**Hemophilia Factor IX Extended Half-Life Products Prior Authorization with Quantity Limit Program Summary**

This program applies to FlexRx Open, FlexRx Closed, GenRx Open, GenRx Closed, Health Insurance Marketplace, KeyRX, and FocusRx formularies.

This is a FlexRx standard and GenRx standard prior authorization.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

**FDA Approved Indications and Dosage**

<table>
<thead>
<tr>
<th>Recombinant Factor IX Concentrates</th>
<th>Indication</th>
<th>Dosing</th>
</tr>
</thead>
</table>
| **Alprolix®** [Coagulation Factor IX (recombinant), Fc Fusion protein] | Adults and children with hemophilia B for:  
- On-demand treatment and control of bleeding episodes  
- Perioperative management of bleeding  
- Routine prophylaxis to reduce the frequency of bleeding episodes  
Limitations of Use: Alprolix is not indicated for induction of immune tolerance in patients with hemophilia B | ● On average, one unit per kilogram body weight of Alprolix increased the circulating Factor IX level by approximately 1% [IU/dL] in adults and children ≥ 6 years of age and by 0.6% [IU/dL] in children under 6 years of age  
● Control/prevention of bleeding episodes and perioperative management:  
  Body weight (kg) x desired increase in plasma factor IX (IU/dL or percent of normal) x Reciprocal of Recovery (IU/kg per IU/dL) = Number of Factor IX IU required  
● See prescribing information for more specific dosing for On-Demand Treatment/Control of Bleeding Episodes and Dosing for Perioperative Management of Bleeding |
| **Idelvion® [Coagulation Factor IX (recombinant), Albumin Fusion Protein (rIX-FP)]** | Children and adults with Hemophilia B (congenital Factor IX deficiency) for:  
- On-demand treatment and control of bleeding episodes  
- Perioperative management of bleeding  
- Routine prophylaxis to reduce the frequency of bleeding episodes  
Limitations of Use: Idelvion is not indicated for immune tolerance induction in patients with Hemophilia B. | • One IU 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  
- Determine the initial dose using the following formula:  
  \[ \text{Required Dose (IU)} = \text{Body Weight (kg)} \times \text{Desired Factor IX rise (% of normal or IU/dL)} \times (1/\text{reciprocal of recovery (IU/kg per IU/dL)}) \]  
- See prescribing information for more specific dosing for On-Demand Treatment/Control of Bleeding Episodes and Dosing for Perioperative Management of Bleeding |
| **Rebinyn® [Coagulation Factor IX (Recombinant), GlycoPEGylated]** | Adults and children with hemophilia B for:  
- On-demand treatment and control of bleeding episodes  
- Perioperative management of bleeding  
Limitations of Use: Rebinyn is not indicated for routine prophylaxis in the treatment of patients with hemophilia B. It is not indicated for immune tolerance induction in patients with hemophilia B. | • On-demand Treatment/Control of Bleeding Episodes and Perioperative management: 40 or 80 IU/kg body weight (see prescribing information for specifics) |

**CLINICAL RATIONALE**

Hemophilia B, also known as Christmas disease, is an X-linked congenital bleeding disorder caused by a deficiency of coagulation factor IX (FIX), with a prevalence of 1 in 30,000 births.\(^{11}\)

Bleeding disorder patients require treatment with clotting factor concentrates for prevention and treatment of bleeding. Prophylaxis is recommended as the optimal treatment modality for individuals with severe hemophilia as recommended by the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation.\(^{12,16}\)
The MASAC suggests the number of doses required for provision of home therapy varies greatly and is dependent upon the type of hemophilia (FVIII, FIX), the level of severity (severe, moderate, mild), the presence of an inhibitor, the prescribed regimen (on-demand, prophylaxis, immune tolerance), the number of bleeding episodes experienced regardless of the prescribed regimen, individual pharmacokinetics, the products utilized, and the level of physical activity. For patients on prophylaxis, a minimum of one major dose and two minor doses should be available in addition to the prophylactic doses utilized monthly. For patients with severe or moderate hemophilia treated on-demand, the number of doses required to be available at home may be based upon historical bleeding patterns, with at least one major and two minor doses added to assure a level of safety.

A major dose is defined as a correction of clotting factor that achieves a level of 60-100+% clotting factor activity that is utilized to treat a bleeding episode that is deemed to require a higher hemostatic level such as occurs when bleeds occur in a target joint, or joint/area with a risk of significant sequelae (e.g., hip, head, GI bleed, etc.). A minor dose is defined as a correction of clotting factor that achieves a level of 30-60% clotting factor activity that is utilized to treat a bleeding episode that is deemed early, in a non-critical area and treatable with a lower hemostatic level (e.g., early non-major joints, small muscle bleeds, and skin/soft tissue, etc.).

**Hemophilia B**

Hemophilia B is characterized as mild (>5% to <40% factor activity), moderate (≥1% to ≤5% factor activity), or severe (<1% factor activity), based on the residual or baseline factor activity level. There are fewer patients that have severe hemophilia B than those with severe hemophilia A (approximately 50% vs 66% respectively).

The Medical and Scientific Advisory Council (MASAC) and National Hemophilia Foundation (NHF) guidelines on treatment of hemophilia B recommend Recombinant FIX (rFIX) products over plasma-derived products as the treatment of choice. All rFIX products are third generation.

In view of the demonstrated benefits of prophylaxis (regular/scheduled administration of clotting factor concentrate to prevent bleeding) begun at a young age in persons with hemophilia B, MASAC recommends that prophylaxis be considered optimal therapy for individuals with severe hemophilia B (factor IX <1%). Prophylactic therapy should be instituted early (prior to the onset of frequent bleeding), with the aim of keeping the trough FIX level above 1% between doses. Optimal dosing and frequency should be determined for each individual by appropriate laboratory monitoring. It is also recommended that individuals on prophylaxis have regular follow-up visits to evaluate joint status, to document any complications such as inhibitors, and to record any bleeding episodes that occur during prophylaxis.

Guidelines for long acting recombinant formulations from the U.K. (2016) state many patient groups were excluded from clinical trials with these formulations (e.g., those with history of inhibitor formation) and there are limited data published on children. Previously untreated patients (PUPs) should not routinely use these formulations, except as part of a clinical trial. In severely affected minimally treated patients (MTPs), switching to a long acting agent can be considered after 50 exposure days (EDs) on a standard half-life clotting factor. In mild/moderate patients switching could be considered after fewer EDs. A limited half-life study should be performed, and patients should be tested for an inhibitor before and at approximately 10 EDs after switching product.
The Canadian National Advisory Committee on blood and blood products lists specific criteria for starting an extended half-life factor product. Criteria for switching to an extended half-life product includes any of the following: evidence that peripheral infusion of standard factor IX concentrates cannot be accomplished without the placement of a central line which could be avoided by using an extended half-life agent, a less than expected half-life of the standard factor IX concentrate with no evidence of inhibitor formation in the patient, to improve compliance with a prophylactic regimen of an extended half-life agent, to improve quality of life by using an extended half-life agent, to decrease frequent breakthrough bleeds or other rationale provided by the treating prescriber.\(^\text{18}\)

The National Hemophilia Foundation states that keeping an accurate treatment log is an essential part of managing bleeding disorders and should include the following information: For bleeding episodes: 1) date and time of the bleed 2) location and severity of the bleed 3) how quickly the bleed was treated 4) the treatment used with brand name, expiration date, lot number, and number of units administered noted 5) additional steps taken to manage the bleed, and 6) level of pain. For infusions not in response to a bleed should include: 1) date and time of the infusion 2) the treatment used with brand name, expiration date, lot number, and number of units administered noted, and 3) reason for the infusion such as prophylaxis, pre-surgery, etc.\(^\text{14}\)

REFERENCES

1. Deleted.
3. Deleted.
4. Deleted.
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7. Deleted.
8. Deleted.
10. Deleted.
Hemophilia Factor IX Extended Half-Life Products Prior Authorization with Quantity Limit

TARGET AGENTS
Extended Half-Life Agents
Alprolix®
Idelvion®
Rebinyn®

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Multisource Code</th>
<th>Quantity Limit</th>
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</thead>
<tbody>
<tr>
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<tr>
<td>250 Unit</td>
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<td>M, N, O, or Y</td>
<td>Determined by patient weight and number of doses</td>
</tr>
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PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Initial Evaluation
The requested agent will be approved for use when ALL of the following are met:
1. The patient has a diagnosis of hemophilia B, is currently bleeding, AND is out of medication (need immediate use)
   OR
2. ALL of the following:
   A. ONE of the following:
i. There is documentation that the patient is currently being treated with the requested agent (starting on samples is not approvable)
   **OR**

ii. The prescriber states the patient is being treated with the requested agent (starting on samples is not approvable) AND is at risk if therapy is changed
   **OR**

iii. The patient has a diagnosis of hemophilia B AND ALL of the following:
   1. If the requested agent is Alprolix or Idelvion, it is being prescribed for one of the following:
      a. Prophylaxis
      **OR**
      b. On-demand use for bleeds
      **OR**
      c. Peri-operative dosing
      **AND**
   2. If the requested agent is Rebinyn, it is being prescribed for ONE of the following:
      a. On-demand use for bleeds only
      **OR**
      b. Perioperative management of bleeding
   **AND**
   3. The prescriber has submitted documentation supporting ONE of the following:
      i. The patient has tried and failed to be adequately controlled on a standard half-life clotting factor agent after at least 50 exposure days
      **OR**
      ii. The patient has poor venous access
      **OR**
      iii. The patient failed to achieve an adequate trough level while on clinically optimal dose and frequency of a standard half-life clotting factor agent
      **OR**
      iv. The prescriber has documented clinical reasoning as to why a standard half-life clotting factor agent cannot be utilized by the patient (convenience alone is not acceptable).
   **AND**
   4. If the client has a preferred agent(s) then ONE of the following:
      i. The patient has tried and had an inadequate response to all of the preferred agent(s)
      **OR**
      ii. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to therapy with all of the preferred agent(s)
   **AND**
   **B.** The prescriber is a specialist in the area of the patient’s diagnosis [e.g., prescriber working in a hemophilia treatment center (HTC), hematologist with hemophilia experience] or has consulted with a specialist in the area of the patient’s diagnosis
   **AND**
   **C.** The prescriber has discussed with the patient the importance of maintaining an accurate treatment log
   **AND**
D. The patient does not have any FDA labeled contraindication(s) to the requested agent

AND

E. The prescriber must provide the **actual prescribed dose** with ALL of the following supporting documentation:
   i. Patient's weight
   ii. Severity of the factor deficiency (i.e., severe is <1% factor activity, moderate is ≥1 to ≤5% factor activity, mild is >5 to 40% factor activity)
   iii. Inhibitor status
   iv. Intended use/regimen: prophylaxis, on-demand, peri-operative

AND

F. ONE of the following:
   i. The patient is not currently using another Factor IX agent (e.g. AlphaNine SD, Alprolix, Bebulin, BeneFIX, Idelvion, Ixinity, Mononine, Profilnine, Rebinyn, Rixubis)
   OR
   ii. The other Factor IX agent will be discontinued prior to beginning therapy with the requested agent
   OR
   iii. The prescriber has submitted documentation supporting the use of more than one unique Factor IX agent

AND

G. ONE of the following:
   i. The dose is within the FDA labeled dosing
   OR
   ii. The prescriber has provided clinical reasoning with supportive documentation for the higher dosing

AND

H. The quantity (number of doses) requested is appropriate based on submitted supportive documentation and intended use (e.g., prophylaxis, on-demand, peri-operative)

**Length of Approval:**
- Immediate Use: up to 2 weeks
- Peri-operative dosing: 1 time
- On-demand: up to 3 months
- Prophylaxis: up to 6 months

**Renewal Evaluation**
The requested agent will be approved when ALL of the following are met:

1. The patient has been previously approved through the Prime Therapeutics Prior Authorization process for the requested agent (if current request is for immediate use or the patient ONLY has previous approval(s) for immediate use, must use Initial Evaluation)

AND

2. The prescriber is a specialist in the area of the patient’s diagnosis [e.g., prescriber working in a hemophilia treatment center (HTC), hematologist with hemophilia experience] or has consulted with a specialist in the area of the patient’s diagnosis

AND

3. ONE of the following:
   A. The patient has shown clinical improvement (e.g. decreased frequency of infusions and/or decreased number of total units used including on-demand infusions)
   OR
B. The patient failed to achieve an adequate trough level while on clinically optimal dose and frequency of a standard half-life clotting factor agent

OR

C. The prescriber has documented clinical reasoning as to why a standard half-life clotting factor cannot be utilized by the patient (convenience alone is not acceptable)

AND

4. The patient does not have any FDA labeled contraindication(s) to the requested agent

AND

5. The prescriber must provide the actual prescribed dose with ALL of the following supporting documentation:
   A. Patient’s weight
   B. Severity of the factor deficiency (i.e., severe is <1% factor activity, moderate is $\geq 1$ to $\leq 5$% factor activity, mild is $>5$ to 40% factor activity)
   C. Inhibitor status
   D. Intended use/regimen: prophylaxis, on-demand, peri-operative

AND

6. ONE of the following:
   A. The prescriber communicated with the patient (via any means) regarding the frequency and severity of the patient’s bleeds and has verified that the patient does not have $>5$ on-demand doses on hand

OR

B. The prescriber has provided information in support of the patient having more than 5 on-demand doses on hand

AND

7. ONE of the following:
   A. The patient is not currently using another Factor IX agent (e.g. AlphaNine SD, Alprolix, Bebulin, BenefIX, Idelvion, Ixinity, Mononine, Profilnine, Rebinyn, Rixubis)

OR

B. The prescriber has submitted documentation supporting the use of more than one unique Factor IX agent

AND

8. ONE of the following:
   A. The dose is within the FDA labeled dosing

OR

B. The prescriber has provided clinical reasoning with supportive documentation for the higher dosing

AND

9. The quantity (number of doses) requested is appropriate based on submitted supportive documentation and intended use (e.g., prophylaxis, on-demand, peri-operative)

**Length of Approval:**

- On-demand: up to 3 months
- Prophylaxis: up to 12 months
Step Therapy Supplement

This program applies to FlexRx Closed, FlexRx Open, GenRx Closed, GenRx Open, Health Insurance Marketplace, FocusRx and KeyRx formularies.

Please note, this does not include or apply to quantity limit questions.

**STEP THERAPY SUPPLEMENT**

**OBJECTIVE**
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

**CONDITIONS FOR APPROVAL**
The requested agent will be approved when ONE of the following are met:

1. **The patient is currently being treated with the requested agent as indicated by ALL of the following:**
   a. A statement by the prescriber that the patient is currently taking the requested agent
   AND
   b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
   AND
   c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

OR

2. **The patient’s medication history include the required prerequisite/preferred agent(s) as indicated by:**
   a. Evidence of a paid claim(s) within the past 999 days
   OR
   b. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days AND the required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event

OR

3. **The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm**

**Length of Approval:** As per program specific criteria