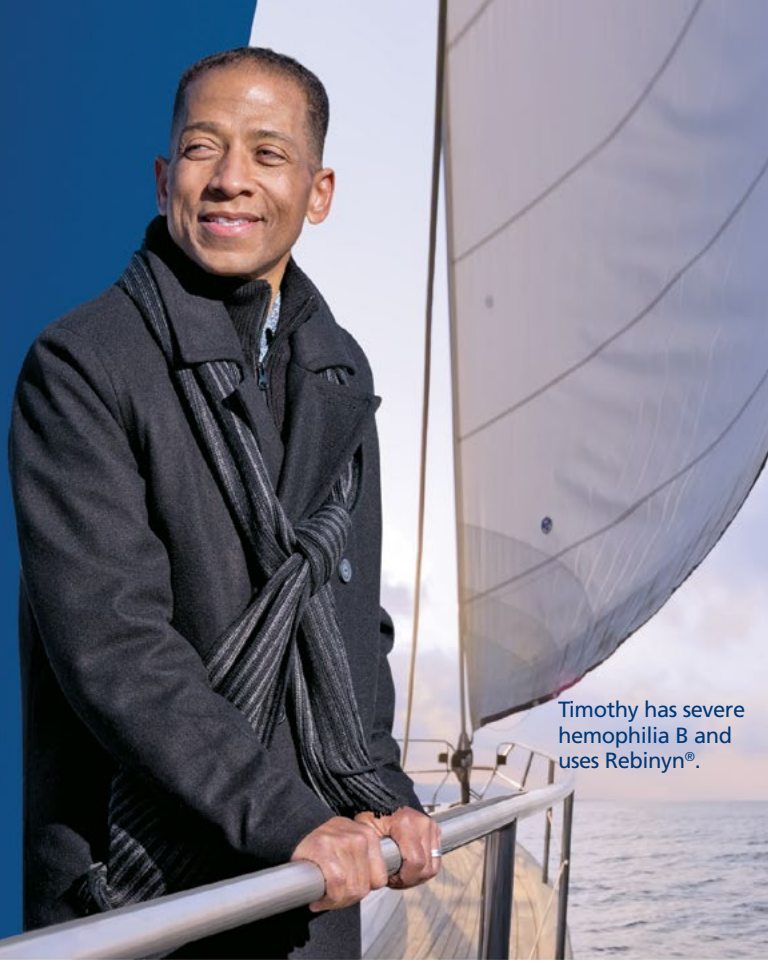
LIFE IS ABOUT THE UNEXPECTED

ONCE-WEEKLY REBINYN® RAISES EXPECTATIONS WITH HIGHER FIX LEVELS FOR LONGER[1,a]

FIX=Factor IX; IR=incremental recovery; pdFIX=plasma-derived Factor IX; PK=pharmacokinetic; rFIX=recombinant Factor IX; SHL=standard half-life.

[a]Based upon a phase 1 study of patients administered 1 of 3 doses of Rebinyn® (25, 50, or 100 IU/kg) compared with 1 dose of their prior SHL rFIX (N=7) or pdFIX (N=8) at the same dose using a 1-stage assay and product-specific standard. Estimated mean PK parameters are adjusted to a dose of 50 IU/kg. IR at 30 minutes (IR_{30}) and half-life were higher and longer with Rebinyn® than rFIX (IR_{30} 0.0131 vs 0.0068 (IU/mL)/(IU/kg) and half-life 93 vs 19 hours). All values were statistically significant ($P<0.001$). The clinical relevance of these PK differences is unknown.[1]



Timothy has severe hemophilia B and uses Rebinyn®.

Indications and Usage

Rebinyn®, Coagulation Factor IX (Recombinant), GlycoPEGylated, is a recombinant DNA derived coagulation Factor IX concentrate indicated for use in adults and children with hemophilia B (congenital Factor IX deficiency) for on demand treatment and control of bleeding episodes, perioperative management of bleeding, and routine prophylaxis to reduce the frequency of bleeding episodes.

Limitations of Use: Rebinyn® is not indicated for immune tolerance induction in patients with hemophilia B.

Important Safety Information

Contraindications

- Rebinyn® is contraindicated in patients with a known hypersensitivity to Rebinyn® or its components, including hamster proteins.

Please see additional Important Safety Information throughout.
Please see Prescribing Information here.

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rebinyn®
Coagulation Factor IX (Recombinant), GlycoPEGylated

Higher factor levels mean less bleeding in hemophilia A and B[2,3]

In patients with non-severe hemophilia A and B

Each **10%** increase in factor level has been associated with

1.8 fewer joint bleeds per year[2,a]

>40% RANGE

The World Federation of Hemophilia (WFH) acknowledges that EHL FIX products allow for more ambitious prophylaxis by having patients' FIX levels in a **non-hemophilic range (>40 IU/dL [40%])** for a substantial proportion of time[3]

Improve bleed prevention and participation in activities with higher FIX trough levels[3]

EHL=extended half-life; FIX=Factor IX.

[a]Based on a retrospective, observational study of the Centers for Disease Control and Prevention (CDC) Universal Data Collection (UDC) system surveillance data to investigate the effects of hemophilia type and factor activity level on rates of joint bleeding and orthopedic procedures. The study included 7941 males, aged ≥2 years, with mild or moderate hemophilia. On average, there were 0.09 fewer bleeds per 6 months with every 1% increase in factor activity.[2]

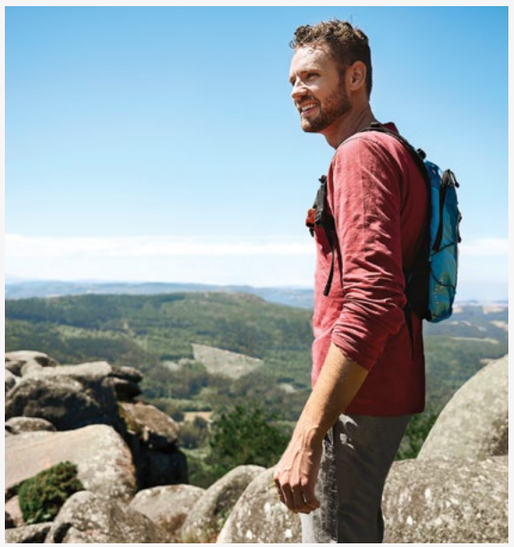
Maintaining higher factor levels matter for many activities[4]

The B-HERO-S study evaluated the impact of hemophilia B on activities[4,a]

- Adult patients administered extra factor in order to participate in activities[4]

46% **(n=137/295)** of adults reported change in the timing of dosing around recreational activity[4]

37% **(n=110/295)** of adults took extra doses before vigorous activity[4]

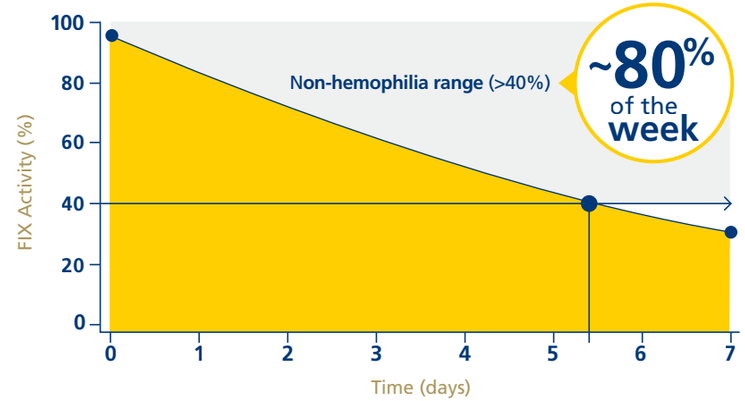


Clayton lives with hemophilia B.

[a]B-Hero-S (Bridging Hemophilia B Experiences, Results, and Opportunities Into Solutions) study included adult males or females (aged ≥18 years) with hemophilia B of any severity or caregivers of a child (aged <18 years) with hemophilia B of any severity. The objective was to describe the impact of hemophilia B on the participation of adults and children in recreational activities and to assess changes made to treatment regimens to accommodate engagement in such activities, as reported by respondents. Participants were recruited via social media and email through patient advocacy organizations.[4]

Raise FIX levels because life is about the unexpected

Rebinyn® once weekly maintains higher[a] FIX levels in the non-hemophilia range for most of the week[5]



~80% of the **week**

Adult and adolescent patients achieved FIX levels in the non-hemophilia range[a] (N=9)

	Adults	Adolescents
High FIX peak levels[6,b]	98% (N=20)	83% (N=9)
Long-lasting half-life[6,c]	115 HOURS (N=6)	103 HOURS (N=3)
High FIX trough levels[6,b]	29% (N=20)	24% (N=9)

Rebinyn® once weekly for prophylaxis delivers high peak factor levels, long half-life, high troughs, and bleed protection[6,b,c]

FIX=Factor IX.

[a]Data represent mean steady-state pharmacokinetic profiles from previously treated adolescent/adult patients with moderate-to-severe hemophilia B (N=9) taking Rebinyn® 40 IU/kg once weekly. FIX levels were within the non-hemophilia range (>40%) for 5.4 days (~80% of the week).[5]

[b]Based on the mean steady-state post-dose peak levels and pre-dose trough levels 168 hours after administered Rebinyn® 40 IU/kg/once weekly in previously treated patients (20 adult and 9 adolescent patients).[6]

[c]Based on analysis using a 1-stage assay in patients (N=6) aged ≥18, the half-life at steady state was 115 following once-weekly (40 IU/kg) dosing; in patients (N=3) aged 13 to 17, the half-life at steady state was 103 hours. Following single-dose administration (40 IU/kg) in the same patient population, the half-life was 83 hours (adults) and 89 hours (adolescents).[6]

Raise FIX levels to help kids be ready for the unexpected[6]

Rebinyn® maintains high factor levels throughout the dosing interval for pediatric patients[6]

Children aged **0 to 6** (N=12)

66%

mean FIX peak levels at steady state[a]

15% mean FIX trough level at Day 7[a]

70 HOUR half-life[b]

Children aged **7 to 12** (N=13)

71%

mean FIX peak levels at steady state[a]

19% mean FIX trough level at Day 7[a]

76 HOUR half-life[b]

FIX=Factor IX; PPx=prophylaxis; Tx=treatment.

[a]Mean steady-state pre-dose trough levels and post-dose peak levels across the clinical trials for all previously treated children aged ≤6 (N=12) and 7 to 12 years (N=13) receiving Rebinyn® 40 IU/kg once weekly.[6]

[b]Based on single-dose pharmacokinetic parameters of Rebinyn® 40 IU/kg in children aged ≤6 (N=12) and 7 to 12 years (N=13).[6]

Important Safety Information (cont'd)

Warnings and Precautions

- **Hypersensitivity Reactions:** Allergic-type hypersensitivity reactions, including anaphylaxis, have occurred with Rebinyn®. Signs may include angioedema, chest tightness, difficulty breathing, wheezing, urticaria, and itching. Discontinue Rebinyn® if allergic- or anaphylactic-type reactions occur and initiate appropriate treatment.

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rebinyn®
Coagulation Factor IX (Recombinant), GlycoPEGylated

Help your patients protect more moments[6,7]

Rebinyn® prophylaxis helps stop bleeds before they start[6,7]

Adults and adolescents achieved a median ABR of[7]:

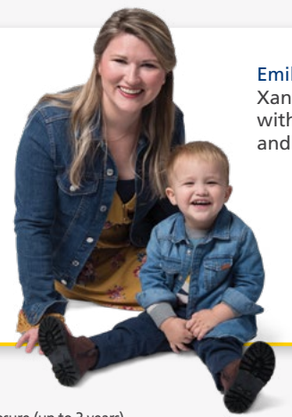
0
Spontaneous bleeds[a]

0
Traumatic bleeds[a]

1
Overall bleed[b]
(n=52)

Children ≤12 years achieved a median ABR of[6,c]:

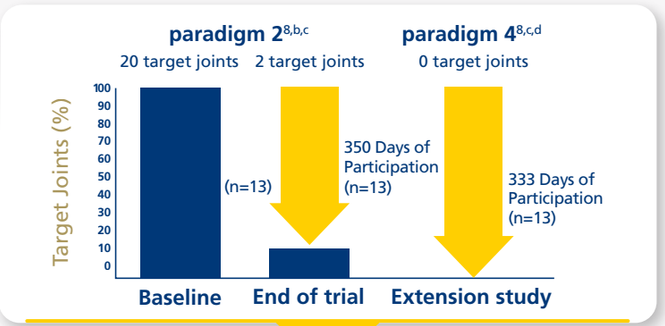
	traumatic bleed	spontaneous bleeds	joint bleed
≤6 years (N=12)	0	0	0
7 to 12 years (N=13)	1	0	1



Emili and her son Xander, who lives with hemophilia B and uses Rebinyn®.

ABR=annualized bleeding rate.
[a]From a phase 3, open-label trial assessing the safety and efficacy of Rebinyn® after long-term exposure (up to 3 years) in 71 previously treated patients (aged 13-70) from paradigm 2 or 3.[7]
[b]ABR of 1 was based on statistical calculation of median ABR for total bleeds in adult/adolescent patients.
[c]25 previously treated children 0 to 12 years old received routine prophylactic administration of Rebinyn® 40 IU/kg once weekly for 52 weeks.[6]

Rebinyn® prophylaxis reduced the number of target joints[8,a]



Adapted from Negrier et al. 2016.

100% of target joints no longer classified as target joints at completion of the extension study[8,a,c,d]

0 joint bleed ABR (median)[7,d] (n=52)

Timothy has severe hemophilia B and uses Rebinyn®.

Target joint resolution with Rebinyn® prophylaxis[7,8]

ABR=annualized bleeding rate; PPx=prophylaxis.
[a]Post hoc analyses of paradigm 2 and paradigm 4 data assessed the bleeding patterns in target joints in a population of patients with hemophilia B who received once-weekly prophylaxis with Rebinyn® 40 IU/kg.
[b]From the main phase of the adult/adolescent trial, 29 previously treated patients (aged 13-65) received Rebinyn® 40 IU/kg once weekly for approximately 52 weeks.[6]
[c]As measured by International Society on Thrombosis and Haemostasis (ISTH) target joint criteria. The most recent definition of a target joint from the ISTH is ≥3 spontaneous bleeds into the joint within a consecutive 6-month period. When there have been ≤2 bleeds into the joint within a consecutive 12-month period, the joint is no longer considered a target joint.[8]
[d]From a phase 3, open-label trial assessing the safety and efficacy of Rebinyn® after long-term exposure (up to 3 years) in 71 previously treated patients (aged 13-70) from paradigm 2 or 3.[7]

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

- **Inhibitors:** The formation of inhibitors (neutralizing antibodies) to Factor IX has occurred following Rebinyn®. If expected plasma factor IX activity levels are not attained, or if bleeding is not controlled as expected with the administered dose, perform an assay that measures Factor IX inhibitor concentration. Monitor all patients using clinical observations and laboratory tests for the development of inhibitors. Factor IX activity assay results may vary with the type of activated partial thromboplastin time reagent used.

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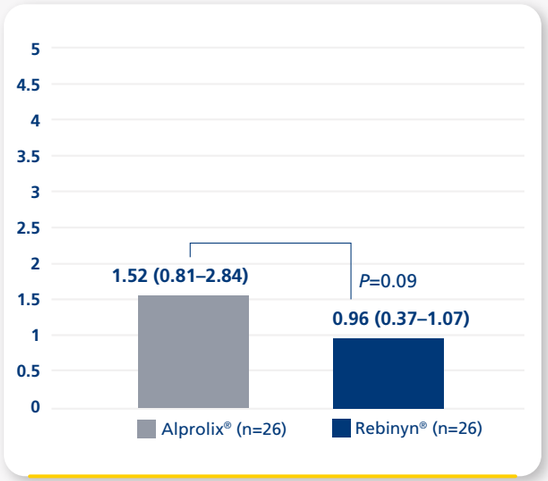
rebinyn®
Coagulation Factor IX (Recombinant), GlycoPEGylated

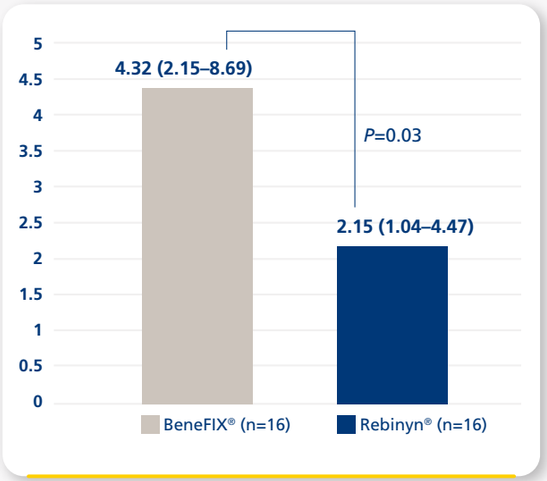
Based on a Canadian Bleeding Disorders Registry study,

In a retrospective, observational, real-world study of 42 patients,[a] fewer bleeds were observed in patients who switched to Rebinyn® [9]

Mean intrapatient ABR when switching from Alprolix® to Rebinyn® prophylaxis



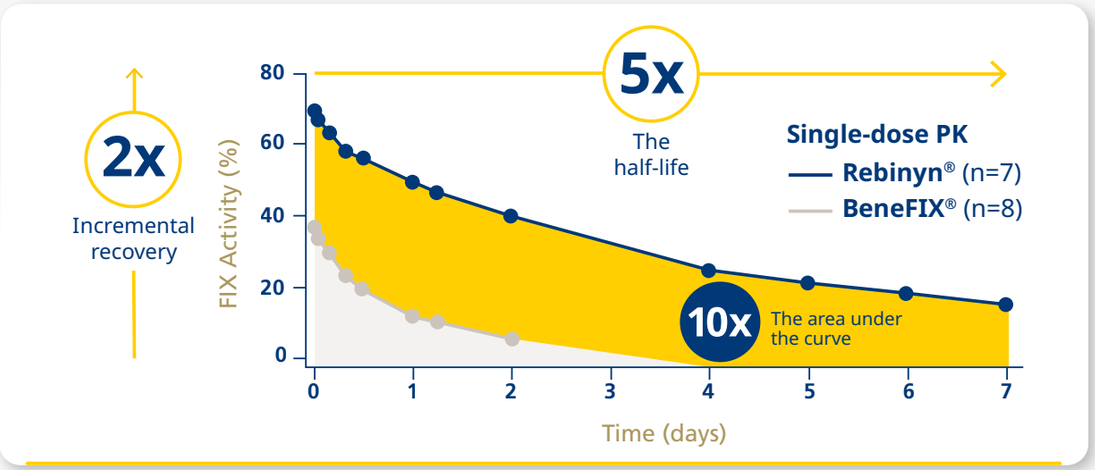
Mean intrapatient ABR when switching from BeneFIX® to Rebinyn® prophylaxis

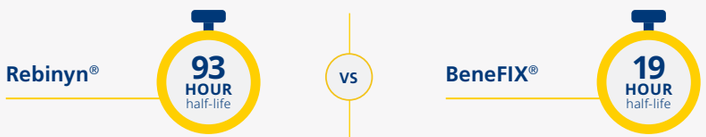


ABR=annualized bleeding rate; Tx=treatment.

[a]Based on a retrospective, observational, real-world study of 42 patients with hemophilia B (5 patients were <18 years old) that switched from either BeneFIX® or Alprolix® prophylaxis to Rebinyn® prophylaxis using published Canadian Bleeding Disorders Registry (CBDR) data. Patients had to be on a previous therapy for at least 6 months and have at least 6 months of follow-up with Rebinyn®. CBDR formulary mandated a switch from Alprolix® to Rebinyn®, and patients had the option to switch from BeneFIX® to Rebinyn®. Intrapatient comparison of ABR was determined using a negative binomial regression model.[9]

Rebinyn® delivered higher FIX levels longer than BeneFIX® [1,a]





AUC=area under the curve; FIX=Factor IX; pdFIX=plasma-derived Factor IX; PK=pharmacokinetic; rFIX=recombinant Factor IX; SHL=standard half-life.

[a]Phase 1 trial comparing PK of Rebinyn® with SHL FIX products (Negrier et al). Based upon a phase 1 study of patients administered 1 of 3 doses of Rebinyn® (25, 50, or 100 IU/kg) compared with 1 dose of their prior SHL rFIX (n=7) or pdFIX (n=8) at the same dose using a 1-stage assay. Estimated mean FIX activity profiles adjusted to a dose of 50 IU/kg. Differences were similar in comparison of Rebinyn® to pdFIX (half-life 93 vs 18 hours, 5.2x, $P<0.001$; AUC 70 vs 9 U x h/mL, 8x, $P<0.001$) and in comparison of Rebinyn® to rFIX (half-life 93 vs 19 hours, $P<0.001$; AUC 72 vs 7 U x h/mL, $P<0.001$). The clinical relevance of these PK differences is unknown.[1]

Important Safety Information (cont'd)

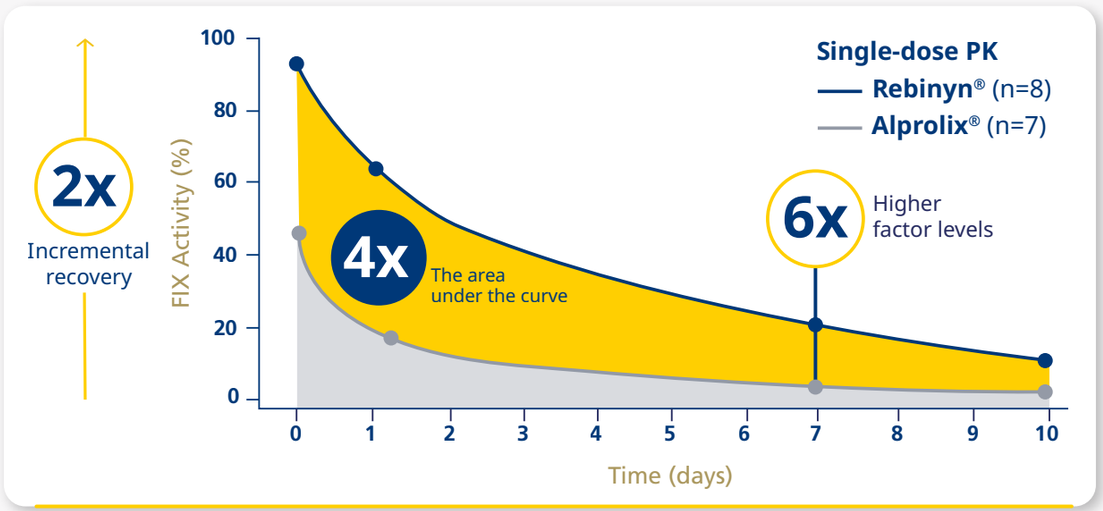
Warnings and Precautions (cont'd)

- **Thrombotic Events:** The use of Factor IX-containing products has been associated with thromboembolic complications. Monitor for thrombotic and consumptive coagulopathy when administering Rebinyn® to patients with liver disease, post-operatively, to newborn infants, or to patients at risk of thrombosis or disseminated intravascular coagulation (DIC).

Please see additional Important Safety Information throughout.
Please see Prescribing Information here.

rebinyn®
Coagulation Factor IX (Recombinant), GlycoPEGylated

Rebinyn® delivered higher FIX levels longer than Alprolix® [10,a]



Rebinyn® 103 HOUR half-life vs Alprolix® 85 HOUR half-life

FIX=Factor IX; PK=pharmacokinetic.

[a]Phase 1 trial comparing PK of Rebinyn® with Alprolix® (Ettingshausen et al). Based upon a phase 1 study of 15 patients administered a single dose of Rebinyn® 50 IU/kg compared with a single dose of Alprolix® 50 IU/kg using both 1-stage (shown above) and chromogenic assays. The standard Alprolix® dose of 50 IU/kg was administered for both products to allow for comparison of dose-dependent parameters; dose normalized to 50 IU/kg to reflect minor differences in dose administered. Geometric mean half-life was also prolonged (Rebinyn®: 103.2 hours, Alprolix®: 84.9 hours). All comparisons were significant ($P<0.0001$) for all assays. The clinical relevance of these PK differences is unknown.[10]

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

- **Nephrotic Syndrome:** Nephrotic syndrome has been reported following 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.

Rebinyn® offers effective bleed control across age groups [6,11,12]

98% (N=143 bleeding episodes)
of bleeds in adults and adolescents treated with 1-2 infusions in paradigm 2 clinical trial[6,a]

95% (N=143 bleeding episodes)
of bleeds were rated as successful (defined as excellent or good) in adults and adolescents in paradigm 2 clinical trial[6,11,b]

93% (N=42 bleeding episodes)
of bleed control in children rated as successful (defined as excellent or good) at the end of the 1-year analysis in paradigm 5 clinical trial[12]

Rebinyn® may reduce the need for additional infusions based on PK modeling [13,14,c,d]

	Rebinyn®	rFIX	pdFIX	rFIXFc
Estimated total infusions for severe bleed	1 80 IU/kg total	6 350 IU/kg total	6 310 IU/kg total	4 230 IU/kg total
Estimated total infusions for surgery	3 160 IU/kg total	17 790 IU/kg total	17 750 IU/kg total	9 480 IU/kg total

Results may vary.

FIX=Factor IX; pdFIX=plasma-derived Factor IX; PK=pharmacokinetic; rFIX=recombinant Factor IX; rFIXFc=recombinant Factor IX-Fc fusion protein.

[a]Results shown are from the on-demand arm of the adolescent/adult trial, in which 15 previously treated adolescent/adult patients were treated for on-demand bleeds. In 14 patients, there were a total of 143 bleeding episodes. In 1 patient, no bleeding episode data were recorded.[11]

[b]Results shown are based on a bleed assessment by either the patient (for home treatment) or the study investigator (for treatment under medical supervision). Bleeds were assessed using a 4-point scale of excellent, good, moderate, or poor.[6]

[c]A single dose should be enough for minor and moderate bleeds. Additional doses of 40 IU/kg can be given.[6]

[d]Based on a PK modeling to WFH guidelines. Simulated results based on a phase 1 PK study of Rebinyn® (N=15), rFIX (n=7), and pdFIX (n=8) and a phase 1 PK study of Rebinyn® and rFIXFc in 15 patients who received single 50 IU/kg doses of each ≥21 days apart.[1,10,13,14]

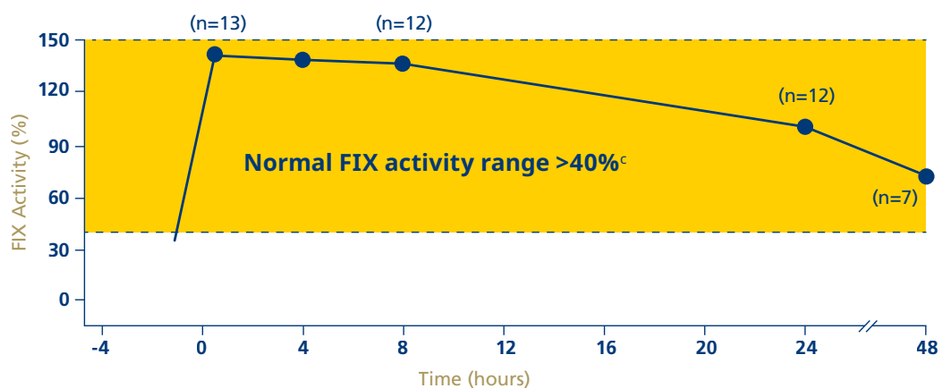
Rebinyn® provides bleed protection for surgery[6,15]

- In all major surgeries studied, single **80 IU/ kg** preoperative dose was administered[6,a]
- Intraoperative hemostatic effect had a **100%** success rate (N=13)[6,a]

- **Days 1 to 6**
  During the first postoperative week (Days 1 to 6), a median of 2 injections was administered and the median consumption was **84.1 IU/kg**[15]
- **Days 1 to 13**
  During the first 2 postoperative weeks (Days 1 to 13), a median of 3 injections was administered and the median consumption was **126.1 IU/kg**[15]

- Postoperative doses of **40 IU/kg** were given at the investigator's discretion for up to 3 weeks after surgery[6]

FIX activity sustained up to 48 hours post surgery[6,15,b]



[a]Results shown are from the surgery trial, which included 13 previously treated adolescent and adult subjects. On the day of their respective surgeries, patients received 1 infusion of Rebinyn® 80 IU/kg. Postoperatively, subjects received infusions of Rebinyn® 40 IU/kg at the investigator's discretion for up to 3 weeks after surgery. Across 13 surgical procedures (9 major)—which included 9 orthopedic, 1 gastrointestinal, and 3 oral cavity procedures—the hemostatic effect during surgery was evaluated on a 4-point scale of excellent, good, moderate, or poor. Treatment success was defined as excellent or good hemostasis.[6]

[b]In the surgery study, mean FIX activity following an initial preoperative infusion of Rebinyn® 80 IU/kg in 13 procedures was assessed by 1-stage assay with product-specific standard. At 8 and 24 hours, 1 subject who had no FIX activity measurement obtained was excluded. At 48 hours, 2 subjects who had no FIX activity measurement obtained were excluded and 4 subjects re-dosed prior to the second day after surgery for whom FIX activity at 24 hours was 84%, 112%, 131%, and 134%. The FIX activity at 48 hours reflects a measurement on the second day after surgery (range 47-57).[6]

[c]Range shaded represents the non-hemophilia population FIX activity range of >40% based on WFH classification.

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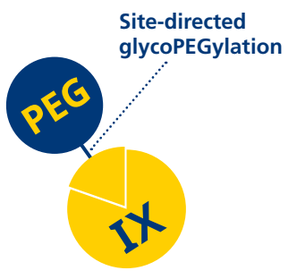
How PEGylation technology extends half-life in Rebinyn®[16]

The FIX in Rebinyn® is conjugated to a 40-kDa polyethylene glycol molecule, which slows down its removal from the blood circulation[6]

Selective Attachment



PEG selectively attaches to the FIX activation peptide by site-directed glycoPEGylation[17]

Prolonged Circulation

GlycoPEGylation keeps Rebinyn® in the bloodstream for longer, where it needs to be to stop bleeding[17]

Activated FIX Release

Rebinyn® releases rFIX similar to native human FIX once activated[6]

kDA=kilodalton; PEG=polyethylene glycol; rFIX=recombinant Factor IX.

Important Safety Information (cont'd)

Adverse Reactions

- The most common adverse reactions reported in previously treated patients in clinical trials (≥1%) were itching and injection site reactions. The most common adverse reactions (≥1%) in previously untreated patients reported in clinical trials were rash, FIX inhibitors, hypersensitivity, itching, injection site reaction, and anaphylactic reaction.
- Animals administered Rebinyn® showed accumulation of PEG in the choroid plexus, pituitary, circumventricular organs, and cranial motor neurons. The potential clinical implications of these animal findings are unknown. Consider whether the patient is vulnerable to cognitive impairment, such as infants and children who have developing brains, and patients who are cognitively impaired.

Please see additional Important Safety Information throughout.
Please see Prescribing Information here.

rebinyn®
Coagulation Factor IX (Recombinant), GlycoPEGylated

Safety and efficacy of Rebinyn® established in 5 clinical trials over 13 years[6,18]

292 PTP patient-years

15,137 exposure days

142 PUP patient-years

6709 exposure days

0 inhibitors in PTPs

The formation of inhibitors (neutralizing antibodies) to Factor IX has occurred following Rebinyn®. Common adverse reactions (≥1%) in PUPs reported in clinical trials for Rebinyn® included FIX inhibitors.

0 thrombotic events in PTPs

The use of Factor IX-containing products has been associated with thromboembolic complications.

Abdiel lives with hemophilia B and uses Rebinyn®.

FIX=Factor IX; PTP=previously treated patient; PUP=previously untreated patient.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in clinical trials of another drug and may not reflect the rates observed in clinical practice.

Once-weekly dosing that fits into life's routines[6]

High FIX protection with once-weekly Rebinyn® helps patients be ready for the unexpected[6]

Recommended dose for routine prophylaxis[6]

40 IU/kg

body weight, once weekly

Dosing regimen can be adjusted based on **individual patient's bleeding pattern and physical activity**

Abdiel lives with hemophilia B and uses Rebinyn®.

Almost two-thirds of patients taking extended half-life therapies use once-weekly dosing regimens[19,a]

EHL=extended half-life; FIX=Factor IX.

[a]Based on American Thrombosis and Hemostasis Network (ATHN) Data Set, the proportion of patients with severe hemophilia aged 0 to 50+ years on prophylaxis (n=4807) were compared with those on demand (n=1280) by age cohort in June 2018 and March 2019. The proportion of subjects on prophylaxis was analyzed by race, ethnicity, insurance status, and hemophilia treatment center region. Treatment frequency for subjects receiving prophylaxis with EHL was analyzed.[19]

Important Safety Information

Contraindications

- Rebinyn® is contraindicated in patients with a known hypersensitivity to Rebinyn® or its components, including hamster proteins.

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rebinyn®
Coagulation Factor IX (Recombinant), GlycoPEGylated

Administration that fits into life's routines[6]

Rebinyn® can be infused in 1 to 4 minutes[6]

With MixPro®, preparing a dose of Rebinyn® is as simple as attach, twist, and mix[6]

ATTACH[a]

Prefilled diluent syringe contains 4 mL of diluent—works with any dose strength

1

TWIST[a]

Adapter connects the syringe and vial, with a 25-µm inline particle filter

2

MIX[a]

After mixing, the reconstituted solution can be administered

3

2000 IU

1000 IU

500 IU

- Contains no preservatives

[a]For complete instructions on reconstitution and administration, please refer to the Instructions for Use.[6]

LabCorp™ partnership helps you monitor high FIX levels

Speak to a Novo Nordisk Representative about:

Option for phlebotomy available at

~1700 LabCorp™ locations

FIX levels available in

48 to 72 HOURS

Heat-modified Bethesda assays available in

7 DAYS

Markus lives with hemophilia B.

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References: **1.** Negrier C, Knobe K, Tiede A, Giangrande P, Møss J. Enhanced pharmacokinetic properties of a glycoPEGylated recombinant factor IX: a first human dose trial in patients with hemophilia B. *Blood*. 2011;118(10):2695-2701. **2.** Soucie JM, Monahan PE, Kulkarni R, Konkle BA, Mazepa MA; US Hemophilia Treatment Center Network. The frequency of joint hemorrhages and procedures in nonsevere hemophilia A vs B. *Blood Adv*. 2018;2(16):2136-2144. **3.** Srivastava A, Santagostino E, Dougall A, et al. WFH guidelines for the management of hemophilia. *Haemophilia*. 2020;26(Suppl6):1-158. **4.** Baumann K, Hernandez G, Witkop M, et al. Impact of mild to severe hemophilia on engagement in recreational activities by US men, women, and children with hemophilia B: The Bridging Hemophilia B Experiences, Results and Opportunities into Solutions (B-HERO-S) study. *Eur J Haematol*. 2017;98:25-34. **5.** Tiede A, Abdul-Karim F, Carcao M, et al. Pharmacokinetics of a novel extended half-life glycoPEGylated factor IX, nonacog beta pegol (N9-GP) in previously treated patients with haemophilia B: results from two phase 3 clinical trials. *Haemophilia*. 2017;23(4):547-555. **6.** Rebinyn® [package insert]. Plainsboro, NJ: Novo Nordisk Inc; July 2022. **7.** Young G, Collins PW, Colberg T, et al. Nonacog beta pegol (N9-GP) in haemophilia B: a multinational phase III safety and efficacy extension trial (paradigm™ 4). *Thromb Res*. 2016;141:69-76. **8.** Negrier C, Young G, Abdul Karim F, et al. Recombinant long-acting glycoPEGylated factor IX (nonacog beta pegol) in haemophilia B: assessment of target joints in multinational phase 3 clinical trials. *Haemophilia*. 2016;22(4):507-513. **9.** Matino D, Iorio A, Keepanasseril A, et al. Switching to nonacog beta pegol in hemophilia B: Outcomes from a Canadian real-world, multicenter, retrospective study. *Res Pract Thromb Haemost*. 2022;6(3):e12661. **10.** Ettingshausen CE, Hegemann I, Simpson ML, et al. Favorable pharmacokinetics in hemophilia B for nonacog beta pegol versus recombinant factor IX-Fc fusion protein: a randomized trial. *Res Pract Thromb Haemost*. 2019;3(2): 268-276. **11.** Collins PW, Young G, Knobe K, et al; paradigm 2 Investigators. Recombinant long-acting glycoPEGylated factor IX in hemophilia B: a multinational randomized phase 3 trial. *Blood*. 2014;124(26):3880-3886. **12.** Carcao M, Zak M, Abdul Karim F, et al. Nonacog beta pegol in previously treated children with hemophilia B: results from an international open-label phase 3 trial. *J Thromb Haemost*. 2016;14(8):1521-1529. **13.** Collins PW, Møss J, Knobe K, Groth A, Colberg T, Watson E. Population pharmacokinetic modeling for dose setting of nonacog beta pegol (N9-GP), a glycoPEGylated recombinant factor IX. *J Thromb Haemost*. 2012;10(11):2305-2312. **14.** Simpson M, Kulkarni R, Ettingshausen C, et al. Population pharmacokinetic modeling of on-demand and surgical use of nonacog beta pegol (N9-GP) and rFIXFc based upon the paradigm 7 comparative pharmacokinetic study. *J Blood Med*. 2019;10:391-398. **15.** Escobar MA, Tehranchi R, Karim FA, et al. Low-factor consumption for major surgery in haemophilia B with long-acting recombinant glycoPEGylated factor IX. *Haemophilia*. 2017;23(1):67-76. **16.** Swierczewska M, Lee KC, Lee S. What is the future of PEGylated therapies? *Expert Opin Emerg Drugs*. 2015;20(4):531-536. **17.** Østergaard H, Bjelke JR, Hansen L, et al. Prolonged half-life and preserved enzymatic properties of factor IX selectively PEGylated on native N-glycans in the activation peptide. *Blood*. 2011;118(8):2333-2341. **18.** Novo Nordisk A/S. Safety of 40K Pegylated Recombinant Factor IX in Non-Bleeding Patients With Haemophilia B. ClinicalTrials.gov identifier: NCT00956345. Updated January 20, 2017. Accessed June 3, 2022. https://clinicaltrials.gov/ct2/show/NCT00956345?term=NCT00956345&draw=2&rank=1 **19.** Malec LM, Cheng D, Witmer CM, et al. The impact of extended half-life factor concentrates on prophylaxis for severe hemophilia in the United States. *Am J Hematol*. 2020;95(8):960-965.

FIX=Factor IX.

Important Safety Information (cont'd)

Warnings and Precautions

- **Hypersensitivity Reactions:** Allergic-type hypersensitivity reactions, including anaphylaxis, have occurred with Rebinyn®. Signs may include angioedema, chest tightness, difficulty breathing, wheezing, urticaria, and itching. Discontinue Rebinyn® if allergic- or anaphylactic-type reactions occur and initiate appropriate treatment.

Please see additional Important Safety Information throughout.
Please see Prescribing Information here.

rebinyn®
Coagulation Factor IX (Recombinant), GlycoPEGylated

Raise expectations because life is about the unexpected

Rebinyn® once weekly for prophylaxis delivers high peak factor levels, long half-life, high troughs, and long-term bleed protection[6,7,a-c]

Higher FIX levels[d]

Rebinyn® helps patients maintain higher FIX levels in the non-hemophilia range (>40%) for **~80% of the week**[5,d]

Bleed protection

Rebinyn® prophylaxis helps stop bleeds before they start, with an overall median ABR of 1[7,c]

Long-term safety

13 years of clinical trial experience, 292 PTP patient-years and 142 PUP patient-years of experience[6,18]

ABR=annualized bleeding rate; FIX=Factor IX; PTP=previously treated patient; PUP=previously untreated patient.

[a]Based on the mean steady-state post-dose peak levels and pre-dose trough levels 168 hours after administered Rebinyn® 40 IU/kg/once weekly in PTPs (20 adult, 9 adolescent, and 25 pediatric patients).[6]

[b]Based on analysis using a 1-stage assay in patients (N=6) aged ≥18, the half-life at steady state was 115 hours following once-weekly (40 IU/kg) dosing; in patients (N=3) aged 13 to 17, the half-life at steady state was 103 hours. Following single-dose administration (40 IU/kg) in the same patient population, the half-life was 83 hours (adults) and 89 hours (adolescents).[6]

[c]Based on a phase 3, open-label trial assessing the safety and efficacy of Rebinyn® after long-term exposure (up to 3 years) in 71 previously treated patients (aged 13-70) from paradigm 2 or 3.[7]

[d]Based on mean steady-state pharmacokinetic profiles from previously treated adolescent/adult patients with moderate-to-severe hemophilia B (N=9) taking Rebinyn® 40 IU/kg once weekly. FIX levels were within the non-hemophilia range (>40%) for 5.4 days (~80% of the week).[5]

Important Safety Information (cont'd)

Warnings and Precautions (cont'd)

- **Inhibitors:** The formation of inhibitors (neutralizing antibodies) to Factor IX has occurred following Rebinyn®. If expected plasma factor IX activity levels are not attained, or if bleeding is not controlled as expected with the administered dose, perform an assay that measures Factor IX inhibitor concentration. Monitor all patients using clinical observations and laboratory tests for the development of inhibitors. Factor IX activity assay results may vary with the type of activated partial thromboplastin time reagent used.

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