All images of hemophilia B patients shown are for illustrative purposes only.

**INDICATIONS AND USAGE**

**What is Rebinyn® Coagulation Factor IX (Recombinant), GlycoPEGylated?**

Rebinyn® is an injectable medicine used to replace clotting Factor IX that is missing in patients with hemophilia B. Rebinyn® is used to treat and control bleeding in people with hemophilia B. Your healthcare provider may give you Rebinyn® when you have surgery. Rebinyn® is not used for routine prophylaxis or for immune tolerance therapy.

Please see Important Safety Information throughout. Please see accompanying Prescribing Information.
PIVOTAL DATA

TAKE CONTROL WITH HIGH FACTOR LEVELS

+94% 17%
achieved after an infusion,repeatedly sustained after 7 days
With a single dose of Rebinyn® 40 IU/kg in adults with <2% Factor IX (FIX) levels

IMPORTANT SAFETY INFORMATION

What is the most important information I need to know about Rebinyn®?

• Do not attempt to do an infusion yourself unless you have been taught how by your healthcare provider or hemophilia treatment center.

Carefully follow your healthcare provider’s instructions regarding the dose and schedule for infusing Rebinyn®.

• In two phase 3 studies, factor levels were evaluated for 1 week after the first dose of Rebinyn® 40 IU/kg. The average levels after 7 days were 16.8% in 6 adults, 14.6% in 3 adolescents, 10.9% in 13 children ages 7 to 12 years, and 8.4% in 12 children up to age 6 years.

• Based upon a 2.34% increase in factor levels per IU/kg infused in adults.

TAKE CONTROL WITH HIGH FACTOR LEVELS

Rebinyn® elevates factor above your normal levels

IMPORTANT SAFETY INFORMATION (cont’d)

Who should not use Rebinyn®?

Do not use Rebinyn® if you:

• are allergic to Factor IX or any of the other ingredients of Rebinyn®.

• are allergic to hamster proteins.

Please see additional Important Safety Information throughout.

Please see accompanying Prescribing Information.

EXTENDED HALF-LIFE WITH REBINYN®

Rebinyn® achieved and maintained high factor levels

Half-life: Time taken for the level of factor in the blood to fall by 50%.

Area under the curve (AUC): Calculated determination of the factor coverage provided while factor is in the body.

In two phase 3 studies, factor levels were evaluated for 1 week after the first dose of Rebinyn® 40 IU/kg. The average levels after 7 days were 16.8% in 6 adults, 14.6% in 3 adolescents, 10.9% in 13 children ages 7 to 12 years, and 8.4% in 12 children up to age 6 years.

Based upon a phase 3 study in 6 adults who received a single dose of Rebinyn® 40 IU/kg.
LONGER HALF-LIFE COMPARED TO BENEFIX®

In a single-dose study, Rebinyn® achieved

5X LONGER HALF-LIFE

[Graph showing estimated Rebinyn® factor levels stayed above 1% for 22.5 days compared to BeneFIX 19 hours.] 2x THE RECOVERY RATE

• Rebinyn® is not used for routine prophylaxis or for immune tolerance therapy.

• Animals given repeat doses of Rebinyn® showed Polyethylene Glycol (PEG) inside cells lining blood vessels in the choroid plexus, which makes the fluid that cushions the brain. The potential human implications of these animal tests are unknown.

HIGHER FACTOR LEVELS FOR LONGER COMPARED TO BENEFIX®

[Table showing FIX activity (%)

Time (hours)

Rebinyn® BeneFIX

0 20 40 60 80 100 120 140 160

5X LONGER HALF-LIFE

93 hours (~4 days) with Rebinyn®

19 hours with BeneFIX

Based upon a phase 1 study comparing 25, 50, and 100 IU/kg doses of Rebinyn® vs a 50 IU/kg dose of standard half-life FIX in 7 adults, and a 50 IU/kg dose of plasma-derived FIX in 8 adults. For Rebinyn®, estimated average FIX activity is adjusted to a dose of 50 IU/kg to allow comparison of all PK parameters.

Based upon a phase 1 study in 7 adults comparing Rebinyn® with BeneFIX. Rebinyn® doses adjusted to 50 IU/kg to allow for comparison of all PK parameters.

Please see accompanying Prescribing Information.

IMPORTANT SAFETY INFORMATION (cont’d)

What should I tell my health care provider before using Rebinyn®?

Tell your health care provider if you:

• have or have had any medical conditions.

• take any medicines, including non-prescription medicines and dietary supplements.

• are nursing, pregnant, or plan to become pregnant.

• have been told you have inhibitors to Factor IX.

Please see additional Important Safety Information throughout. Please see accompanying Prescribing Information.
**REBINYN® MAY REDUCE THE NEED FOR ADDITIONAL INFUSIONS**\(^{a,b,c}\)

Estimated number of doses and amount of FIX per episode

<table>
<thead>
<tr>
<th>Days</th>
<th>0</th>
<th>0.5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Infusions</strong></td>
<td><strong>Total Dosage (IU/kg)</strong></td>
<td></td>
</tr>
<tr>
<td>Mild to moderate bleed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rebinyn®</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>rFIX</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>pdFIX</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Severe bleed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rebinyn®</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>rFIX</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>pdFIX</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rebinyn®</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>rFIX</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>pdFIX</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

\(^{a}\) A single 40 IU/kg dose should be enough for minor and moderate bleed. Your doctor may recommend additional doses of 40 IU/kg based on pharmacokinetic (PK) modeling to the World Federation of Hemophilia (WFH) guidelines. Simulated results based on phase 1 PK study of Rebinyn® (n=15), recombinant FIX (rFIX) (n=7), and plasma-derived FIX (pdFIX) (n=8).

\(^{b}\) Compared with SHL products.

\(^{c}\) Estimated number of doses and amount of FIX per episode. In a phase 3 study in previously treated adolescents and adults:

- Half of the patients treated on-demand were able to resolve all bleeds with a single dose of Rebinyn®.
- Of the remaining patients, those previously treated with multiple high doses saw a meaningful decrease in FIX use with Rebinyn®.

**IMPORTANT SAFETY INFORMATION (cont’d)**

**What are the possible side effects of Rebinyn®?**

- Common side effects include swelling, pain, rash or redness at the location of the infusion, and itching.

Please see additional Important Safety Information throughout. Please see accompanying Prescribing Information.
**IMPORTANT SAFETY INFORMATION (cont’d)**

What are the possible side effects of Rebinyn®? (cont’d)

- Call your healthcare provider right away or get emergency treatment right away if you get any of the following signs of an allergic reaction: hives, chest tightness, wheezing, difficulty breathing, and/or swelling of the face.

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

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**COMPARISON VS EHL**

**GREATER FACTOR COVERAGE COMPARED TO ALPROLIX®**

In a single-dose study, Rebinyn® achieved a 4X greater factor coverage compared to Alprolix.

- **96.6 IU x h/mL** with Rebinyn®
- **22.0 IU x h/mL** with Alprolix

Compared upon a phase I study comparing a single 50 IU/kg dose of Rebinyn® to a single 50 IU/kg dose of extended half-life rFIXFc in 15 adults. To allow for direct comparison between standards, all patients received the Alprolix standard 50 IU/kg dose, dose normalized to 50 IU/kg.

**IMPORTANT SAFETY INFORMATION (cont’d)**

What are the possible side effects of Rebinyn®? (cont’d)

- Call your healthcare provider right away or get emergency treatment right away if you get any of the following signs of an allergic reaction: hives, chest tightness, wheezing, difficulty breathing, and/or swelling of the face.

**HIGHER FACTOR LEVELS FOR LONGER COMPARED TO ALPROLIX®**

- **6x higher factor levels as 7 days vs Alprolix**

The half-life of Rebinyn® was 103 hours vs 85 hours for Alprolix.

**IMPORTANT SAFETY INFORMATION (cont’d)**

What are the possible side effects of Rebinyn®? (cont’d)

- Tell your healthcare provider about any side effect that bothers you or that does not go away.
**HOW REBINYN® MEASURES UP AGAINST OTHER FIX PRODUCTS**

When considering FIX treatment options, Rebinyn® may be the right fit for you.

<table>
<thead>
<tr>
<th>Comparison of FIX products</th>
<th>Simplified dosing</th>
<th>Storage conditions</th>
<th>Mixing device includes prefilled diluent syringe</th>
<th>3 or more vial sizes</th>
<th>Diluent volume consistent across all vial sizes</th>
<th>Peel-off label for tracking infusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rebinyn® (EHL)</td>
<td>✔</td>
<td>Up to 85°F</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>BeneFIX (SHL)</td>
<td>Calculation required</td>
<td>Unspecified</td>
<td>Up to 3 hours</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Alprolix (EHL)</td>
<td>Calculation required</td>
<td>Up to 3 hours</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Idelvion® (SHL)</td>
<td>Calculation required</td>
<td>Up to 77°F</td>
<td>Not included</td>
<td>✔</td>
<td>2 diluent volumes</td>
<td>✔</td>
</tr>
<tr>
<td>Ixinity® (SHL)</td>
<td>Calculation required</td>
<td>Unspecified</td>
<td>✔</td>
<td>✔</td>
<td>Not included</td>
<td>✔</td>
</tr>
<tr>
<td>Rixubis® (SHL)</td>
<td>Calculation required</td>
<td>Up to 3 hours</td>
<td>Not included</td>
<td>✔</td>
<td>Not included</td>
<td>✔</td>
</tr>
</tbody>
</table>

**IMPORTANT SAFETY INFORMATION (cont’d)**

What are the possible side effects of Rebinyn®?

**INDICATIONS AND USAGE**

Rebinyn® is not used for routine prophylaxis or for immune tolerance therapy.

Animals given repeat doses of Rebinyn® showed Polyethylene Glycol (PEG) inside cells lining blood vessels in the choroid plexus, which makes the fluid that cushions the brain. The potential human implications of these animal tests are unknown.

As of June 2018, Rebinyn®, BeneFIX, and Ixinity are not indicated for routine prophylaxis.

Data from Rebinyn® PI, 2017; Alprolix PI, 2018; Idelvion® PI, 2017; BeneFIX PI, 2017; Ixinity PI, 2016; and Rixubis® PI, 2016.
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The above table does not imply that one FIX product is more effective than another product. Data from Rebinyn® PI, 2017; Alprolix PI, 2018; Idelvion PI, 2017; BeneFIX PI, 2017; Ixinity PI, 2016; and Rixubis PI, 2016.

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