFCs), as well as other hemostasis products when appropriate can be used for treatment of bleeding and prophylaxis in people with hemophilia
- Prophylaxis is the standard of care for people with severe hemophilia, and for some people with moderate hemophilia or for those with a severe bleeding phenotype and/or a high risk of spontaneous life-threatening bleeding
- Episodic CFC replacement should not be considered a long-term option for the management of hemophilia as it does not alter its natural history of spontaneous bleeding and related complications
- Emerging therapies in development with alternative modes of delivery (e.g., subcutaneous injection) and novel targets may overcome the limitations of standard CFC replacement therapy (i.e., need for intravenous administration, short half-life, risk of inhibitor formation)
- The development of gene therapies for hemophilia has advanced significantly, with product registration likely in the near future
- Gene therapy should make it possible or some people with hemophilia to aspire to and attain much better health outcomes and quality of life than that attainable with currently available hemophilia therapies
- Given the ongoing advances transforming the hemophilia treatment landscape, it is important to establish systems to constantly monitor developments in emerging and gene therapies for hemophilia and make them available as soon as possible following approval by regulatory authorities

The MASAC suggests the number of doses required for provision of home therapy varies greatly and is dependent upon the type of hemophilia (FVIII, FIX), the level of severity (severe, moderate, mild), the presence of an inhibitor, the prescribed regimen (on-demand, prophylaxis, immune tolerance), the number of bleeding episodes experienced regardless of the prescribed regimen, individual pharmacokinetics, the products utilized, and the level of physical activity. For patients on prophylaxis, a minimum of one major dose and two minor doses should be available in addition to the prophylactic doses utilized monthly. For patients with severe or moderate hemophilia treated on-demand, the number of doses required to be available at home may be based upon historical bleeding patterns, with at least one major and two minor doses added to assure a level of safety.[11]

A major dose is defined as a correction of clotting factor that achieves a level of 60-100+% clotting factor activity that is utilized to treat a bleeding episode that is expected to require a higher hemostatic level such as when bleeds occur in a target joint, or joint/area with a risk of significant sequelae (e.g., hip, head, GI bleed, etc.). A minor dose is defined as a correction of clotting factor that achieves a level of 30-60% clotting factor activity that is utilized to treat a bleeding episode that is treated early, in a non-critical area and treatable with a lower hemostatic level (e.g., early non-major joints, small muscle bleeds, and skin/soft tissue, etc.).[11]

The Medical and Scientific Advisory Council (MASAC) and National Hemophilia Foundation (NHF) guidelines on treatment of hemophilia B recommend Recombinant FIX (rFIX) products over plasma-derived products as the treatment of choice.[13]

In view of the demonstrated benefits of prophylaxis (regular/scheduled administration of clotting factor concentrate to prevent bleeding) begun at a young age in persons with hemophilia B, MASAC recommends that prophylaxis be considered optimal therapy for individuals with severe hemophilia B (factor IX <1%). Prophylactic therapy should be instituted early (prior to the onset of frequent bleeding), with the aim of keeping the trough FIX level above 1% between doses. Optimal dosing and frequency should be determined for each individual by appropriate laboratory monitoring. It is also recommended that individuals on prophylaxis have regular follow-up visits to evaluate joint status, to document any complications such as inhibitors, and to record any bleeding episodes that occur during prophylaxis.[12]

Safety[1-9]

- **AlphaNine SD** has no known FDA labeled contraindications
- **Alprolix** is contraindicated in:
  - Individuals who have a known history of hypersensitivity reactions, including anaphylaxis, to the product or its excipients
- **BeneFIX** is contraindicated in:
  - Patients who have manifested life-threatening, immediate hypersensitivity reactions, including anaphylaxis, to the product or its components, including hamster protein
- **Idelvion** is contraindicated in:
  - Patients who have had life-threatening hypersensitivity reactions to Idelvion or its components, including hamster proteins
- **Ixinity** is contraindicated in:
  - Patients with known hypersensitivity to Ixinity or its excipients, including hamster protein
- **Mononine** is contraindicated in:
  - Known hypersensitivity to mouse protein
- **Profilnine** has no known FDA labeled contraindications
- **Rebinyn** is contraindicated in:
  - Patients who have known hypersensitivity to Rebinyn or its components, including hamster proteins
- **Rixubis** is contraindicated in:
  - Known hypersensitivity to Rixubis or its excipients including hamster protein
  - Disseminated intravascular coagulation (DIC)
  - Signs of fibrinolysis

References

1. AlphaNine SD prescribing information. Grifols. June 2018.
2. Alprolix prescribing information. Bioverativ. October 2020.
3. BeneFIX prescribing information. Pfizer. June 2020.
4. Idelvion prescribing information. CSL Behring. July 2020.
5. Ixinity prescribing information. Aptevo BioTherapeutics. September 2020.
6. Mononine prescribing information. CSL Behring. December 2019.
7. Profilnine prescribing information. Grifols Biologicals Inc. June 2018.
8. Rebinyn prescribing information. Novo Nordisk. June 2020.
9. Rixubis prescribing information. Baxalta. June 2020.

10. National Hemophilia Foundation. Bleeding Disorders A-Z/Types/Hemophilia B. Accessed at: https://www.hemophilia.org/bleeding-disorders-a-z/types/hemophilia-b.
11. Medical and Scientific Advisory Committee. MASAC recommendation regarding doses of clotting factor concentrate in the home. MASAC Document #242. June 2016.
12. Medical and Scientific Advisory Committee. MASAC recommendation concerning prophylaxis. MASAC Document #241. February 2016.
13. Medical and Scientific Advisory Council (MASAC) MASAC recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders. Document #263. September 2020.
14. Srivastave A, Santagostino E, Dougall A, et al. World Federation of Hemophilia Guidelines for the Management of Hemophilia. 3rd edition. August 2020.

Document History
Original Prime Standard Part B criteria, approved by P&T UM Committee 12/2021

Medicare Part B Hemophilia Factor IX Prior Authorization

Coverage and policy application are contingent on National Coverage Determinations (NCD) and Local Coverage Determinations (LCD). An NCD or LCD that is applicable to the drug or product must be used in lieu of applicable medical necessity criteria. Also, please note that Prior Authorization criteria cannot be stricter than an NCD or LCD with specified step therapy requirements.

TARGET PREFERRED AGENT(S)	TARGET NON-PREFERRED AGENT(S)
Target preferred and non-preferred agent(s) to be determined client	Target preferred and non-preferred agent(s) to be determined client
AlphaNine SD® [Coagulation Factor IX (Human)] **Alprolix®** [Coagulation Factor IX (recombinant), Fc Fusion protein] **BeneFIX®** [Coagulation Factor IX (Recombinant)] **Idelvion®** [Coagulation Factor IX (recombinant), Albumin Fusion Protein (rIX-FP)] **Ixinity®** [Coagulation Factor IX (Recombinant)] **Mononine®** [Coagulation Factor IX (Human)] **Profilnine SD®** (Factor IX complex) **Rebinyn®** [Coagulation Factor IX (Recombinant), GlycoPEGylated] **Rixubis®** [Coagulation Factor IX (Recombinant)]	

Brand (generic)	GPI	Multisource Code	HCPCS/J Code
AlphaNine SD [Coagulation Factor IX (Human)]			
500 Unit Single-dose vial	85100028002170	M, N, O, or Y	J7193
1000 Unit Single-dose vial	85100028002180	M, N, O, or Y	J7193
1500 Unit Single-dose vial	85100028002185	M, N, O, or Y	J7193
Alprolix [Coagulation Factor IX (recombinant), Fc Fusion protein]			
250 Unit Single-use vial	85100028402105	M, N, O, or Y	J7201
500 Unit Single-use vial	85100028402110	M, N, O, or Y	J7201

Brand (generic)	GPI	Multisource Code	HCPCS/J Code
1000 Unit Single-use vial	85100028402120	M, N, O, or Y	J7201
2000 Unit Single-use vial	85100028402130	M, N, O, or Y	J7201
3000 Unit Single-use vial	85100028402140	M, N, O, or Y	J7201
4000 Unit Single-use vial	85100028402150	M, N, O, or Y	J7201
BeneFIX [Coagulation Factor IX (Recombinant)]			
250 Unit Single-use vial	85100028206420	M, N, O, or Y	J7195
500 Unit Single-use vial	85100028206430	M, N, O, or Y	J7195
1000 Unit Single-use vial	85100028206440	M, N, O, or Y	J7195
2000 Unit Single-use vial	85100028206450	M, N, O, or Y	J7195
3000 Unit Single-use vial	85100028206460	M, N, O, or Y	J7195
Idelvion [Coagulation Factor IX (recombinant), Albumin Fusion Protein (rIX-FP)]			
250 Unit Single-use vial	85100028352110	M, N, O, or Y	J7202
500 Unit Single-use vial	85100028352120	M, N, O, or Y	J7202
1000 Unit Single-use vial	85100028352130	M, N, O, or Y	J7202
2000 Unit Single-use vial	85100028352140	M, N, O, or Y	J7202
3500 Unit Single-use vial	85100028352150	M, N, O, or Y	J7202
Ixinity [Coagulation Factor IX (Recombinant)]			

Brand (generic)	GPI	Multisource Code	HCPCS/J Code
250 Unit Single-use vial	85100028202120	M, N, O, or Y	J7195
500 Unit Single-use vial	85100028202130	M, N, O, or Y	J7195
1000 Unit Single-use vial	85100028202140	M, N, O, or Y	J7195
1500 Unit Single-use vial	85100028202145	M, N, O, or Y	J7195
2000 Unit Single-use vial	85100028202150	M, N, O, or Y	J7195
3000 Unit Single-use vial	85100028202160	M, N, O, or Y	J7195
Mononine [Coagulation Factor IX (Human)]			
1000 Unit Single-dose vial	85100028002180	M, N, O, or Y	J7193
Profilnine SD (Factor IX complex)			
500 Unit Single-dose vial	85100030002105	M, N, O, or Y	J7194
1000 Unit Single-dose vial	85100030002110	M, N, O, or Y	J7194
1500 Unit Single-dose vial	85100030002115	M, N, O, or Y	J7194
Rebinyn [Coagulation Factor IX (Recombinant), GlycoPEGylated]			
500 Unit Single-use vial	85100028452120	M, N, O, or Y	J7203
1000 Unit Single-use vial	85100028452130	M, N, O, or Y	J7203
2000 Unit Single-use vial	85100028452140	M, N, O, or Y	J7203
Rixubis [Coagulation Factor IX (Recombinant)]			

Brand (generic)	GPI	Multisource Code	HCPCS/J Code
250 Unit Single-use vial	85100028202120	M, N, O, or Y	J7200
500 Unit Single-use vial	85100028202130	M, N, O, or Y	J7200
1000 Unit Single-use vial	85100028202140	M, N, O, or Y	J7200
2000 Unit Single-use vial	85100028202150	M, N, O, or Y	J7200
3000 Unit Single-use vial	85100028202160	M, N, O, or Y	J7200

CRITERIA FOR APPROVAL
Evaluation
Target Agent(s) will be approved when ALL of the following are met:

1. The requested agent is being used for ONE of the following:
    a. An FDA approved indication
    OR
    b. An indication in CMS approved compendia

    AND
2. If the client has preferred agents, then ONE of the following:
    a. The requested agent is the preferred agent
    OR
    b. Information has been provided that indicates the patient has been treated with the requested agent in the past 365 days
    OR
    c. There is documentation that the patient has had an ineffective treatment response to the active ingredient(s) of ALL preferred agent(s)
    OR
    d. The patient has a documented intolerance, hypersensitivity, or FDA labeled contraindication to the active ingredient(s) of ALL preferred agent(s)
    OR
    e. The prescriber has submitted documentation indicating ALL preferred agent(s) are likely to be ineffective or are likely to cause an adverse reaction or other harm to the patient

    AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent
    AND
4. The requested quantity (dose) is within FDA labeled dosing or supported in compendia for the requested indication

Length of Approval: up to 12 months