INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview
This policy supports medical necessity review for emicizumab-kxwh (Hemlibra®).

Medical Necessity Criteria

Emicizumab-kxwh (Hemlibra®) is considered medically necessary when the following are met:

1. **Hemophilia A with Factor VIII Inhibitors.** Individual meets ALL of the following criteria (A, B, C, D, E and F):
   A. Emicizumab-kxwh (Hemlibra) is being used for routine prophylaxis to prevent or reduce the frequency of bleeding episodes  
   B. Individual meets ONE of the following (i or ii):
      i. Individual has had a positive Factor VIII inhibitor titer greater than 5 Bethesda Units  
      ii. Individual has had a positive Factor VIII inhibitor titer less than or equal to 5 Bethesda Units and meets ONE of the following (a or b):
a. Individual had an anamnestic response (current or past) to Factor VIII product dosing
b. Individual experienced an inadequate clinical response (current or past) to increased Factor VIII product dosing
C. According to the prescriber, the individual will NOT be undergoing immune tolerance induction therapy while receiving Hemlibra
D. Individual meets BOTH of the following regarding the use of bypassing agents (i and ii):
   i. If the individual is currently receiving a bypassing agent for prophylaxis, the bypassing agent therapy will be discontinued the day prior to initiation of Hemlibra
   ii. Prophylactic use of bypassing agents will not occur while using Hemlibra
Note: Use of bypassing agents for the treatment of breakthrough bleeding is permitted. Examples of bypassing agents include NovoSeven® RT (coagulation Factor VIIa [recombinant] for intravenous use), Sevenfact® (Factor VIIa [recombinant]-jncw for intravenous infusion), and FEIBA® (anti-inhibitor coagulant complex for intravenous use).
E. Individual meets BOTH of the following regarding the use of Factor VIII products (i and ii):
   i. If the individual is currently receiving a Factor VIII product for prophylaxis, the Factor VIII product will be discontinued within the initial 4-week loading dose period with Hemlibra
   ii. Prophylactic use of Factor VIII products will not occur while using Hemlibra
Note: Use of Factor VIII products for the treatment of breakthrough bleeding is permitted.
F. Medication is being prescribed by or in consultation with a hemophilia specialist

2. **Hemophilia A without Factor VIII Inhibitors.** Individual meets ALL of the following criteria (A, B, C, D, and E):
   A. Emicizumab-kxwh (Hemlibra) is being used for routine prophylaxis to prevent or reduce the frequency of bleeding episodes.
   B. Individual meets ONE of the following criteria (i or ii):
      i. Individual has severe to moderate severe disease as defined by pretreatment Factor VIII levels ≤ 2% of normal
      ii. Individual has moderate to mild disease as defined by pretreatment Factor VIII levels greater than 2% to < 40% of normal and meets ONE of the following criteria (a, b, or c):
         a. Individual has experienced a severe, traumatic, or spontaneous bleeding episode as determined by the prescriber (for example, a bleed involving the central nervous system)
         b. Individual has hemophilia-related joint damage, has experienced a joint bleed, or has a particular joint that is subject to recurrent bleeding (presence of a target joint)
         c. Individual is in a perioperative situation and/or has an additional clinical scenario regarding bleeding/bleeding risk in which the prescriber determines the use of Hemlibra is warranted (for example, iliopsoas bleeding or severe epistaxis)
   C. Individual meets BOTH of the following regarding the use of bypassing agents (i and ii):
      i. If the individual is currently receiving a bypassing agent for prophylaxis, the bypassing agent therapy will be discontinued the day prior to initiation of Hemlibra
      ii. Prophylactic use of bypassing agents will not occur while using Hemlibra
Note: Use of bypassing agents for the treatment of breakthrough bleeding is permitted. Examples of bypassing agents include NovoSeven® RT (coagulation Factor VIIa [recombinant] for intravenous use), Sevenfact® (Factor VIIa [recombinant]-jncw for intravenous infusion), and FEIBA® (anti-inhibitor coagulant complex for intravenous use).
D. Individual meets BOTH of the following regarding the use of Factor VIII products (i and ii):
   i. If the individual is currently receiving a Factor VIII product for prophylaxis, the Factor VIII product will be discontinued within the initial 4-week loading dose period with Hemlibra
   ii. Prophylactic use of Factor VIII products will not occur while using Hemlibra
Note: Use of Factor VIII products for the treatment of breakthrough bleeding is permitted.
E. Medication is being prescribed by, or in consultation with a hemophilia specialist
When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

**Reauthorization Criteria**
Emicizumab-kxwh (Hemlibra) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response (for example, a reduction in bleeding events, in the severity of bleeding episodes, in the number of bleeding episodes that required treatment, and/or in the number of spontaneous bleeding events).

**Authorization Duration**
Initial approval duration is up to 12 months.

Reauthorization approval duration is up to 12 months.

**Conditions Not Covered**
Emicizumab-kxwh (Hemlibra) is considered experimental, investigational or unproven for ANY other use.

**Coding / Billing Information**
Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Covered when medically necessary when used to report emicizumab-kxwh (Hemlibra):

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J7170</td>
<td>Injection, emicizumab-kxwh, 0.5 mg</td>
</tr>
</tbody>
</table>

**Background**

**OVERVIEW**
Hemlibra, a bispecific Factor IXa- and Factor X-directed antibody, is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in patients aged newborn and older with hemophilia A (congenital Factor VIII deficiency) with or without Factor VIII inhibitors.¹

**FDA Recommended Dosing**
The recommended loading dose of Hemlibra is 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks, followed by a maintenance dose of
- 1.5 mg/kg once every week, or
- 3 mg/kg once every two weeks, or
- 6 mg/kg once every four weeks.

The selection of a maintenance dose should be based on healthcare provider preference with consideration of regimens that may increase patient adherence.

**Disease Overview**
Hemophilia A is an X-linked bleeding disorder caused by a deficiency in Factor VIII.²⁻⁴ In the US, the incidence of hemophilia A in males is 1:5,000 with an estimated 20,000 people in the US living with hemophilia A. Sometimes the disorder is caused by a spontaneous genetic mutation. Males primarily have the disorder and most times females are asymptomatic carriers. The condition is characterized by bleeding in joints, either spontaneously or
in a provoked joint. Bleeding can occur in many different body areas (e.g., muscles, central nervous system, gastrointestinal). Hemarthrosis is the main sign of hemophilia in older children and adults. In newborns and toddlers, bleeding in the head (intracranial hemorrhage and extracranial hemorrhage), bleeding from circumcision, and in the oral cavity are more common. The bleeding manifestations can lead to substantial morbidity, as well as mortality, if not properly treated. Disease severity is usually defined by the plasma levels of Factor VIII and have been classified as follows: severe (levels less than 1% of normal [normal plasma levels are 50 to 100 U/dL]), moderate (levels 1% to 5% of normal), and mild (levels > 5%); phenotypic expression may also vary. Approximately 25% to 30% of patients with hemophilia A have severe deficiency whereas 3% to 13% of patients have moderate to mild deficiency. Diagnoses can be substantially delayed, especially in patients with mild disease, as bleeding may not clinically occur. Higher doses than that typically used for these uses of standard half-life products can be given if the patient develops an inhibitor, which develop in approximately 25% of patients. Products that contains Factor VIII, which are given intravenously, are utilized as well as agents such as Hemlibra.

**Guidelines**

Two documents from the National Hemophilia Foundation Medical and Scientific Advisory Council provide recommendations regarding Hemlibra. In general, Hemlibra has been shown to prevent or reduce the occurrence of bleeding in patients with hemophilia A in adults, adolescent, children and infants, both with and without inhibitors. Subcutaneous administration at more prolonged dosing intervals is viewed as having advantages for some patients compared with intravenous administration of Factor VIII products.

**Safety**

Hemlibra has a Boxed Warning regarding thrombotic microangiopathy and thromboembolism. Cases of thrombotic microangiopathy are thrombotic events were reported when on average a cumulative amount of > 100 U/kg/24 hours of activated prothrombin complex concentrate (aPCC) was given for 24 hours or more to patients receiving Hemlibra prophylaxis. Monitor for the development of thrombotic microangiopathy and thrombotic events when aPCC is given.

**References**