PRIOR AUTHORIZATION POLICY

POLICY: Hemophilia – Non-Factor Routine Prophylaxis Products – Hemlibra Prior Authorization Policy
- Hemlibra® (emicizumab-kxwh subcutaneous injection – Genentech/Roche/Chugai)

REVIEW DATE: 06/11/2025

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.

CIGNA NATIONAL FORMULARY COVERAGE:

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 adults 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 a genetic bleeding disorder caused by a dysfunction or deficiency in Factor VIII.[2-5] Because hemophilia is an X-linked condition, males are primary impacted. In the US, the incidence of hemophilia A in males is 1:5,000 with an estimated 26,400 people in the US living with hemophilia A. Patients who have hemophilia A are not able to properly form clots in the blood and may bleed for a longer time than normal following injury or surgery. Patients may also experience spontaneous bleeding in muscles, joints, and organs. Bleeds may be life-threatening. A main morbidity is hemophilic arthropathy, which limits mobility. The condition is characterized by bleeding in joints, either spontaneously or in a provoked joint by trauma. The disease can be classified as mild, moderate, or severe based on reduced Factor VIII; approximately 50% of patients with hemophilia A have severe disease. The formation of inhibitors (antibodies) to factor products is a challenging complication as it causes Factor VIII therapies to be ineffective, which increases bleeding frequency and severity. Inhibitors develop in around 30% and 10% of patients with severe hemophilia A and hemophilia B, respectively.

Guidelines

Various guidelines discuss Hemlibra.[6-9]

- **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] Continuation of Factor VIII prophylaxis 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.
- **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.
- **International Society on Thrombosis and Hemostasis:** In 2024, the International Society on Thrombosis and Hemostasis published a practice guideline for the treatment of congenital hemophilia A and B.[9] There are many recommendations. In patients with severe or moderately severe hemophilia A or B without inhibitors, prophylaxis is recommended over episodic treatment of bleeding events (strong recommendation based on moderate-certainty evidence). For hemophilia A for this population, prophylaxis with Hemlibra or Factor VIII concentrates is recommended (conditional recommendation based on very low certainty-evidence). In patients with severe hemophilia A with

inhibitors, prophylaxis with Hemlibra is recommended over bypassing agents (conditional recommendation based on very low-certainty evidence).

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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Hemlibra. All approvals are provided for the duration noted below. 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 hemophilia specialist.

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

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

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, and v):
     - **i.** Patient is using Hemlibra for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; AND
     - **ii.** Patient meets BOTH of the following (a and b):
       - **a)** Factor VIII inhibitor titer testing has been performed within the past 30 days; AND
       - **b)** Patient has a positive test for Factor VIII inhibitors of ≥ 0.6 Bethesda units/mL; AND
     - **iii.** According to the prescriber, prophylactic use of bypassing agents will be discontinued; 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.** Patient is not undergoing immune tolerance induction therapy; AND
     - **v.** The 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. According to the prescriber, prophylactic use of bypassing agents will not occur while receiving 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).

iii. Patient is not undergoing immune tolerance induction therapy; AND

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

v. According to the prescriber, the patient experienced a beneficial response to therapy.

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 bleeds.

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, and iv):

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 meets BOTH of the following [(1) and (2)]:

(1) Factor VIII inhibitor titer testing has been performed within the past 30 days; AND

(2) Patient does not have a positive test for Factor VIII inhibitors of ≥ 1.0 Bethesda units/mL; OR

b) Patient has not received Factor VIII therapy in the past; AND

iii. According to the prescriber, prophylactic use of Factor VIII products will be discontinued no later than 4 weeks following the initial Hemlibra dose; AND

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

iv. The 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, and iv):

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

ii. According to the prescriber, prophylactic use of Factor VIII products will not occur while receiving Hemlibra; AND

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

iii. The medication is prescribed by or in consultation with a hemophilia specialist; AND

iv. According to the prescriber, the patient experienced a beneficial response to therapy.

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 bleeds.

CONDITIONS NOT COVERED

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

is(are) considered not medically necessary for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as newly published data are available):

1. **Concurrent Use with Alhemo (concixumab-mtci subcutaneous injection), Hympavzi (marstacimab-hncq subcutaneous injection), or Qfitlia (fitusiran subcutaneous injection).** These are also non-factor products used for routine prophylaxis in hemophilia A and B.[10-12] There is no evidence to support concomitant use of Hemlibra with Alhemo, Hympavzi, or Qfitlia.

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. Chowdary P, Carcao M, Kenet G, Pipe SW. Haemophilia. *Lancet*. 2025;405(10480):736-750.
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 October 2, 2024). MASAC Document #290. Available at: https://www.bleeding.org/sites/default/files/document/files/MASAC-Products-Licensed.pdf. Accessed on June 6, 2025.
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 June 6, 2025.
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.
9. Rezende SM, Neumann I, Angchaisuksiri P, et al. International Society on Thrombosis and Haemostasis clinical practice guideline for the treatment of congenital hemophilia A and B based on the Grading of Recommendations Assessment, Development, and Evaluation methodology. *J Thromb Haemost*. 2024;22:2629-2652.

10. Alhemo® subcutaneous injection [prescribing information]. Plainsboro, NJ: Novo Nordisk; May 2025.
11. Hympavzi™ subcutaneous injection [prescribing information]. New York, NY: Pfizer; October 2024.
12. Qfitlia™ subcutaneous injection [prescribing information]. Cambridge, MA: Genzyme/Sanofi; March 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	05/24/2023
Annual Revision	No criteria changes.	06/05/2024
Annual Revision	"Non-Factor Routine Prophylaxis Products" was added to the title of the Policy. In addition, the following changes were made: **Hemophilia A with Factor VIII Inhibitors:** In Initial Therapy, requirements were added that Factor VIII inhibitor titer testing has been performed within the past 30 days, and that the patient has a positive test for Factor VIII inhibitors of ≥ 0.6 Bethesda units/mL. The following requirements were deleted: the patient has had a positive Factor VIII inhibitor titer > than 5 Bethesda Units or that the patient has had a positive Factor VIII inhibitor titer ≤ to 5 Bethesda units and either has had an anamnestic response (current or past) to Factor VIII product dosing or that the patient experienced an inadequate clinical response (current or past) to increased Factor VIII product dosing. The requirement that the prescriber attests that if the patient is currently receiving a bypassing agent for prophylaxis, that the bypassing agent therapy will be discontinued the day prior to initiation of Hemlibra was changed to "According to the prescriber, prophylactic use of bypassing agents will be discontinued". The requirement that prophylactic use of bypassing agents will not occur while using Hemlibra was removed. The requirement that the prescriber attests that the patient will not be undergoing immune tolerance induction therapy while receiving Hemlibra was changed to "The patient is not undergoing immune tolerance induction therapy". The requirement that the prescriber attests the following regarding Factor VIII product was deleted: 1) that 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 2) prophylactic use of Factor VIII products will not occur while using Hemlibra; the related Note was also removed. For a Patient Currently Receiving Hemlibra, the requirement that the "Prescriber attests that prophylactic use of bypassing agents will not occur while using Hemlibra" was changed to "According to the prescriber prophylactic use of bypassing agents will not occur while receiving Hemlibra". The requirement that the "prescriber attests that the patient will not be undergoing immune tolerance induction while receiving Hemlibra" was changed to "Patient is not undergoing immune tolerance induction therapy". The requirement was deleted that the prescriber attests that prophylactic use of Factor VIII products will not occur while using Hemlibra was deleted; the related Note was also removed. In the Note regarding examples of a beneficial response, the phrase "to therapy" was added and "spontaneous bleeding events" was changed to "spontaneous bleeds." **Hemophilia A without Factor VIII Inhibitors:** In Initial Therapy, the requirement that the patient either had Factor VIII inhibitor titer testing performed within the past 30 days and the patient does not have a positive test for Factor VIII inhibitors of ≥ 1.0 Bethesda	06/11/2025

	units/mL, or the patient has not received Factor VIII therapy in the past was added. The following requirement was deleted: that the patient either has severe to moderate severe disease as defined by pretreatment Factor VIII levels ≤ 2% of normal or that the patient has moderate to mild disease as defined by pretreatment Factor VIII levels > 2% to < 40% of normal and meets one of the following: 1) patient has experienced a severe, traumatic, or spontaneous bleeding episode as determined by the prescriber, 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. Also, Notes related to these requirements were deleted. The requirement that the prescriber attests that prophylactic use of bypassing agents will not occur while using Hemlibra (along with the related Note) was removed. The requirement regarding use of Factor VIII products was changed to state that "according to the prescriber, prophylactic use of Factor VIII products will be discontinued no later than 4 weeks following the initial Hemlibra dose". Previously, the requirement was that the prescriber attested that if the patient was receiving a Factor VIII product for prophylactic use, that therapy will be discontinued within the initial 4-week loading dose period with Hemlibra and that prophylactic use of Factor VIII products will not occur while using Hemlibra. For a Patient Currently Receiving Hemlibra, the requirement that the prescriber attests that prophylactic use of bypassing agents will not occur while using Hemlibra was deleted, along with the related Note. Regarding prophylactic use of Factor VIII products, the phrase "Prescriber attests" was changed to "According to the prescriber" and the word "using" was changed to "receiving". In the Note regarding examples of a beneficial response, the phrase "to therapy" was added and "spontaneous bleeding events" was changed to "spontaneous bleeds." **Conditions Not Covered** **:** Concurrent Use of Alhemo, Hympavzi, or Qfitlia is not permitted was added.	