PDL DRUG REVIEW

Proprietary Name: Rebinyn®
Common Name: coagulation factor IX (recombinant), glyco-pegylated
PDL Category: Antihemophilic Agents

Comparable Products	Preferred Drug List Status
Benefix	Preferred
Mononine	Preferred

Summary

Pharmacology/Usage: Rebinyn® is a purified recombinant human Factor IX (rFIX) with a polyethylene-glycol (PEG) conjugated to the protein. This PEG molecule slows down its removal from circulation. This product goes through a purification process. Hemophilia B patients are deficient in coagulation Factor IX, which is needed for effective hemostasis. Treatment with Rebinyn® temporarily replaces the missing coagulation Factor IX.

Indication: A recombinant DNA-derived coagulation Factor IX concentrate indicated for use in adults and children with hemophilia B for:

- On-demand treatment and control of bleeding episodes
- Perioperative management of bleeding

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.

There is no pregnancy category for this medication; however, the risk summary indicates that there are no data with use in pregnant women to determine whether there is a drug-associated risk. Animal studies have not been conducted. Use during pregnancy only if clearly needed. The safety and efficacy of use in the pediatric population have been established. Studies included children ages 1 through 17 years of age.

Dosage Forms: Lyophilized powder in single-use vials containing nominally 500, 1000, or 2000 IU per vial. Each carton and vial states the actual Factor IX potency in IU. After reconstitution with 4ml of histidine diluent, the reconstituted solution contains about 125, 250, or 500 IU per ml of Rebinyn®, respectively.

Recommended Dosage: For IV infusion after reconstitution only. Dose and duration of treatment depend on the location and extent of bleeding, as well as the patient's clinical condition. If monitoring of Factor IX activity is performed, use a chromogenic assay or selected one-stage clotting assay validated for use with Rebinyn®.

For on-demand treatment and control of bleeding episodes, the recommended dose is 40IU/kg for minor and moderate bleeding (a single dose should be sufficient, but additional doses of 40IU/kg can be given) or 80IU/kg for major bleeding (additional doses of 40IU/kg can be given). *For perioperative management*, the recommended dose is 40IU/kg for minor surgical procedures (a single pre-op dose should be sufficient, but additional doses can be given

prn) or 80IU/kg for major surgical procedures (given pre-op and then 40IU/kg given as clinically needed for the perioperative management of bleeding).

Drug Interactions: There were no reported drug interactions listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Rebinyn®). There was no placebo data to compare with.* The most frequently reported adverse events included injection site reaction (4%), hypersensitivity (1%), and itching (3%).

Nephrotic syndrome has been reported after immune tolerance induction therapy with Factor IX products in hemophilia B patients with Factor IX inhibitors, often with a history of allergic reactions to Factor IX. The safety and efficacy of using Rebinyn® for immune tolerance induction have not been established.

The use of Factor IX-containing products has been associated with thrombotic complications. Thus, monitor patients for early signs of thrombotic and consumptive coagulopathy when giving this product to patients with liver disease, post-operatively, to newborn infants, or to patients at risk of thrombosis or disseminated intravascular coagulation.

Contraindications: In patients who have known hypersensitivity to Rebinyn® or its components (including hamster proteins)

Manufacturer: Novo Nordisk

Analysis: There were 4 multicenter, non-controlled studies performed to assess the safety and efficacy of Rebinyn® in routine treatment, on-demand treatment and perioperative management in previously treated male patients with hemophilia B. The efficacy evaluation included 105 subjects, with 62 adults, 18 adolescents (13 to 17 years), and 25 children (1 to 12 years).

- The adult/adolescent trial included 74 adolescents and adults previously treated. There were 2 routine treatment arms, with single-blind randomization for 52 weeks and an open-label on-demand treatment arm for 28 weeks.
- The surgery trial included 13 previously treated adolescent and adult patients who received one infusion of Rebinyn® the day of the surgery and post-operatively received infusions at the investigators discretion for up to 3 weeks.
- The adult/adolescent extension trial included 71 subjects from the adult/adolescent trial and surgery trial who continued routine treatment or on-demand treatment with Rebinyn® in an open-label extension trial.
- The pediatric trial included 25 pediatric previously treated patients where subjects received routine Rebinyn® treatment once weekly for 52 weeks.

There was a total of 597 bleeding episodes reported in 79 out of 105 patients in the clinical program in previously treated patients. An overall assessment of efficacy was performed by the subjects (for home treatment) or the study site investigator (for treatment under medical supervision), using a 4-point scale of excellent, good, moderate, or poor. The overall success rate, defined as excellent or good, for treatment of bleeding episodes was 93.2%. The table below, adapted from the prescribing information, illustrates the results.

New Bleeding Episodes	N=597
Efficacy Assessment	
Excellent or Good	551 (93%)
Moderate or Poor	40 (7%)
Number of injections to treat a bleeding episode	

New Bleeding Episodes	N=597
1 injection	521 (87%)
2 injections	60 (10%)
>2 injections	16 (3%)

In the on-demand arm, there were 143 bleeding episodes in 14 of 15 subjects. The overall success rate was 95.1%. A total of 120 bleeds (83.9%) of the 143 bleeding episodes were treated with one injection, and 20 (14%) were treated with 2 injections.

In the surgery trial, the efficacy analysis of Rebinyn® in perioperative management included 13 surgical procedures of which 9 were major and performed in 13 previously treated adolescent and adult patients. The hemostatic effect during surgery was assessed on a 4-point scale of excellent, good, moderate, or poor. The intraoperative hemostatic effect was rated as excellent or good for the 13 surgeries, for a success rate of 100%. A pre-operative dose of 80IU/kg Rebinyn® was effective, and no subjects required additional doses on the day of the surgery. The median number of additional 40IU/kg doses in the post-op period was 2 for days 1 to 6, 1.5 for days 7-13 days, and 3 for days 1 to 13. There was no unexpected postoperative bleeding.

There were 3 additional major surgeries and 18 minor surgery procedures that were assessed in the extension trial for Rebinyn® in previously treated patients. The hemostatic effect during major and minor surgery was confirmed with a success rate of 100%.

Place in Therapy: Rebinyn® is an IV infusion, recombinant DNA-derived coagulation Factor IX concentrate indicated for use in adults and children with hemophilia B for on-demand treatment and control of bleeding episodes and for perioperative management of bleeding. The Factor IX in Rebinyn® is conjugated to a polyethylene glycol molecule, which slows down its removal from the blood circulation.

There is no evidence that Rebinyn® is safer or more effective than the currently available, more cost-effective medications. It is therefore recommended that Rebinyn® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred**

References

[1] Rebinyn [package insert]. Plainsboro, NJ: Novo Nordisk; 2017.