Drug Coverage Policy

Effective Date.....7/15/2025
Coverage Policy Number IP0121
Policy Title.....Hemlibra

Hemophilia – Hemlibra

- Hemlibra® (emicizumab-kxwh subcutaneous injection - Genentech/Roche/Chugai)

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. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. 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

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

Hemlibra is recommended to be given as a loading dose by subcutaneous injection once weekly for the first 4 weeks, followed by a maintenance dose given either once weekly, once every 2 weeks, or once every 4 weeks.[1] Discontinue prophylactic use of bypassing medications the day before starting Hemlibra. The prophylactic use of Factor VIII products may be continued during the first week of Hemlibra prophylaxis. If appropriate, a patient or caregiver may self-inject Hemlibra. Self-administration is not recommended for children < 7 years of age.

Disease Overview
Hemophilia A is an X-linked bleeding disorder primarily impacting males caused by a deficiency in Factor VIII.[2-5] 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. The condition is characterized by bleeding in joints, either spontaneously or in a provoked joint by trauma. Bleeding can occur in many different body areas as well (e.g., muscles, central nervous system). The bleeding manifestations can lead to substantial morbidity such as hemophilic arthropathy. Disease severity is usually defined by the plasma levels or activity of Factor VIII classified as follows: severe (levels < 1% of normal), moderate (levels 1% to 5% of normal), and mild (levels > 5% to < 40% of normal); phenotypic expression may vary. Approximately 50% of patients with hemophilia A are categorized as having severe disease.

Guidelines
Various guidelines discuss Hemlibra.[6-8]

- **National Bleeding Disorders Foundation:** Two documents from the National Bleeding Disorders Foundation's Medical and Scientific Advisory Council (MASAC) provide recommendations regarding Hemlibra.[6,7] In general, Hemlibra has been shown to prevent or reduce the occurrence of bleeding in patients with hemophilia A in adults, adolescents, children and infants, both with and without inhibitors.[6] Factor VIII prophylaxis continuation during the week after initiation of Hemlibra is a reasonable approach.[7] However, because Hemlibra steady-state levels are not achieved until after four weekly doses, it may be reasonable to continue Factor VIII prophylaxis in selected patients based on bleeding history, as well as physical history, until they are ready to initiate maintenance dosing. Factor VIII products may be used for breakthrough bleeding events. Data are limited regarding the use of Hemlibra prophylaxis during immune tolerance induction.
- **World Federation of Hemophilia (WFH):** Guidelines from the WFH regarding hemophilia (2020) feature Hemlibra in a variety of clinical scenarios.[8] It is noted that the subcutaneous administration permits patients to initiate prophylaxis at a very young age. Other key benefits include its long half-life, high efficacy in bleed prevention, and reduction in bleeding episodes in patients with or without inhibitors.

Safety
Hemlibra has a Boxed Warning regarding thrombotic microangiopathy and thromboembolism.[1] 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 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. Discontinue prophylactic use of bypassing agents the day before starting Hemlibra.

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of Hemlibra. Approval is recommended for those who meet the Criteria and Dosing for the listed indications. Extended approvals are allowed for the duration noted below if the patient continues to meet the criteria and dosing for the indication provided. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). Because of the specialized skills required for evaluation and diagnosis of patients treated with Hemlibra as well as the monitoring required for adverse events and long-term efficacy, approval requires Hemlibra to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required where noted in the criteria. Documentation may include, but not limited to, chart notes, laboratory tests, claims records, and/or other information.

Hemlibra is considered medically necessary when the following criteria are met:

FDA-Approved Indications

1. **Hemophilia A with Factor VIII Inhibitors.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, iv, v, and vi):
     - **i.** Patient is using Hemlibra for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; AND
     - **ii.** Patient meets ONE of the following (a or b):
       - **a)** Patient has had a positive Factor VIII inhibitor titer greater than 5 Bethesda Units **[documentation required]**; OR
       - **b)** Patient has had a positive Factor VIII inhibitor titer less than or equal to 5 Bethesda Units **[documentation required]** and meets ONE of the following [(1) or (2)]:
         - **(1)** Patient has had an anamnestic response (current or past) to Factor VIII product dosing; OR
         - **(2)** Patient experienced an inadequate clinical response (current or past) to increased Factor VIII product dosing; AND
     - **iii.** Prescriber attests that the patient will not be undergoing immune tolerance induction therapy while receiving Hemlibra; AND
     - **iv.** Prescriber attests the following regarding use of bypassing agents (a and b):
       - **a)** If the patient is currently receiving a bypassing agent for prophylaxis, the bypassing agent therapy will be discontinued the day prior to initiation of Hemlibra; AND
       - **b)** Prophylactic use of bypassing agents will not occur while using Hemlibra; AND
         Note: Use of bypassing agents for the treatment of breakthrough bleeding is permitted. Examples of bypassing agents include NovoSeven RT (coagulation Factor VIIa [recombinant] intravenous infusion), Sevenfact (Factor VIIa [recombinant]-jncw intravenous infusion), and FEIBA (anti-inhibitor coagulant complex intravenous infusion).
     - **v.** Prescriber attests BOTH of the following regarding Factor VIII products (a and b):
       - **a)** If the patient is currently receiving a Factor VIII product for prophylactic use, the Factor VIII product will be discontinued within the initial 4-week loading dose period with Hemlibra; AND
       - **b)** Prophylactic use of Factor VIII products will not occur while using Hemlibra; AND
         Note: Use of Factor VIII products for the treatment of breakthrough bleeding is permitted.
     - **vi.** Medication is prescribed by or in consultation with a hemophilia specialist; OR
   - **B)** Patient is Currently Receiving Hemlibra. Approve if the patient meets ALL of the following (i, ii, iii, iv, v, and vi)

- **i.** Patient is using Hemlibra for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; AND
- **ii.** Prescriber attests that the patient will not be undergoing immune tolerance induction therapy while receiving Hemlibra; AND
- **iii.** Prescriber attests that prophylactic use of bypassing agents will not occur while using Hemlibra; AND
  Note: Use of bypassing agents for the treatment of breakthrough bleeding is permitted. Examples of bypassing agents include NovoSeven RT (coagulation Factor VIIa [recombinant] intravenous infusion), Sevenfact (Factor VIIa [recombinant]-jncw intravenous infusion), and FEIBA (anti-inhibitor coagulant complex intravenous infusion).
- **iv.** Prescriber attests that prophylactic use of Factor VIII products will not occur while using Hemlibra; AND
  Note: Use of Factor VIII products for the treatment of breakthrough bleeding is permitted.
- **v.** Medication is prescribed by or in consultation with a hemophilia specialist; AND
- **vi.** Patient experienced a beneficial response to therapy according to the prescriber.
  Note: Examples of a beneficial response to therapy include a reduction in bleeding events, in the severity of bleeding episodes, in the number of bleeding events that required treatment, and/or in the number of spontaneous bleeding events.

2. **Hemophilia A without Factor VIII Inhibitors.** Approve for 1 year if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, iv, and v):
      - **i.** Patient is using Hemlibra for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; AND
      - **ii.** Patient meets ONE of the following (a or b):
        - **a)** Patient has severe to moderate severe disease as defined by pretreatment Factor VIII levels ≤ 2% of normal **[documentation required]**; OR
        - **b)** Patient has moderate to mild disease as defined by pretreatment Factor VIII levels greater than 2% to less than 40% of normal **[documentation required]** and meets ONE of the following [(1), (2), or (3)]:
          - **(1)** Patient has experienced a severe, traumatic, or spontaneous bleeding episode as determined by the prescriber; OR
            Note: An example is a bleed involving the central nervous system.
          - **(2)** Patient has hemophilia-related joint damage, has experienced a joint bleed, or has a specific joint that is subject to recurrent bleeding (presence of a target joint); OR
          - **(3)** Patient 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.
            Note: Examples include iliopsoas bleeding or severe epistaxis.
      - **iii.** Prescriber attests that prophylactic use of bypassing agent will not occur while using Hemlibra; AND
        Note: Examples of bypassing agents include NovoSeven RT (coagulation Factor VIIa [recombinant] intravenous infusion), Sevenfact (Factor VIIa [recombinant]-jncw intravenous infusion), and FEIBA (anti-inhibitor coagulant complex intravenous infusion).
      - **iv.** Prescriber attests BOTH of the following regarding Factor VIII products (a and b):
        - **a)** If receiving a Factor VIII product for prophylactic use, therapy will be discontinued within the initial 4-week loading dose period with Hemlibra; AND
        - **b)** Prophylactic use of Factor VIII products will not occur while using Hemlibra; AND

Note: Use of Factor VIII products for the treatment of breakthrough bleeding is permitted.

v. Medication is prescribed by or in consultation with a hemophilia specialist; OR

B) Patient is Currently Receiving Hemlibra. Approve if the patient meets ALL of the following (i, ii, iii, iv, and v):

i. Patient is using Hemlibra for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; AND

ii. Prescriber attests that prophylactic use of bypassing agent will not occur while using Hemlibra; AND
Note: Examples of bypassing agents include NovoSeven RT (coagulation Factor VIIa [recombinant] intravenous infusion), Sevenfact (Factor VIIa [recombinant]-jncw intravenous infusion), and FEIBA (anti-inhibitor coagulant complex intravenous infusion).

iii. Prescriber attests that prophylactic use of Factor VIII product will not occur while using Hemlibra; AND
Note: Use of Factor VIII products for the treatment of breakthrough bleeding is permitted.

iv. Medication is prescribed by or in consultation with a hemophilia specialist; AND

v. Patient experienced a beneficial response to therapy according to the prescriber.
Note: Examples of a beneficial response include a reduction in bleeding events, in the severity of bleeding episodes, in the number of bleeding events that required treatment, and/or in the number of spontaneous bleeding events.

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.

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

Conditions Not Covered

Hemlibra for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

Coding 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.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J7170	Injection, emicizumab-kxwh, 0.5 mg

References

1. Hemlibra® subcutaneous injection [prescribing information]. South San Francisco, CA and Tokyo, Japan: Genentech/Roche and Chugai; January 2024.

2. Mancuso ME, Mahlangu JN, Pipe SW. The changing treatment landscape in haemophilia: from standard half-life clotting factor concentrates to gene editing. *Lancet*. 2021;397:630-640.
3. Croteau SE. Hemophilia A/B. *Hematol Oncol Clin North Am*. 2022;36(4):797-812.
4. Franchini M, Mannucci PM. The more recent history of hemophilia treatment. *Semin Thromb Hemost*. 2022;48(8):904-910.
5. Mannucci PM. Hemophilia treatment innovation: 50 years of progress and more to come. *J Thromb Haemost*. 2023;21(3):403-412.
6. National Bleeding Disorders Foundation. MASAC (Medical and Scientific Advisory Council) recommendations concerning products licensed for the treatment of hemophilia and other selected disorders of the coagulation system (endorsed by the National Bleeding Disorders Foundation Board of Directors on April 11, 2024). MASAC Document #284. Available at: https://www.bleeding.org/sites/default/files/document/files/MASAC-Products-Licensed.pdf. Accessed on May 30, 2024
7. National Bleeding Disorders Foundation. MASAC (Medical and Scientific Advisory Council) recommendations on the use and management of emicizumab-kxwh (Hemlibra®) for hemophilia A with and without inhibitors. MASAC Document #268. Adopted by the National Hemophilia Foundation Board of Directors on April 27, 2022. Available at: https://www.hemophilia.org/sites/default/files/document/files/268_Emicizumab.pdf. Accessed on May 30, 2024.
8. Srivastava A, Santagostino E, Dougall A, et al, on behalf of the WFH guidelines for the management of hemophilia panelists and co-authors. WFH guidelines for the management of hemophilia, 3rd edition. *Hemophilia*. 2020;26(Suppl 6):1-158.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Updated** coverage policy title from *Emicizumab-kxwh* to *Hemophilia – Hemlibra*.	10/1/2024
Selected Revision	**Added** documentation requirements throughout policy.	7/15/2025

The policy effective date is in force until updated or retired.