ONCE-WEEKLY REBINYN® HELPS YOU KEEP FACTOR 9 LEVELS HIGHER FOR LONGER[a]

[a]Rebinyn® achieved and maintained higher factor levels than recombinant Factor 9 based upon a phase 1 study comparing 25, 50, and 100 IU/kg doses of Rebinyn® to a 50 IU/kg dose of standard half-life recombinant Factor 9 in 7 adults and a 50 IU/kg dose of plasma-derived Factor 9 in 8 adults. For Rebinyn®, estimated average Factor 9 activity is adjusted to a dose of 50 IU/kg. Incremental recovery at 30 minutes (IR_{30}) and half-life were higher and longer with Rebinyn® than recombinant Factor 9 (IR_{30} 0.0131 vs 0.0068 (IU/mL)/(IU/kg) and half-life 93 vs 19 hours). The clinical relevance of these pharmacokinetic differences is unknown.

Incremental Recovery: The increase in plasma concentration per IU/kg of factor administered.
Half-life: The time it takes for the level of factor in the blood to fall by half (50%).

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, prevent, or reduce the frequency (number) of bleeding episodes in people with hemophilia B. Your healthcare provider may give you Rebinyn® when you have surgery. Rebinyn® is not used for immune tolerance therapy.

Please see Important Safety Information throughout.
Please see Prescribing Information at novo-pi.com/rebinyn.pdf

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rebinyn®
Coagulation Factor IX (Recombinant), GlycoPEGylated

Expect more from your hemophilia B treatment

Higher factor levels mean less bleeding in mild and moderate hemophilia A and B

Each
10%
increase in factor level has been associated with

1.8
fewer joint bleeds per year[a]

Markus lives with hemophilia B.

[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 2 years and older with mild or moderate hemophilia. On average, there were 0.09 fewer bleeds every 6 months with every 1% increase in factor activity.

Higher factor levels are important for many activities

Higher factor levels may lead to more participation in activities, with less risk of bleeding

> 40%
RANGE

The World Federation of Hemophilia (WFH)[b] says an extended half-life prophylaxis can allow individuals to keep Factor 9 levels in the **non-hemophilia range (greater than 40%)** for a significant amount of time

Clayton lives with hemophilia B.

[b]WFH offers guidelines that inform shared decision-making between patients, caregivers, and healthcare providers based on data from existing peer-reviewed findings.

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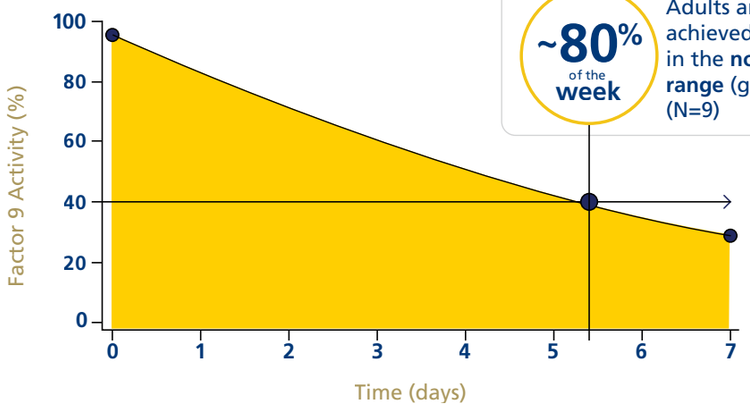
Rebinyn® helps you achieve high factor levels so you can be ready for the unexpected

Rebinyn® once weekly helped previously treated adults and adolescents achieve Factor 9 levels in the non-hemophilia range (greater than 40%)[a]



~80% of the **week** Adults and adolescents achieved Factor 9 levels in the **non-hemophilia range** (greater than 40%)[a] (N=9)

In adults the half-life was **115** hours[b] (N=6) Factor 9 levels after an infusion were 98% (N=20), and Factor 9 levels at Day 7 were 29% (N=20).[c]

In adolescents the half-life was **103** hours[b] (N=3) Factor 9 levels after an infusion were 83% (N=9), and Factor 9 levels at Day 7 were 24% (N=9).[c]

[a]Data represent mean steady-state pharmacokinetic profiles from previously treated adolescent/adult patients with moderate-to-severe hemophilia B (N=9) taking repeated doses of Rebinyn® 40 IU/kg once weekly. Factor 9 levels were within the non-hemophilia range (greater than 40%) for 5.4 days (about 80% of the week).
[b]Based on analysis using a 1-stage assay in patients (N=6) aged 18 and older, 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).
[c]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).

Protect more moments with long-term bleed protection

Rebinyn® helps prevent bleeds before they start in adults and adolescents

Overall ABR[d] (n=52)	Spontaneous ABR[d] (n=52)	Traumatic ABR[d] (n=52)	Joint ABR[d] (n=52)
1	0	0	0

100% **Target joint resolution**[d,e]

Rebinyn® once weekly delivers high Factor 9 activity and provides long-term bleed protection[d,f]

ABR=annualized bleeding rate.
[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 to 70) from paradigm 2 or 3.
[e]20 target joints were reported in 13 patients in the 40 IU/kg once weekly arm at baseline, and 18 out of 20 (90%) of these target joints were considered resolved at the end of the main phase. There were 2 target joints at the start of the extension trial in patients in the 40 IU/kg once weekly arm. Upon conclusion of the extension phase, both of these target joints were resolved. As measured by International Society on Thrombosis and Haemostasis (ISTH) target joint criteria. The definition of target joint from the ISTH is greater than or equal to 3 spontaneous bleeds into the joint within a consecutive 6-month period. When there have been less than or equal to 2 bleeds into the joint within a consecutive 12-month period, the joint is no longer considered a target joint.
[f]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).

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®.

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 Prescribing Information at novo-pi.com/rebinyn.pdf

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Coagulation Factor IX (Recombinant), GlycoPEGylated

High levels with Rebinyn® can help kids be ready for the unexpected

High Factor 9 levels in children 12 years or younger

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

66% Factor 9 levels after an infusion[a]

15% Factor 9 levels at Day 7[a]

70 HOUR half-life[b]

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

71% Factor 9 levels after an infusion[a]

19% Factor 9 levels at Day 7[a]

76 HOUR half-life[b]

[a]Mean steady-state pre-dose trough levels and post-dose peak levels across the clinical trials for all previously treated children receiving Rebinyn® 40 IU/kg once weekly. Based on an analysis using a 1-stage assay of previously treated children aged 0 to 12 years old (N=25). Children were stratified into 2 groups; ≤6 years old (N=12) and 7 to 12 years old (N=13). All patients received a fixed dose of 40 IU/kg of Rebinyn® intravenously once weekly for prophylaxis.

[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). A single-dose pharmacokinetic assessment was conducted after administration of the the first dose of Rebinyn®. The last pharmacokinetic sample was collected 1 week later, just prior to administration of the second dose.

Protect more moments for little ones

Children 12 and under receiving once-weekly Rebinyn® prophylaxis achieved a yearly bleed rate of[c]:

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

	Traumatic bleed	Spontaneous bleeds	Joint bleed
6 years and under (N=12)	0	0	0
7 to 12 years (N=13)	1	0	1

[c]25 previously treated children 0 to 12 years old received routine prophylactic administration of Rebinyn® 40 IU/kg once weekly for 52 weeks.

Important Safety Information (cont'd)

What should I tell my healthcare provider before using Rebinyn®?

Tell your healthcare 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.

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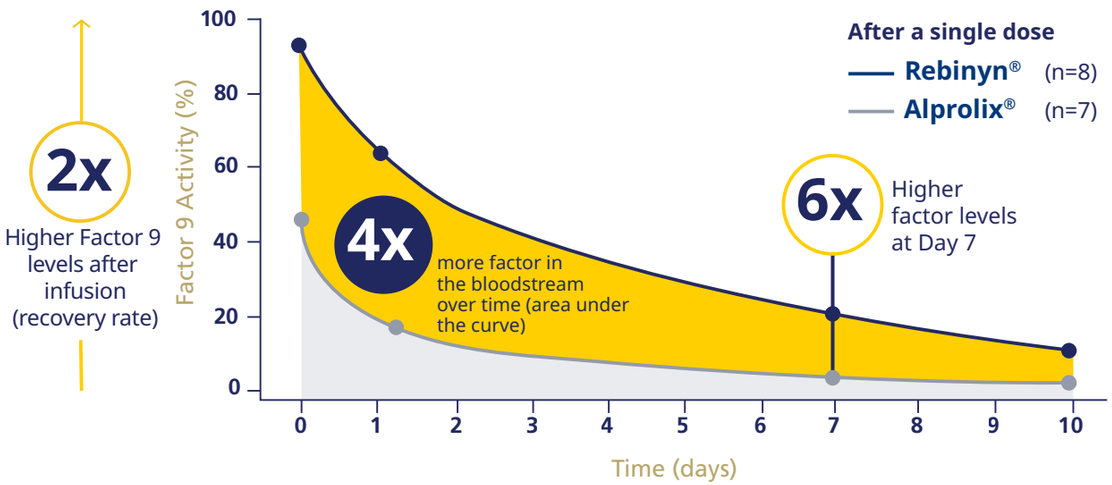
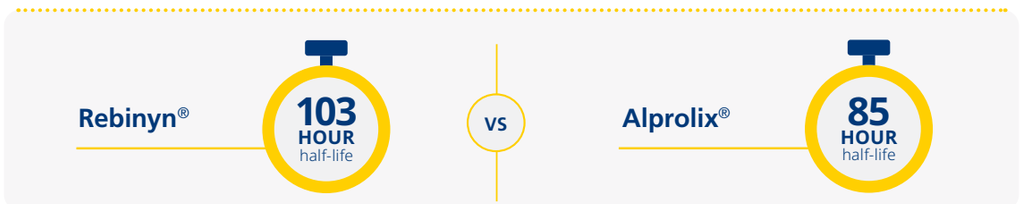
Coagulation Factor IX (Recombinant), GlycoPEGylated

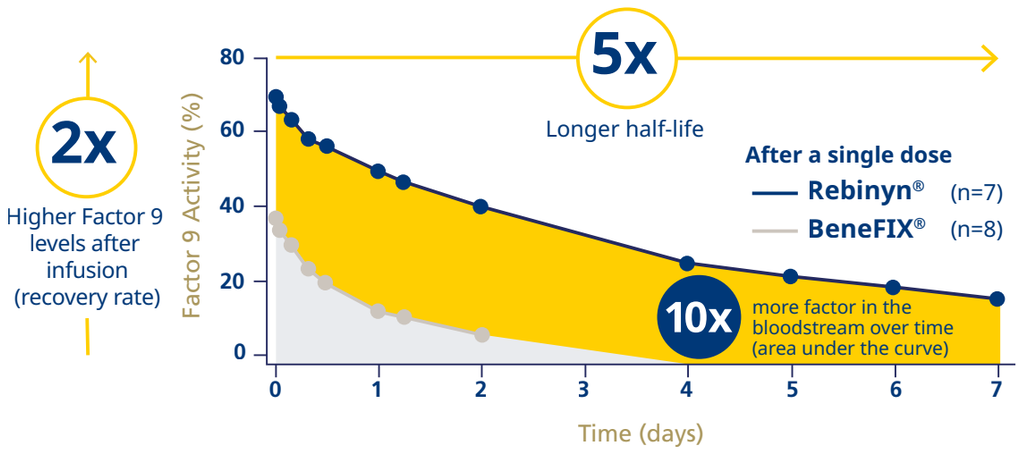
Rebinyn® delivered higher Factor 9 levels longer than Alprolix® a

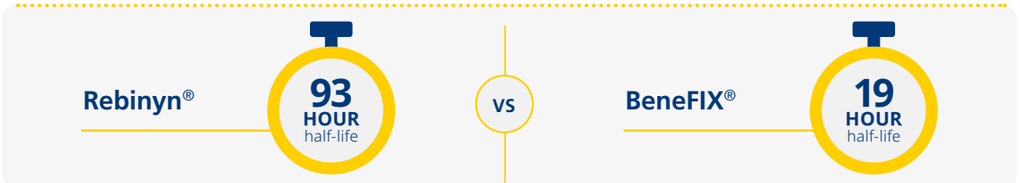




[a]Phase 1 trial comparing pharmacokinetics of Rebinyn® with Alprolix®. Based upon a phase 1 study of 15 patients administered a single dose of Rebinyn® 50 IU/kg compared with a single dose of Alprolix® 50 IU/kg using both 1-stage (shown above) and chromogenic assays. The standard Alprolix® dose of 50 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 pharmacokinetic differences is unknown.

Rebinyn® delivered higher Factor 9 levels longer than BeneFIX® b





h=hours; pdFIX=plasma-derived Factor 9; PK=pharmacokinetic; rFIX=recombinant Factor 9; SHL=standard half-life; U=units.

[b]Phase 1 trial comparing PK of Rebinyn® with SHL Factor 9 products. 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 PK parameters are 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.

Important Safety Information (cont'd)

How should I use Rebinyn®?

- Rebinyn® is given as an infusion into the vein.
- **Call your healthcare provider right away if your bleeding does not stop after taking Rebinyn®.**
- Do not stop using Rebinyn® without consulting your healthcare provider.

Please see additional Important Safety Information throughout.
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Coagulation Factor IX (Recombinant), GlycoPEGylated

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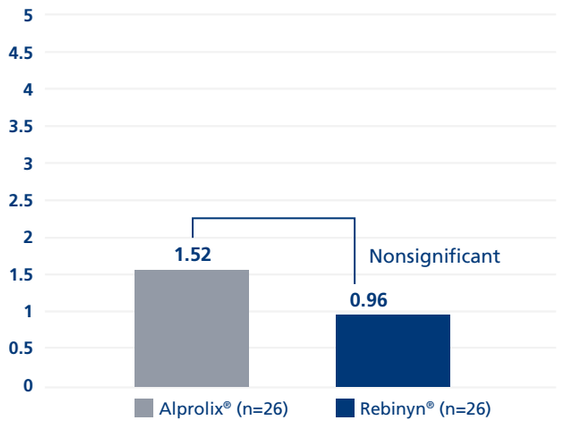
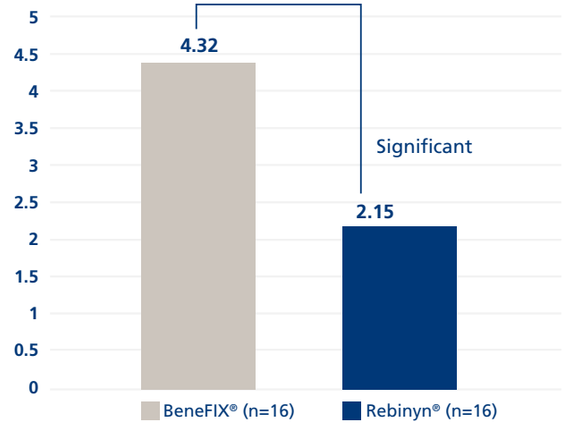
Based on a Canadian Bleeding Disorders Registry study,

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

Total mean ABR when switching from Alprolix® to Rebinyn® prophylaxis



Total mean ABR when switching from BeneFIX® to Rebinyn® prophylaxis



High Factor 9 protection with Rebinyn® helps you to be ready for the unexpected

ABR=annualized bleeding rate.

[a]Based on a retrospective, observational, real-world study of 42 patients with hemophilia B (5 patients were less than 18 years old) who 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 required a switch from Alprolix® to Rebinyn®, and patients had the option to switch from BeneFIX® to Rebinyn®. Total mean ABR is based on intrapatient bleeding, which is the bleeding rate in each patient before and after switching from BeneFIX® or Alprolix® prophylaxis to Rebinyn® prophylaxis.

Over 13 years of clinical trial safety data

Timothy has severe hemophilia B and uses Rebinyn®.

The formation of inhibitors (neutralizing antibodies) to Factor 9 has occurred following Rebinyn®. Common adverse reactions (incidence ≥1%) in PUPs reported in clinical trials for Rebinyn® included Factor 9 inhibitors. The use of Factor 9-containing products has been associated with blood clots.

[b]Patient-years of experience defined as the total number of years all patients have been treated with Rebinyn®.
[c]An exposure day is defined as a unit of time (1 day) during which a patient receives factor treatment.

Important Safety Information (cont'd)

What are the possible side effects of Rebinyn®?

- **Common side effects include** infusion site reaction (bruising, bleeding, swelling, pain, or redness), itching, and rash.
- Your body can also make antibodies called "inhibitors" against Factor IX, including Rebinyn®, which may stop Rebinyn® from working properly. Your healthcare provider may need to test your blood for inhibitors from time to time.

Please see additional Important Safety Information throughout.
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rebinyn®
Coagulation Factor IX (Recombinant), GlycoPEGylated

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Rebinyn® on demand helps you achieve higher factor levels[a]

Rebinyn® elevates factor above your normal levels[b]

+94% achieved after an infusion[c]

17% sustained after 7 days[b]

With a single dose of Rebinyn® 40 IU/kg in adults with less than or equal to 2% Factor 9 levels[b]

- Rebinyn® achieved an 83-hour average half-life in adults (approximately 3.5 days)

Rebinyn® may reduce the need for additional infusions based on PK modeling[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.

In a clinical study, Rebinyn® provided[e]

100% success rate in bleed control during major surgery (N=13)

pdFIX=plasma-derived Factor 9; PK=pharmacokinetic; rFIX=recombinant Factor 9; rFIXFc=recombinant Factor 9-Fc fusion protein.

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

[b]In a pharmacokinetic assessment of a single dose of Rebinyn® 40 IU/kg upon enrollment 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 aged 7 to 12 years, and 8.4% in 12 children up to age 6 years.

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

[d]Based on a PK modeling (mathematical simulation) 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 with hemophilia B who received single 50 IU/kg doses of each ≥21 days apart.

[e]Results shown are from the surgery clinical study, which included 13 previously treated adolescent and adult patients. Patients received 1 infusion of Rebinyn® 80 IU/kg on the day of their surgeries. At the doctor's discretion, patients received infusions of Rebinyn® 40 IU/kg for up to 3 weeks after surgery. Across 13 surgical procedures, the success rate in bleed control during surgery was evaluated on a 4-point scale of excellent, good, moderate, or poor. Treatment success was defined as excellent or good bleed control.

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Patient support with NovoCare® (NovoSecure™)

You may be eligible for:

FREE TRIAL OFFER

Visit **NOVOCARE.COM** or call **1-844-NOVOSEC (1-844-668-6732)** to speak with a NovoSecure™ Specialist to find out if you're eligible to receive a limited supply of Rebinyn® for free.[f] Ask your healthcare provider about the free trial offer through **Novocare.com**.

FOR MORE AFFORDABILITY OPTIONS

Go to **NOVOCARE.COM**

CO-PAY ASSISTANCE PROGRAM

Get help with co-pay costs up to $12,000 per calendar year[g]

NNI=Novo Nordisk.

[f]Patients who have been prescribed a Novo Nordisk hemophilia and rare bleeding disorder product for an FDA-approved indication, and who have commercial insurance or who are uninsured, may be eligible to receive a limited supply of free product. Patients who participate in any government, state, or federally funded medical or prescription benefit program, including Medicare, Medicaid, Medigap, VA, DOD, and TRICARE, including patients who participate in a managed Medicaid program or have Medicaid as secondary insurance, are not eligible to receive product support. Product is provided at no cost to the patient or the HCP, is not contingent on any product purchase, and the patient and HCP must not: (1) bill any third party for the free product, or (2) resell the free product.

[g]Novo Nordisk Hemophilia and Rare Bleeding Disorders Co-Pay/Coinsurance Terms and Conditions: Enrolled patients are eligible for up to $12,000 in co-pay/coinsurance assistance per calendar year for each NNI hemophilia or rare bleeding disorder product. Assistance is retroactive to 60 days. Patients must be commercially insured and may not be participating in any government, state, or federally funded medical or prescription benefit programs, including Medicare, Medicaid, Medigap, VA, DOD, and TRICARE, including patients who participate in a managed Medicaid program or have Medicaid as secondary insurance. Uninsured, cash-paying patients are not eligible to participate. Patients are eligible to receive co-pay/coinsurance assistance on an annual basis (12 months). Offer good only in the USA, Puerto Rico, Guam, Saipan, and Virgin Islands with participating pharmacies and cannot be redeemed at government-subsidized clinics. Void where taxed, restricted, or prohibited by law. Absent a change in Massachusetts law, effective July 1, 2019, the Savings Card will no longer be valid for residents of Massachusetts. Patient is responsible for complying with any insurance carrier co-payment disclosure requirements, including disclosing any savings received from this program. Re-confirmation of information may be requested periodically to ensure accuracy of data and compliance with terms. This is not an insurance program. Novo Nordisk reserves the right to rescind, revoke, or amend this offer without notice at any time. Nonmedication expenses, such as ancillary supplies or administration-related costs, are not eligible. Must have a current prescription for an FDA-approved indication.

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, for example, 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.
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rebinyn®
Coagulation Factor IX (Recombinant), GlycoPEGylated

Simple, once-weekly dosing that fits into your routine

40 IU/kg

Simple dosing for routine prophylaxis with Rebinyn® that may be easier to remember

Your doctor may adjust your dosing regimen based on your bleeding pattern and physical activity.

Recommended dose for bleed treatment for all patients is[a]

40 IU/kg
for minor or moderate bleeds[a]

80 IU/kg
for major bleeds[a]

- Follow your healthcare provider's instructions regarding the dose and schedule for infusing Rebinyn®

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

[a]A single dose should be enough for minor and moderate bleeds. Your doctor may recommend additional doses of 40 IU/kg.

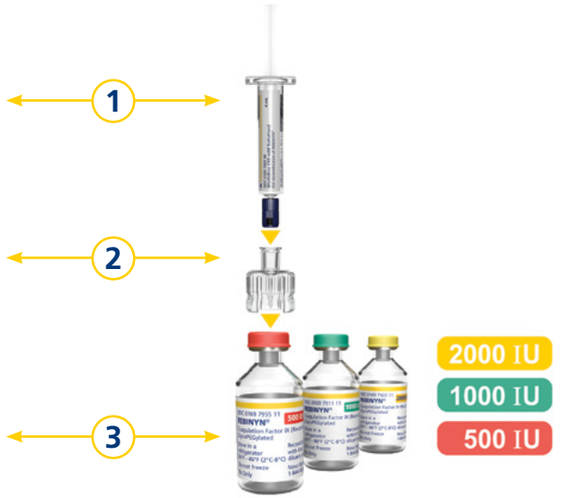
Fast infusions and flexible storage

Rebinyn® can be infused in 1 to 4 minutes
With MixPro®, preparing a dose of Rebinyn® is as simple as attach, twist, and mix

ATTACH[b]
Prefilled diluent syringe contains 4 mL of diluent—works with any dose strength

TWIST[b]
Adapter connects the syringe and vial with a 25-µm inline particle filter

MIX[b]
After mixing, the reconstituted solution can be administered



No refrigeration required

Up to 86°F

- Room temperature stable **for up to 6 months**
- Post-reconstitution storage **for up to 4 hours**

- If storing Rebinyn® at room temperature, do not return to refrigerator
- Rebinyn® can be stored in the refrigerator at 36 °F to 46 °F for up to 24 months

[b]For complete instructions on reconstitution and use, please refer to the Instructions for Use.

Important Safety Information (cont'd)

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

- You may be at an increased risk of forming blood clots in your body, especially if you have risk factors for developing blood clots. Call your healthcare provider if you have chest pain, difficulty breathing, leg tenderness, or swelling.

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rebinyn®
Coagulation Factor IX (Recombinant), GlycoPEGylated

novo nordisk®

Be ready for the unexpected with higher factor levels[a]

Rebinyn® once weekly delivers high Factor 9 activity and long-term bleed protection[b-d]

High factor levels
Rebinyn® helps you maintain high Factor 9 levels in the non-hemophilia range (greater than 40%) for **about 80% of the week**[a]

Achieve bleed protection
Rebinyn® helps prevent bleeds before they start, with an annual spontaneous or traumatic ABR of 0[d]

Established long-term safety so you can be ready for the unexpected
13 years of clinical trial experience and 292 previously treated patient-years of experience

Ask your healthcare provider about once-weekly Rebinyn®

Timothy has severe hemophilia B and uses Rebinyn®.

Scan this code to visit Rebinyn.com

ABR=annualized bleeding rate.

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

[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, 9 adolescent, and 25 pediatric patients).

[c]Based on analysis using a 1-stage assay in patients (N=6) aged 18 and older, 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).

[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 to 70) from paradigm 2 or 3.

Important Safety Information (cont'd)

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

- Animals given repeat doses of Rebinyn® showed Polyethylene Glycol (PEG) in certain cells in the brain. The potential human implications of these animal tests are unknown.

Please see additional Important Safety Information throughout.
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Novo Nordisk Inc., 800 Scudders Mill Road, Plainsboro, New Jersey 08536 U.S.A.

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