Hemophilia Products – Factor IX: AlphaNine SD, Alprolix, BeneFIX, Idelvion, Ixinity, Profilnine, Rebinyn, and Rixubis

(Intravenous)

Effective date: 01/01/2020
Review date: 10/02/2019, 12/18/19, 1/22/20, 4/1/2021, 06/24/2021, 7/22/2021, 6/16/2022, 9/22/2022, 6/22/2023, 12/07/2023, 01/04/2024, 05/15/2024, 08/14/2024, 09/17/2025
Pharmacy Scope: Medicaid
Medical Scope: Medicaid, Commercial, Medicare

I. Length of Authorization

Coverage is provided for 3 months and may be renewed thereafter, unless otherwise specified*.

Note: The cumulative amount of medication the patient has on-hand will be taken into account for authorizations. Up to 5 'on-hand' doses for the treatment of acute bleeding episodes will be permitted at the time of the authorization request.

** Initial and renewal authorization periods may vary by specific covered indication*

*** Requests will also be reviewed to National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) if applicable. ***

II. Dosing Limits

A. Max Units (per dose and over time) [HCPCS Unit]:

Alprolix,	34,500 billable units per 28-day supply
Idelvion, Rebiyn	18,400 billable units per 28-day supply
Ixinity	64,000 billable units per 28-day supply
AlphaNine SD, Ixinity, Profilnine	36,800 billable units per 28-day supply
BeneFIX	46,000 billable units per 28-day supply
Rixubis	55,200 billable units per 28-day supply

III. Initial Approval Criteria[1-11,15]

Hemophilia Management Program
Requirements for half-life study and inhibitor tests are a part of the hemophilia management program. This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide.

Coverage is provided in the following conditions:

Universal Criteria [1-5,7-9]

- Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements
- Therapy NOT used for induction of immune tolerance in members with Hemophilia B [ONLY the following products]:
  - Alprolix
  - Rixubis
  - Ixinity
  - Idelvion
  - Rebinyn
  - AlphaNine SD
  - BeneFIX; **AND**

Hemophilia B (congenital factor IX deficiency aka Christmas disease) † Φ [1-9]

- Diagnosis of congenital factor IX deficiency has been confirmed by blood coagulation testing; **AND**
- Will NOT be used in combination with another agent used as prophylactic therapy for Hemophilia B;***See chart below **AND**
- Used as treatment in at least one of the following:
  - On-demand treatment and control bleeding episodes; **OR**
  - Perioperative management *(*Authorizations valid for 1 month)*; **OR**
  - Routine prophylaxis to prevent or reduce the frequency of bleeding episodes; **AND**
    - Member must have severe hemophilia B (factor IX level of <1%); **OR**
    - Member has at least two documented episodes of spontaneous bleeding into joints

Hemophilia Management Program
• If the request is for prophylaxis and the requested dose exceeds dosing limits under part II, a half-life study should be performed to determine the appropriate dose and dosing interval.

- If the request is for Alprolix, Idelvion, or Rebinyn, a half-life study should be performed to determine the appropriate dose and dosing interval.
  - For Alprolix, 50 IU/kg every 7 days is the preferred dosing regimen. To obtain 100 IU every 10 days, a half-life study must be submitted showing a significant clinical benefit over 50 IU/kg every 7 days.
  - Prior to switching to Alprolix, Idelvion, or Rebinyn, a half-life study should also be performed on current non- EHL factor IX product to ensure that clinical benefit will be achieved.
- For members with a BMI ≥ 30, a half-life study should be performed to determine the appropriate dose and dosing interval.
- For minimally treated members (< 50 exposure days to factor products) previously receiving a different factor product, inhibitor testing is required at baseline, then at every comprehensive care visit (yearly for the mild and moderate members, semi-annually for the severe members)

† FDA Approved Indication(s); **Φ** Orphan Drug

*** Drugs to treat Hemophilia A or B

Hemophilia A & B Drug Chart	
Factor VIIa (Hemophilia A or B)	
Novoseven RT	J7189
Sevenfact	J7212
Anti-Inhibitor Coagulant Complex (Hemophilia A or B)	
Feiba	J7198
Factor VIII (Hemophilia A)	
Advate	J7192
Kogenate FS	J7192
Helixate FS	J7192
Recombinate	J7192

Kovaltry	J7211
Eloctate	J7205
Koate / Koate-DVI	J7190
Hemofil M	J7190
Novoeight	J7182
Nuwiq	J7209
Obizur	J7188
Xyntha / Xyntha Solofuse	J7185
Afstyla	J7210
Adynovate	J7207
Jivi	J7208
Esperoct	J7204
Altuviiio	J7214
Factor IX (Hemophilia B)	
AlphaNine SD	J7193
Mononine	J7193
Alprolix	J7201
Profilnine	J7194
BeneFIX	J7194
Ixinity	J7213
Rixubis	J7200
Idelvion	J7202
Rebinyn	J7203

IV. Dispensing Requirements for Rendering Providers (Hemophilia Management Program)

- Prescriptions cannot be filled without an expressed need from the member, caregiver or prescribing practitioner. Auto-filling is not allowed.
- Monthly, rendering provider must submit for authorization of dispensing quantity before delivering factor product. Information submitted must include:
  - Original prescription information, requested amount to be dispensed, vial sizes available to be ordered from the manufacturer, and member clinical history (including member product inventory and bleed history)
  - Factor dose should not exceed +1% of the prescribed dose and a maximum of three vials may be dispensed per dose. If unable to provide factor dosing within the required threshold, below the required threshold, the lowest possible dose able to be achieved above +1% should be dispensed. Prescribed dose should not be increased to meet assay management requirements.
- The cumulative amount of medication(s) the member has on-hand should be taken into account when dispensing factor product. Members should not have more than 5 extra doses on-hand for the treatment of acute bleeding episodes.
- Dispensing requirements for renderings providers are a part of the hemophilia management program. This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide.

V. Renewal Criteria [1-11,15]

Coverage can be renewed based upon the following criteria:

- Member continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: symptoms of anaphylaxis and hypersensitivity reactions (e.g., angioedema, chest tightness, hypotension, urticaria, wheezing, dyspnea, thromboembolic events, (pulmonary embolism venous thrombosis, and arterial thrombosis), development of neutralizing antibodies (inhibitors), nephrotic syndrome, etc.; **AND**
- Any increases in dose must be supported by an acceptable clinical rationale (i.e., weight gain, half-life study results, increase in breakthrough bleeding when member is fully adherent to therapy, etc.); **AND**
- The cumulative amount of medication(s) the member has on-hand will be taken into account when authorizing. The authorization will allow up to 5 doses on-hand for the treatment of acute bleeding episodes as needed for the duration of the authorization; **AND**

On-demand treatment of bleeding episodes and control bleeding episodes

- Renewals will be approved for a 6-month authorization period

Perioperative management of bleeding

- Coverage may NOT be renewed.

Routine prophylaxis to prevent or reduce the frequency of bleeding episode

- Renewals will be approved for a 12 month authorization period; **AND**
- Member has demonstrated a beneficial response to therapy (i.e., the frequency of bleeding episodes has decreased from pre-treatment baseline)

VI. Dosage/Administration[1-9]

Alprolix

Indication	Dose
On-demand treatment and control of bleeding episodes Hemophilia B	One unit per kilogram body weight increases the circulating Factor IX level by 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 required dose or the expected in vivo peak increase in Factor IX level expressed as IU/dL (or % of normal) using the following: IU/dL (or % of normal) = [Total Dose (IU)/Body Weight (kg)] x Recovery (IU/dL per IU/kg) <u>Minor and Moderate</u> Circulating Factor IX required (% of normal) = 30-60 IU/dL - Repeat every 48 hours as needed <u>Major</u> Circulating Factor IX required (% of normal) = 80-100 IU/dL - Consider repeat dose after 6-10 hours, then every 24 hours for 3 days, then every 48 hours until healing achieved.
Perioperative management Hemophilia B	One unit per kilogram body weight increases the circulating Factor IX level by 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 required dose or the expected in vivo peak increase in Factor IX level expressed as IU/dL (or % of normal) using the following: IU/dL (or % of normal) = [Total Dose (IU)/Body Weight (kg)] x Recovery (IU/dL per IU/kg) <u>Minor</u>

	Circulating Factor IX required (% of normal) = 50-80 IU/dL - Repeat every 24-48 hours as needed, until bleeding stops and healing is achieved. Major Circulating Factor IX required (% of normal) = 60-100 IU/dL (initial level) - Consider repeat dose after 6-10 hours, then every 24 hours for 3 days, then every 48 hours until bleeding stops and healing achieved.
Routine prophylaxis Hemophilia B	Adults and adolescents ≥12 years of age 50 IU/kg once weekly or 100 IU/kg once every 10 days. Adjust dosing regimen based on individual response. Children <12 years of age Start with 60 IU/kg once weekly. Adjust dosing regimen based on individual response. More frequent or higher doses may be needed in children <12 years of age, especially in children <6 years of age.

AlphaNine SD

Indication	Dose
On-demand treatment and control of bleeding episodes Hemophilia B	One unit per kilogram body weight increases the circulating Factor IX level by 1% (IU/dL). Number of Factor IX IU required = body wt (kg) x Desired increase in Plasma Factor IX (percent) x 1.0 IU/kg Minor Circulating Factor IX required (20 – 30 % of normal) = 20-30 IU/kg - Repeat every 12 hours as needed for 1-2 days Moderate Circulating Factor IX required (25 - 50% of normal) = 25-50 IU/kg - Repeat every 12 hours as needed for 2-7 days Major Circulating Factor IX required (50% of normal) = 30-50 IU/kg - Repeat dose every 12 hours as needed for 3-5 days. Following this treatment period, FIX levels should be maintained at 20% (20 IU FIX/kg/twice daily) until healing has been achieved. Major hemorrhages may require treatment for up to 10 days
Routine prophylaxis Hemophilia B §	25-40 IU/kg two times weekly or 15-30 IU/kg two times weekly. Adjust dosing regimen based on individual response.

Perioperative management Hemophilia B	Prior to surgery, FIX should be brought to 50-100% of normal (50-100 IU/kg repeat every 12 hours). For the next 7 to 10 days, or until healing has been achieved, the member should be maintained at 50-100%FIX levels (50-100 IU/kg every 12 hours).

BeneFIX

Indication	Dose
On-demand treatment and control of bleeding episodes and Perioperative management Hemophilia B	One IU per kilogram body weight increases the circulating Factor IX level by 0.8 ± 0.2 IU/dL in adolescents/adults (≥12 years) and 0.7 ± 0.3 IU/dL in children (< 12 years). Initial dose: Number of Factor IX IU required (IU) = body weight (kg) x desired factor IX increase (% of normal or IU/dL) x reciprocal of observed recovery (IU/kg per IU/dL) • Minor hemorrhage: Circulating Factor IX activity required [% of normal or (IU/dL)]: 20-30, dosed every 12 to 24 hours for 1 to 2 days. • Moderate hemorrhage: Circulating Factor IX activity required [% of normal or (IU/dL)]: 25-50, dosed every 12 to 24 hours for 2 to 7 days until bleeding stops and healing begins. • Major hemorrhage: Circulating Factor IX activity required [% of normal or (IU/dL)]: 50-100, dosed every 12 to 24 hours for 7 to 10 days. *Dosage and duration of treatment with BeneFIX depend on the severity of the factor IX deficiency, the location and extent of bleeding, and the member's clinical condition, age and recovery of factor IX.*
Routine prophylaxis Hemophilia B	• 100 IU/kg once weekly • Adjust the dosing regimen (dose or frequency) based on the member's clinical response.

Idelvion

Indication	Dose
On-demand treatment and control of bleeding episodes Hemophilia B	• One IU of IDELVION per kg body weight is expected to increase the circulating activity of Factor IX as follows: o Adolescents and adults: 1.3 IU/dL per IU/kg o Pediatrics (<12 years): 1 IU/dL per IU/kg

	• Dosage and duration of treatment with IDELVION depends on the severity of the Factor IX deficiency, the location and extent of bleeding, and the member's clinical condition, age and recovery of Factor IX. • 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)) • Adjust dose based on the member's clinical condition and response. <u>Minor/Moderate</u> Desired peak Factor IX Level (% of normal or IU/dL): 30-60, dosed every 48-72 hours for at least 1 day until healing is achieved <u>Major</u> Desired peak Factor IX Level (% of normal or IU/dL): 60-100**,** dosed every 48-72 hours for 7-14 days until healing is achieved. Maintenance dose is weekly.

Perioperative management
Hemophilia B
	• One IU of IDELVION per kg body weight is expected to increase the circulating activity of Factor IX as follows:
	  ○ Adolescents and adults: 1.3 IU/dL per IU/kg
	  ○ Pediatrics (<12 years): 1 IU/dL per IU/kg
	Dosage and duration of treatment with IDELVION depends on the severity of the Factor IX deficiency, the location and extent of bleeding, and the member's clinical condition, age and recovery of Factor IX
	<u>Minor</u>
	Desired peak Factor IX Level (% of normal or IU/dL): 50-80, dosed every 48-72 hours for at least 1 day until healing is achieved
	<u>Major</u>
	Desired peak Factor IX Level (% of normal or IU/dL): 60-100**,** dosed every 48-72 hours for 7-14 days until healing is achieved. Repeat dose every 48-72 hours for the first week or until healing is achieved. Maintenance dose is once or twice weekly.

Routine prophylaxis Hemophilia B	<u>Members ≥12 years of age</u>: 25-40 IU/kg body weight every 7 days. Members who are well-controlled on this regimen may be switched to a 14-day interval at 50-75 IU/kg body weight. <u>Members <12 years of age</u>: 40-55 IU/kg body weight every 7 days.

Ixinity

Indication	Dose
On-demand treatment and control of bleeding episodes Congenital Hemophilia B	One IU per kg body weight increases the circulating activity of factor IX by 0.98 IU/dL. Members ≥ 12 years of age: • Initial dose: Required factor IX units (IU) = body weight (kg) x desired factor IX increase (% of normal of IU/dL) x reciprocal of observed recovery (IU/kg per IU/dL) • Maintenance dose: Depends upon the type of bleed or surgery, clinical response, and the severity of the underlying factor IX deficiency • Minor bleeding episode: Desired peak Factor IX Level (% of normal or IU/dL): 30-60, dosed every 24 hours on days 1-3 until healing is achieved • Moderate bleeding episode: Desired peak Factor IX Level (% of normal or IU/dL): 40-60, dosed every 24 hours on days 2-7 until healing is achieved • Major or life threatening bleeding episode: Desired peak Factor IX Level (% of normal or IU/dL): 60-100, dosed every 12-24 hours on days 2-14 until healing is achieved
Perioperative management Hemophilia B	Members ≥ 12 years of age: Minor surgery: • Pre-op: Desired peak Factor IX Level (% of normal or IU/dL) 50-80 • Post-op: Desired peak Factor IX Level (% of normal or IU/dL) 30-80, dosed every 24 hours on days 1-5, depending on type of procedure Major surgery: • Pre-op: Desired peak Factor IX Level (% of normal or IU/dL) 60-80 • Post-op: Desired peak Factor IX Level (% of normal or IU/dL) 40-60, dosed every 8-24 hours on days 1-3, then 30-50 dosed every 8-24 hours on days 4-6, and then 20-40 dosed every 8 -24 hours on days 7-14
Routine prophylaxis Hemophilia B	Members ≥ 18 years of age: • 40 to 70 IU/kg twice weekly • Adjust the dose based on the individual member's bleeding pattern and physical activity.

Profilnine

Indication	Dose
On-demand treatment and control of bleeding episodes Hemophilia B	Members ≥ 18 years of age: One unit per kilogram body weight increases the circulating Factor IX level by 1% (IU/dL). Number of Factor IX IU required = body wt (kg) x Desired increase in Plasma Factor IX (percent) x 1.0 IU/kg Minor to Moderate Single dose of product sufficient to raise plasma Factor IX levels to 20-30% of normal. 20-30 IU/kg every 16-24 hours until hemorrhage stops and healing is achieved. For minor, may repeat for 1-2 days, for moderate, may repeat for 2-7 days. Major Single dose of product sufficient to raise plasma Factor IX levels to 30-50% of normal. 30-50 IU/kg every 16-24 hours for up to 3-10 days. Following this treatment period, maintain Factor IX levels at 20% of normal until healing has been achieved.
Routine prophylaxis Hemophilia B §	Members ≥ 18 years of age: 25-40 IU/kg two times weekly or 15-30 IU/kg two times weekly. Adjust dosing regimen based on individual response.
Perioperative management Hemophilia B	Members ≥ 18 years of age: Surgery associated with bleeding in Factor IX deficient members require Factor IX levels of 30-50% of normal. For dental extractions, the Factor IX level should be raised to 50% of normal immediately prior to procedure. 30-50 IU/kg every 16-24 hours for 7-10 days until healing is achieved. Maintain Factor IX levels at 30-50% of normal until healing has been achieved.

Rebinyn

Indication	Dose
On-demand treatment and control of bleeding episodes Hemophilia B	Minor and Moderate 40 IU/kg of actual body weight. A single dose should be sufficient for minor and moderate bleeds. Additional doses of 40 IU/kg can be given. Major 80 IU/kg of actual body weight. Additional doses of 40 IU/kg can be given.

Perioperative management Hemophilia B	Minor Pre-op: 40 IU/kg of actual body weight (single pre-op dose should be sufficient) Post-op: Additional doses can be given if required Major Pre-op: 80 IU/kg of actual body weight Peri/Post-op: 40 IU/kg of actual body weight. 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. Due to the long half-life, the frequency of dosing in the post-surgical setting may be extended to once weekly after the first week until bleeding stops and healing is achieved.
Routine prophylaxis Hemophilia B	40 IU/kg once weekly. Adjust the dose based on the individual member's bleeding pattern and physical activity.

Rixubis

Indication	Dose
On-demand treatment and control of bleeding episodes Hemophilia B	One IU per kilogram body weight increases the circulating activity of Factor IX by 0.7 IU/dL for members <12 years of age and 0.9 IU/dL for members ≥ 12 years of age. Initial dose = body wt (kg) x desired factor IX increase (percent of normal or IU/dL) x reciprocal of observed recovery (IU/kg per IU/dL) Minor Circulating Factor IX level required (% or IU/dL) = 20-30 every 12 - 24 hours for at least 1 day, until healing is achieved Moderate Circulating Factor IX level required (% or IU/dL) = 25-50 every 12 - 24 hours for 2-7 days, until bleeding stops and healing is achieved Major Circulating Factor IX level required (% or IU/dL) = 50-100 every 12 - 24 hours for 7-10 days, until bleeding stops and healing is achieved
Routine prophylaxis Hemophilia B	Dosing for previously treated members (PTPs): Members <12 years of age 60 – 80 IU/kg twice weekly Members ≥ 12 years of age

Indication	Dose
	40 – 60 IU/kg twice weekly Adjust the dose based on the individual member's age, bleeding pattern, and physical activity.
Perioperative management Hemophilia B	One IU per kilogram body weight increases the circulating activity of Factor IX by 0.7 IU/dL for members <12 years of age and 0.9 IU/dL for members ≥ 12 years of age. Minor Circulating Factor IX level required (% or IU/dL) = 30-60 every 24 hours for at least 1 day, until healing is achieved Major Circulating Factor IX level required (% or IU/dL) = 80-100 every 8 - 24 hours for 7-10 days, until bleeding stops and healing is achieved

§ Utrecht and/or Malmö protocols used as basis for dosing

VII. Summary of Evidence

Rebinyn, Aprolix, Ixinity, Benefix, Rixubis and Idelvion are recombinant DNA-derived coagulation factor IX concentrate indicated for on-demand treatment and control of bleeding episodes, perioperative management of bleeding and routine prophylaxis in patients with Hemophilia B. To note, Rebinyn has not been approved for routine prophylaxis in patients with hemophilia B. The safety and efficacy of Rebinyn in routine treatment, on-demand treatment and perioperative management was assessed through four multicenter, non-controlled trials with 105 patients who had met the inclusion criteria. The safety and efficacy of Idelvion was evaluated through a prospective, open-label, multicenter clinical trial with 63 patients as part of treatment for on-demand treatment, perioperative management and routine prophylaxis. The safety and efficacy of Aprolix was evaluated in a multicenter, prospective, open-label study. Despite each having its own clinical trials conducted, all three uses a four-point scale of excellent, good, moderate or poor/no evidence to evaluate each bleeding episode by the investigator. In investigation of use in on-demand treatment and control of bleeding episodes, Rebinyn, Aprolix and Idelvion proved to show success in controlling bleeding episodes, at ratings of excellent or good of 93%, 83.7% and 94%, respectively. A similar rating scale was used when assessing the effect in perioperative management. Homeostatic efficacy was rated as excellent or good in all points of surgery for all three, except in Idelvion with one evaluation rated as moderate. Only Idelvion and Aprolix had clinical trials evaluating use in routine prophylaxis. Prophylaxis treatment with Idelvion resulted in a 93% and 88% reduction in the spontaneous and total annualized bleeding rate, respectively, when using the Poisson Model. Using a negative binomial model, an 83% reduction in annualized bleeding rate (ABR) for subjects in the fixed weekly interval arm and an 87% reduction for subjects in the individualized interval arm, compared to the episodic (on-demand) treatment arm of Aprolix.

The efficacy of Ixinity was assessed in a multicenter study of 77 subjects with hemophilia B, including 68 previously treated patients who either received routine prophylaxis or on-demand treatment. The study found that Ixinity effectively managed bleeding episodes and provided coverage during 19 major surgeries. Routine prophylaxis with doses of 40-70 IU/kg twice weekly and on-demand treatment with mean doses of 60 IU/kg demonstrated positive outcomes in managing hemophilia B. Ixinity was used to treat 508 bleeding episodes, with

70.9% resolving after a single infusion and 13.0% after two infusions; 4.7% required five or more infusions, often due to trauma or muscle bleeds. Hemostatic efficacy was rated as excellent or good in 84% of episodes, with "excellent" indicating dramatic relief and "good" indicating effective pain or hemorrhage reduction. The treatment demonstrated overall effective management of bleeding episodes. In the efficacy analysis of Ixinity for perioperative management, 19 major surgeries were evaluated in 16 male previously treated patients. Ixinity was administered as a bolus or continuous infusion, and the treatment effectively controlled hemostasis with no transfusions required during the procedures. Surgeons rated the hemostatic control as adequate or better, and blood loss was consistently assessed as 'expected' or 'less than expected.'

The efficacy of BeneFIX was assessed in clinical trials with 153 subjects, including both previously treated patients (PTPs) and previously untreated patients (PUPs). For on-demand treatment, 88% of infusions in PTPs were rated as "excellent" or "good" for bleeding episodes, and 93% of PTPs receiving routine prophylaxis one to two times per week rated it as "excellent" or "effective." Additionally, prophylaxis therapy was effective for 93% of PTPs and PUPs, with some experiencing spontaneous bleeding episodes within 48 hours of infusion. In perioperative management with BeneFIX, 36 surgical procedures were conducted in 28 previously treated patients (PTPs), including 23 major surgeries, and 30 procedures in 23 previously untreated patients (PUPs), with 28 considered minor. Hemostasis was generally maintained, though two PTPs needed additional interventions for complications. The median increase in circulating factor IX activity for PTPs was 0.7 IU/dL per IU/kg infused, with a median half-life of 19.4 hours. Continuous infusion regimens were used in nine major surgeries for eight PUPs, but clinical trial experience is too limited to fully establish the safety and efficacy of this approach. In an open-label trial comparing on-demand treatment with prophylaxis, 25 patients receiving prophylaxis at 100 IU/kg once weekly had a significantly lower annualized bleed rate (ABR) of 3.6 ± 4.6 episodes, compared to 32.9 ± 17.4 episodes with on-demand treatment ($p < 0.0001$). In another crossover trial involving 87 patients, prophylaxis with 100 IU/kg once weekly resulted in an ABR of 4.4 ± 10.0 episodes, while 50 IU/kg twice weekly led to a lower ABR of 2.8 ± 5.7 episodes.

In a prospective, open-label trial evaluating Rixubis in 73 male previously treated patients (PTPs) aged 12 to 65, the drug was used for either routine prophylaxis or on-demand treatment. In the prophylaxis group (59 subjects), Rixubis administered at 40 to 60 IU/kg twice weekly resulted in a mean annualized bleeding rate (ABR) of 4.3 for all bleeds, 1.7 for spontaneous bleeds, and 2.9 for joint bleeds. In contrast, the on-demand group (14 subjects) had a higher mean ABR of 33.9, with a median of 27, and a treatment duration averaging 3.5 months. In the perioperative management of Rixubis. In the perioperative management of Rixubis, 14 surgeries were evaluated across 14 previously treated patients (PTPs) aged 19 to 54, including 11 major and 3 minor procedures. The initial dosing aimed to maintain factor IX activity levels of 80-100% for major and 30-60% for minor surgeries, administered via intravenous bolus infusions. Hemostasis was rated as 'excellent' for all intraoperative assessments and for 11 of 14 surgeries at discharge, with 3 surgeries rated as 'good'. Common adverse events include hypersensitivity reactions, formation of neutralizing antibodies, thromboembolism, and nephrotic syndrome.

Alphanine SD is a purified, solvent detergent treated, virus preparation of Factor IX derived from human plasma used in the prevention and control of bleeding in patients with factor IX deficiency due to Hemophilia B. The safety and efficacy of AlphaNine was evaluated in a clinical trial with 13 patients during and after surgeries ranging from total knee replacement with synovectomy, below the knee amputation and oral surgery. No bleeding episodes were reported, and hemostasis was maintained during the course of the post-surgery therapy. Common adverse effects include Creutzfeldt-Jakob disease, viral infections, hypersensitivity reactions and nephrotic syndrome.

Profilnine is a sterile, lyophilized concentrate of Factor IX, II, X, and low levels of Factor VII used in the prevention and control of bleeding in patients with Factor IX deficiency due to hemophilia B. In a clinical study evaluating Profilnine SD, involving twelve subjects with hemophilia B, the in vivo half-life of Factor IX was found to be 24.68 ± 8.29 hours, and the recovery rate was 1.15 ± 0.16 IU/dL per IU infused per kg. Common adverse events include CJD, risk of infections, and DIC.

VIII. Billing Code/Availability Information

HCPCS Code(s) & NDC(s):

Drug	Manufacturer	HCPCS Code	1 Billable Unit Equiv.	Vial Size	NDC
AlphaNine SD	Grifols Biologicals Inc.	J7193	1 IU	500 units	68516-3601 68516-3607
				1000 units	68516-3602 68516-3608
				1500 units	68516-3603 68516-3609
Alprolix	Bioverativ Therapeutics Inc.	J7201	1 IU	250 units	71104-0966
				500 units	71104-0911
				1000 units	71104-0922
				2000 units	71104-0933
				3000 units	71104-0944
				4000 units	71104-0977
Profilnine	Grifols Biologicals LLC.	J7194	1 IU	500 units	68516-3201 68516-3207
				1000 units	68516-3202 68516-3208
				1500 units	68516-3203 68516-3209
BeneFIX	Wyeth Pharmaceuticals LLC	J7195	1 IU	250 units	58394-0633
				500 units	58394-0634
				1000 units	58394-0635
				2000 units	58394-0636
				3000 units	58394-0637
Ixinity	Medexus Pharma, Inc.	J7213	1 IU	250 units	70504-0287
				500 units	70504-0282
				1000 units	70504-0283
				1500 units	70504-0284
				2000 units	70504-0288
				3000 units	70504-0289
Rixubis		J7200	1 IU	250 units	00944-3026
				500 units	00944-3028

	Takeda Pharmeuticals U.S.A			1000 units	00944-3030
				2000 units	00944-3032
				3000 units	00944-3034
Idelvion	CSL Behring LLC	J7202	1 IU	250 units	69911-0864
				500 units	69911-0865
				1000 units	69911-0866
				2000 units	69911-0867
				3500 units	69911-0869
Rebinyn	Novo Nordisk Inc.	J7203	1 IU	500 units	00169-7905
				1000 units	00169-7901
				2000 units	00169-7902

IX. References

1. AlphaNine SD [package insert]. Los Angeles, CA; Grifols Biologicals LLC.; November 2021. Accessed May 2025.
2. Alprolix [package insert]. Waltham, MA; Bioverativ Therapeutics Inc.; May 2023. Accessed May 2025.
3. BeneFIX [package insert]. Philadelphia, PA; Wyeth Biopharma; March 2023. Accessed May 2025.
4. Ixinity [package insert]. Seattle, WA. Aptevo BioTherapeutics LLC; December 2022. Accessed May 2025.
5. Profilnine [package insert]. Los Angeles, CA; Grifols Biologicals Inc.; June 2023. Accessed May 2025.
6. Rebinyn [package insert]. Plainsboro, NJ; Novo Nordisk Inc.; August 2022. Accessed May 2025.
7. Rixubis [package insert]. Cambridge, MA; Takeda Inc.; March 2025; Accessed May2025.
8. Idelvion [package insert]. Kankakee, IL; CSL Behring LLC; June 2023. Accessed May 2025.
9. MASAC Recommendations Concerning Products Licensed For The Treatment Of Hemophilia And Selected Disorders of the Coagulation System. Revised April 11, 2024. National Hemophilia Foundation. MASAC Document #284; April 2024. Available at: https://www.bleeding.org. Accessed May 2024.
10. Guidelines for the Management of Hemophilia. 3rd Edition. World Federation of Hemophilia 2020. Available at: https://www1.wfh.org/publications/files/pdf-1863.pdf. Accessed April 2022.
11. Annual Review of Factor Replacement Products. Oklahoma Health Care Authority Review Board. Updated April 2016. Accessed April 2022.
12. Graham A1, Jaworski K. Pharmacokinetic analysis of anti-hemophilic factor in the obese patient. Haemophilia. 2014 Mar;20(2):226-9.
13. Croteau SE1, Neufeld EJ. Transition considerations for extended half-life factor products. Haemophilia. 2015 May;21(3):285-8.
14. Mingot-Castellano, et al. Application of Pharmacokinetics Programs in Optimization of Haemostatic Treatment in Severe Hemophilia a Patients: Changes in Consumption, Clinical Outcomes and Quality of Life. Blood. 2014 December; 124 (21).

15. MASAC Recommendation Concerning Prophylaxis for Hemophilia A and B with and without Inhibitors. Revised April 27, 2022. National Hemophilia Foundation. MASAC Document #267; April 2022. Available at: https://www.bleeding.org. Accessed May 2024.
16. Rayment R, Chalmers E, Forsyth K, et al. Guidelines on the use of prophylactic factor replacement for children and adults with Haemophilia A and B. B J Haem:190;5, Sep 2020. https://doi.org/10.1111/bjh.16704. Accessed May 2024.
17. Hoots, WK. (2024). Hemophilia A and B: Routine management including prophylaxis. In Leung LLK, Tirnauer JS (Eds.), UptoDate. Last updated: April 16, 2024. Accessed May 13, 2024. Available from https://www.uptodate.com/contents/hemophilia-a-and-b-routine-management-including-prophylaxis?search=hemophilia%20a&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H978189854
18. First Coast Service Options, Inc. Local Coverage Article: Billing and Coding: Hemophilia Clotting Factors (A56482). Centers for Medicare & Medicaid Services Inc. Updated on 02/05/2021 with effective date 01/01/2021. Accessed April 2022.
19. Palmetto GBA. Local Coverage Article: Billing and Coding: Guidance for Anti-Inhibitor Coagulant Complex (AICC) National Coverage Determination (NCD) 110.3 (A56065). Centers for Medicare & Medicaid Services Inc. Updated on 02/01/2021 with effective date 01/01/2021. Accessed April 2022.
20. Novitas Solutions, Inc. Local Coverage Article: Billing and Coding: Hemophilia Factor Products (A56433). Centers for Medicare & Medicaid Services Inc. Updated on 04/01/2021 with effective date 04/08/2021. Accessed April 2022.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D67	Hereditary factor IX deficiency

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs), and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes		
Jurisdiction	**NCD/LCA/LCD Document (s)**	**Contractor**
H,L	A56433	Novitas Solutions, Inc.
J, M	A56065	Palmetto GBA
N	A56482	First Coast Service Options, Inc. Insurance

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT,	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
15	KY, OH	CGS Administrators, LLC

Policy Rationale: AlphaNine SD, Alprolix, BeneFIX, Idelvion, Ixinity, Profilnine, Rebinyn, and Rixubis were reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Alprolix, Indelvion, and Rebinyn according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.