Clinical Policy: Emicizumab-kxwh (Hemlibra)
Reference Number: CP.PHAR.370
Effective Date: 03.01.18
Last Review Date: 11.20
Line of Business: Commercial, HIM, Medicaid

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

Description
Emicizumab-kxwh (Hemlibra®) is a bispecific factor IXa- and factor X-directed antibody.

FDA Approved Indication(s)
Hemlibra is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.

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 Hemlibra is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Congenital Hemophilia A With Inhibitors (must meet all):
      1. Prescribed for routine prophylaxis of bleeding episodes in patients with congenital hemophilia A (factor VIII deficiency);
      2. Prescribed by or in consultation with a hematologist;
      3. Member meets one of the following (a or b):
         a. Member has severe hemophilia (defined as factor VIII level of < 1%);
         b. Member has experienced at least one life-threatening or serious spontaneous bleed (see Appendix D);
      4. Member has inhibitor level ≥ 5 Bethesda units (BU);
      5. Provider confirms that member will discontinue any use of bypassing agents or factor VIII products as prophylactic therapy while on Hemlibra (on-demand usage may be continued);
      6. Dose does not exceed 3 mg/kg per week during the first four weeks of therapy, followed by either 1.5 mg/kg per week, 3 mg/kg once every two weeks, or 6 mg/kg once every four weeks thereafter.
   
   Approval duration: 6 months

   B. Congenital Hemophilia A Without Inhibitors (must meet all):
      1. Prescribed for routine prophylaxis of bleeding episodes in patients with congenital hemophilia A (factor VIII deficiency);
      2. Prescribed by or in consultation with a hematologist;
3. Member meets one of the following (a or b):
   a. Member has severe hemophilia (defined as factor VIII level of < 1%);
   b. Member has experienced at least one life-threatening or serious spontaneous bleed 
      (see Appendix D);

4. Member meets one of the following (a or b):
   a. Failure of a factor VIII product (e.g., Advate®, Adynovate®, Eloctate®) used for 
      routine prophylaxis as assessed and documented by prescriber (see Appendix D), 
      unless contraindicated or clinically significant adverse effects are experienced;
      *Prior authorization is required for factor VIII products
   b. Member has poor venous access, does not tolerate frequent venous access, or has 
      central line or port placement;

5. Provider confirms that member will discontinue any use of factor VIII products as 
   prophylactic therapy while on Hemlibra (on-demand usage may be continued);

6. Member meets one of the following (a or b):
   a. Member has not received treatment with valoctocogene roxaparvovec;
   b. Request is for prophylaxis post-valoctocogene roxaparvovec gene therapy 
      administration;

7. Dose does not exceed 3 mg/kg per week during the first four weeks of therapy, 
   followed by either 1.5 mg/kg per week, 3 mg/kg once every two weeks, or 6 mg/kg 
   once every four weeks thereafter.

   Approval duration: 1 month (if immediately following valoctocogene roxaparvovec 
   gene therapy administration) or 6 months (other indications)

C. 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): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance 
      marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy
   A. Congenital Hemophilia A With or Without Inhibitors (must meet all):
      1. Currently receiving medication via Centene benefit or member has previously met 
         initial approval criteria;
      2. Member meets one of the following (a or b):
         a. Member is responding positively to therapy (see Appendix D) and has not 
            received treatment with valoctocogene roxaparvovec;
         b. Member is responding positively to therapy (see Appendix D) and request is for 
            prophylaxis post-valoctocogene roxaparvovec gene therapy administration;
      3. Provider confirms that member will discontinue any use of bypassing agents (if 
         member has inhibitors) or factor VIII products as prophylactic therapy while on 
         Hemlibra (on-demand usage may be continued);
      4. If request is for a dose increase, new dose does not exceed 3 mg/kg per week during 
         the first four weeks of therapy, followed by either 1.5 mg/kg per week, 3 mg/kg once 
         every two weeks or 6 mg/kg once every four weeks thereafter.

   Approval duration: 6 months (prophylaxis) or 1 month (if following valoctocogene 
   roxaparvovec gene therapy administration)
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): CP.CPA.09 for commercial, 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 policies – CP.CPA.09 for commercial, 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**
   - aPCC: activated prothrombin complex concentrate
   - BU: Bethesda unit
   - FDA: Food and Drug Administration
   - FEIBA: factor eight inhibitor bypassing activity

   **Appendix B: Therapeutic Alternatives**
   Not applicable

   **Appendix C: Contraindications/Boxed Warnings**
   - Contraindication(s): none reported
   - Boxed warning(s): thrombotic microangiopathy and thromboembolism. Cases of thrombotic microangiopathy and thrombotic events were reported when on average a cumulative amount of >100 U/kg/24 hours of activated prothrombin complex concentrate (aPCC) was administered for 24 hours or more to patients receiving Hemlibra prophylaxis. Monitoring is recommended for the development of thrombotic microangiopathy and thrombotic events if aPCC is administered. Discontinuation of aPCC and suspended dosing of Hemlibra is also recommended if symptoms occur.

   **Appendix D: General Information**
   - The elimination half-life of Hemlibra is 27.8 ± 8.1 days. Therefore, the “on-demand” use of Hemlibra for the treatment of acute bleeding episodes is inappropriate.
   - There is insufficient data to support the use of Hemlibra for the treatment of hemophilia B either with or without inhibitors.
   - There is potential for thrombotic microangiopathy and thrombotic events when used concurrently with FEIBA > 100 U/kg/day for 24 hours or more. Additional monitoring is recommended with concomitant use of the two agents. Discontinuation of FEIBA and suspended dosing of Hemlibra is recommended if symptoms occur.
• The World Federation of Hemophilia recommends starting primary prophylaxis before the second clinically evident large joint bleed, and before 3 years of age, to prevent future bleeding episodes and the resulting complications.
• Examples of member responding positively to therapy may include: reduction in number of all bleeds over time, reduction in number of joint bleeds over time, or reduction in number of target joint bleeds over time.
• There are no strict criteria for failing factor VIII product for routine prophylaxis; however, the following reasons are acceptable to fulfill the criteria:
  o Prescriber has documented clinical criteria which support his or her assessment that the member has failed factor VIII therapy;
  o Clinically significant bleeding, hemarthroses, life-threatening bleeding episodes, joint swelling, upcoming surgery/procedure not responding to current therapy, or other clinical assessment as determined by prescriber.
• Examples of life-threatening bleeding episodes include, but are not limited to, bleeds in the following sites: intracranial, neck/throat, or gastrointestinal.
• Examples of serious bleeding episodes include bleeds in the following site: joints (hemarthrosis).
• A spontaneous bleed is defined as a bleeding episode that occurs without apparent cause and is not the result of trauma.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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<tbody>
<tr>
<td>Routine prophylaxis of bleeding episodes</td>
<td>Loading dose of 3 mg/kg SC weekly for four weeks, followed by a maintenance dose of 1.5 mg/kg SC weekly or 3 mg/kg once every two weeks or 6 mg/kg once every four weeks</td>
<td>3 mg/kg/week for the first 4 weeks, followed by 1.5 mg/kg/week thereafter</td>
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VI. Product Availability
Single-dose vials for injection: 30 mg/mL, 60 mg/0.4 mL, 105 mg/0.7 mL, 150 mg/mL

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>HCPHC Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>J7170</td>
<td>Injection, emicizumab-kxwh, 0.5 mg</td>
</tr>
<tr>
<td>Reviews, Revisions, and Approvals</td>
<td>Date</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------------------------</td>
<td>------------</td>
</tr>
<tr>
<td>Policy created</td>
<td>01.16.18</td>
</tr>
<tr>
<td>Criteria updated for new FDA indication: hemophilia A without inhibitors; references reviewed and updated.</td>
<td>11.20.18</td>
</tr>
<tr>
<td>Criteria updated to distinguish between hemophilia A with and without inhibitors; new approval criteria added for hemophilia A without inhibitors.</td>
<td>07.16.19</td>
</tr>
<tr>
<td>1Q 2020 annual review: no significant changes; added HIM line of business from HIM-Medical Benefit; references reviewed and updated.</td>
<td>11.27.19</td>
</tr>
<tr>
<td>Added 1 month approval duration for use post-valoctocogene gene therapy administration in hemophilia A.</td>
<td>04.17.20</td>
</tr>
<tr>
<td>Added requirement for severe hemophilia classification or at least one life-threatening or serious spontaneous bleed for classification of non-severe hemophilia; added requirement for prescriber attestation of not partaking in contact sports.</td>
<td>05.27.20</td>
</tr>
<tr>
<td>Removed requirement for prescriber attestation of not partaking in contact sports.</td>
<td>10.01.20</td>
</tr>
</tbody>
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**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 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.

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**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.

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