Clinical Policy: Factor IX (Human, Recombinant)
Reference Number: CP.PHAR.218
Effective Date: 05.01.16
Last Review Date: 02.20
Line of Business: Medicaid, HIM

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The following are factor IX products requiring prior authorization: human – AlphaNine SD®, Mononine®, recombinant – Alprolix®, BeneFIX®, Idelvion®, Ixinity®, Rebinyn®, Rixubis®.

FDA Approved Indication(s)
Factor IX products are indicated for patients with hemophilia B (congenital factor IX deficiency or Christmas disease) for the following uses:
- Prevention and control of bleeding (on-demand treatment)
  - Adults and children: AlphaNine SD (≥ 17 years), Alprolix, BeneFIX, Idelvion, Ixinity (≥ 12 years), Mononine, Rebinyn, and Rixubis
- Perioperative management of bleeding
  - Adults and children: Alprolix, BeneFIX, Idelvion, Ixinity (≥ 12 years), Rebinyn, and Rixubis
- Routine prophylaxis to reduce the frequency of bleeding episodes
  - Adults and children: Alprolix, Idelvion, and Rixubis

Limitation(s) of use:
- AlphaNine SD, BeneFIX, and Mononine contain low, non-therapeutic levels of factors II, VII, and X, and, therefore, are not indicated for the treatment of factor II, VII or X deficiencies. They are also not indicated for the reversal of coumarin anticoagulant-induced hemorrhage, nor in the treatment of hemophilia A patients with inhibitors to factor VIII.
- BeneFIX and Mononine are also not indicated in a hemorrhagic state caused by hepatitis-induced lack of production of liver dependent coagulation factors.
- Alprolix, Idelvion, Ixinity, Rebinyn, and Rixubis are not indicated for induction of immune tolerance in patients with hemophilia B.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that AlphaNine SD, Alprolix, BeneFIX, Idelvion, Ixinity, Mononine, Rebinyn, and Rixubis are medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Congenital Hemophilia B (must meet all):
      1. Diagnosis of congenital hemophilia B (factor IX deficiency);
Clinical Policy
Factor IX (Human, Recombinant)

2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 17 years (AlphaNine only) or ≥ 12 years (Ixinity only);
4. Request is for one of the following uses (a, b, or c):
   a. Control and prevention of bleeding episodes;
   b. Perioperative management;
   c. Routine prophylaxis to prevent or reduce the frequency of bleeding episodes (Alprolix, Idelvion, or Rixubis only);
5. Dose does not exceed the FDA approved maximum recommended dose for the relevant indication.

Approval duration: 3 months (surgical/acute bleeding) or 6 months (prophylaxis)

B. Other diagnoses/indications
   1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy
   A. Congenital Hemophilia B (must meet all):
      1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
      2. Member is responding positively to therapy;
      3. If request is for a dose increase, new dose does not exceed the FDA approved maximum recommended dose for the relevant indication.

Approval duration: 3 months (surgical/acute bleeding) or 6 months (prophylaxis)

B. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or
   2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   FDA: Food and Drug Administration
Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s):
  - All products except AlphaNine SD: known history of hypersensitivity reactions, including anaphylaxis, to the product or its excipients*
    *Including mouse or hamster protein for BeneFix, Idelvion, Ixinity, Mononine, Rebinyn, and Rixubis
  - Rixubis: disseminated intravascular coagulation, signs of fibrinolysis
- Boxed warning(s): none reported

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor IX, human</td>
<td>Control and</td>
<td>Minor episodes: 20-30 IU/kg IV twice daily</td>
<td>Bleeding episodes: 100 IU/kg/day</td>
</tr>
<tr>
<td>(AlphaNine SD)</td>
<td>prevention of</td>
<td>Moderate episodes: 25-50 IU/kg IV twice daily</td>
<td>Surgery: 200 IU/kg/day</td>
</tr>
<tr>
<td></td>
<td>bleeding</td>
<td>Major episodes: 30-50 IU/kg IV twice daily for at least 3-5 days, followed</td>
<td></td>
</tr>
<tr>
<td></td>
<td>episodes</td>
<td>by 20 IU/kg IV twice daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Surgery: 50-100 IU/kg IV twice daily before surgery, followed by the same</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>regimen for 7-10 days thereafter</td>
<td></td>
</tr>
<tr>
<td>Factor IX, human</td>
<td></td>
<td>Minor episodes: 20-30 IU/kg IV every 24 hours</td>
<td>Minor episodes: 30 IU/kg/day</td>
</tr>
<tr>
<td>(Mononine)</td>
<td></td>
<td>Major trauma or surgery: 75 IU/kg IV every 18-30 hours</td>
<td>Major trauma or surgery: 750 IU/kg/18 hours</td>
</tr>
<tr>
<td>Factor IX, recombinant</td>
<td>Control and</td>
<td>Minor and moderate episodes: 30-60 IU/dL/kg IV every 48 hours if there is</td>
<td>Bleeding episodes: 100 IU/dL/kg/dose</td>
</tr>
<tr>
<td>(Alprolix)</td>
<td>prevention of</td>
<td>further evidence of bleeding after the first dose</td>
<td>Surgery: 80 IU/dL/kg/dose</td>
</tr>
<tr>
<td></td>
<td>bleeding</td>
<td>Major episodes: 80-100 IU/dL/kg IV initially; consider a repeat dose after</td>
<td></td>
</tr>
<tr>
<td></td>
<td>episodes,</td>
<td>6-10 hours and then every 24 hours for the first</td>
<td></td>
</tr>
<tr>
<td></td>
<td>perioperative</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>management</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug Name</td>
<td>Indication</td>
<td>Dosing Regimen</td>
<td>Maximum Dose</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>-------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>------------------------------</td>
</tr>
</tbody>
</table>
| Factor IX, recombinant (BeneFIX)  | Control and prevention of bleeding episodes, perioperative management | Minor episodes: 20-30 IU/dL/kg IV every 12-24 hours  
Moderate episodes: 25-50 IU/dL/kg IV every 12-24 hours  
Major episodes: 50-100 IU/dL/kg IV every 12-24 hours  
Surgery: 50-100 IU/dL/kg IV every 12-24 hours | 200 IU/dL/kg/day            |
| Factor IX, recombinant (Idelvion) | Control and prevention of bleeding episodes, perioperative management | Minor and moderate episodes: 30-60 IU/dL/kg IV every 48-72 hours  
Major episodes: 60-100 IU/dL/kg IV every 48-72 hours until bleeding stops and healing is achieved; maintenance dose is weekly | Bleeding episodes: 100 IU/dL/kg/48 hours  
Surgery: 80 IU/dL/kg/48 hours |
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
</table>
| **Factor IX, recombinant** (Ixinity) | Control and prevention of bleeding episodes, perioperative management | Minor episodes: 30-60 IU/dL/kg IV every 24 hours  
Moderate episodes: 40-60 IU/dL/kg IV every 24 hours  
Major episodes: 60-100 IU/dL/kg IV every 12-24 hours  
Minor surgery: 50-80 IU/dL/kg IV pre-operatively followed by 50-80 IU/dL/kg IV every 24 hours  
Major surgery: 60-80 IU/dL/kg IV pre-operatively followed by 40-60 IU/dL/kg IV every 8-24 hours for 1-3 days or 30-50 IU/dL/kg IV every 8-24 hours for 4-6 days or 20-40 IU/dL/kg IV every 8-24 hours for 7-14 days | 100 IU/dL/kg/dose |
| **Factor IX, recombinant** (Rixubis) | Control and prevention of bleeding episodes, perioperative management | Minor episodes: 20-30 IU/dL/kg IV every 12-24 hours until healing is achieved  
Moderate episodes: 25-50 IU/dL/kg IV every 12-24 hours | 100 IU/dL/kg/dose |
| **Routine prophylaxis** | | | 55 IU/dL/kg/week |
## Clinical Policy

### Factor IX (Human, Recombinant)

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor IX, human (AlphaNine SD)</td>
<td>On-demand treatment and control of bleeding episodes</td>
<td>40 IU/kg body weight for minor and moderate bleeds, and 80 IU/kg body weight for major bleeds. Additional doses of 40 IU/kg can be given</td>
<td>80 IU/kg/dose</td>
</tr>
<tr>
<td>Factor IX, human (Mononine)</td>
<td>Perioperative management of bleeding</td>
<td>Pre-operative dose of 40 IU/kg body weight for minor surgery, and 80 IU/kg body weight for major surgery. As clinically needed for the perioperative management of bleeding, repeated doses of 40 IU/kg (in 1-3 day intervals) within the first week after major surgery may be administered. Frequency may be extended to once weekly after the first week until bleeding stops and healing is achieved</td>
<td>80 IU/kg pre-operatively; 40 IU/kg/dose after surgery</td>
</tr>
</tbody>
</table>

### VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor IX, human (AlphaNine SD)</td>
<td>Vial: 500, 1,000, 1,500 IU</td>
</tr>
<tr>
<td>Factor IX, human (Mononine)</td>
<td>Vial: 500, 1,000 IU</td>
</tr>
</tbody>
</table>
**Drug Name** | **Availability**
--- | ---
Factor IX, recombinant (Alprolix) | Vial: 250, 500, 1,000, 2,000, 3,000, 4,000 IU
Factor IX, recombinant (BeneFIX) | Vial: 250, 500, 1,000, 2,000, 3,000 IU
Factor IX, recombinant (Idelvion) | Vial: 250, 500, 1,000, 2,000, 3500 IU
Factor IX, recombinant (Ixinity) | Vial: 250, 500, 1,000, 1,500, 2,000, 3,000 IU
Factor IX, recombinant (Rixubis) | Vial: 250, 500, 1,000, 2,000, 3,000 IU
Factor IX, recombinant, glycopegylated (Rebinyn) | Vial: 500, 1,000, 2,000 IU

**VII. References**

**Coding Implications**
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J7194</td>
<td>Factor IX complex, per IU</td>
</tr>
<tr>
<td>J7195</td>
<td>Injection, factor IX (antihemophilic factor, recombinant) per IU, not otherwise specified</td>
</tr>
<tr>
<td>J7200</td>
<td>Injection, factor IX, (antihemophilic factor, recombinant), Rixubis, per IU</td>
</tr>
</tbody>
</table>
**HCPCS Codes** | **Description** | **Date** | **P&T Approval Date**
--- | --- | --- | ---
J7201 | Injection, factor IX, FC fusion protein (recombinant), per IU |  |  
J7202 | Injection, factor IX, albumin fusion protein, (recombinant), Idelvion, per IU. |  |  

**Reviews, Revisions, and Approvals**

Policy split from CP.PHAR.12.Blood Factors and converted to new template. Removed requests for documentation. Added age requirement per PI for Ixinity. Under initial criteria, removed requirement for “history of 2 or more joint bleeds.” Delineated Alprolix and Rixubis for prophylaxis per PIs. Approval period for non-prophylactic use is edited to provide 3 months on initial approval and one 3-month re-auth; approval period for prophylactic use is retained at 6 months initial/6 months continuing therapy. Removed denial based on inhibitor titer of ≥5 BU/mL as PIs do not specify a limit. Reviewed by specialist.  

| Policy split from CP.PHAR.12.Blood Factors and converted to new template. Removed requests for documentation. Added age requirement per PI for Ixinity. Under initial criteria, removed requirement for “history of 2 or more joint bleeds.” Delineated Alprolix and Rixubis for prophylaxis per PIs. Approval period for non-prophylactic use is edited to provide 3 months on initial approval and one 3-month re-auth; approval period for prophylactic use is retained at 6 months initial/6 months continuing therapy. Removed denial based on inhibitor titer of ≥5 BU/mL as PIs do not specify a limit. Reviewed by specialist. | 04.01.16 | 05.16  

Safety information removed. Wording for uses of all blood factor products made consistent across all policies. Added indication for Alprolix and Rixubis for routine prophylaxis. Approval periods across all blood factor policies made consistent. Efficacy statement added to renewal criteria. Hemophilias are specified as “congenital” versus “acquired” across blood factor policies where indicated. Reviewed by specialist-hematology/internal medicine.  

| Safety information removed. Wording for uses of all blood factor products made consistent across all policies. Added indication for Alprolix and Rixubis for routine prophylaxis. Approval periods across all blood factor policies made consistent. Efficacy statement added to renewal criteria. Hemophilias are specified as “congenital” versus “acquired” across blood factor policies where indicated. Reviewed by specialist-hematology/internal medicine. | 04.01.17 | 05.17  

1Q18 annual review:  
- Converted to new template  
- Added Idelvion to the policy under the same coverage criteria as the other recombinant factor IX agents.  
- Specified routine prophylaxis indication is only for certain agents, per package labeling for those agents.  
- Added age limit for AlphaNine per package labeling  
- References reviewed and updated.  

| 1Q18 annual review: | 11.28.17 | 02.18  

1Q 2019 annual review: added HIM-Medical Benefit; no significant changes; added Rebinyn; references reviewed and updated.  

| 1Q 2019 annual review: added HIM-Medical Benefit; no significant changes; added Rebinyn; references reviewed and updated. | 11.08.18 | 02.19  

RT4: added new strength of Idelvion 3,500 IU.  

| RT4: added new strength of Idelvion 3,500 IU. | 06.21.19 |  

1Q 2020 annual review: no significant changes; added HIM line of business; references reviewed and updated.  

| 1Q 2020 annual review: no significant changes; added HIM line of business; references reviewed and updated. | 11.27.19 | 02.20  

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted
CLINICAL POLICY
Factor IX (Human, Recombinant)

standards of medical practice; peer-reviewed medical literature; government agency/program
approval status; evidence-based guidelines and positions of leading national health professional
organizations; views of physicians practicing in relevant clinical areas affected by this clinical
policy; and other available clinical information. The Health Plan makes no representations and
accepts no liability with respect to the content of any external information used or relied upon in
developing this clinical policy. This clinical policy is consistent with standards of medical
practice current at the time that this clinical policy was approved. “Health Plan” means a health
plan that has adopted this clinical policy and that is operated or administered, in whole or in part,
by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a
component of the guidelines used to assist in making coverage decisions and administering
benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage
decisions and the administration of benefits are subject to all terms, conditions, exclusions and
limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy,
contract of insurance, etc.), as well as to state and federal requirements and applicable Health
Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting
may not be the effective date of this clinical policy. This clinical policy may be subject to
applicable legal and regulatory requirements relating to provider notification. If there is a
discrepancy between the effective date of this clinical policy and any applicable legal or
regulatory requirement, the requirements of law and regulation shall govern. The Health Plan
 retains the right to change, amend or withdraw this clinical policy, and additional clinical
policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is
not intended to dictate to providers how to practice medicine. Providers are expected to exercise
professional medical judgment in providing the most appropriate care, and are solely responsible
for the medical advice and treatment of members. This clinical policy is not intended to
recommend treatment for members. Members should consult with their treating physician in
connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent
judgment and over whom the Health Plan has no control or right of control. Providers are not
agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and
distribution of this clinical policy or any information contained herein are strictly prohibited.
Providers, members and their representatives are bound to the terms and conditions expressed
herein through the terms of their contracts. Where no such contract exists, providers, members
and their representatives agree to be bound by such terms and conditions by providing services to
members and/or submitting claims for payment for such services.
Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.