UTILIZATION MANAGEMENT MEDICAL POLICY

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

REVIEW DATE: 06/11/2025

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 medical 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Hemlibra is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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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; 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, 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.

Dosing. Approve the following dosing regimens (A and B):

A) Loading dose is 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks; AND

B) The patient is receiving ONE of the following maintenance doses (i, ii, or iii):

i. 1.5 mg/kg by subcutaneous injection once every week, OR

ii. 3 mg/kg by subcutaneous injection once every 2 weeks; OR

iii. 6 mg/kg by subcutaneous injection once every 4 weeks.

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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, 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.

Dosing. Approve the following dosing regimens (A and B):

A) Loading dose is 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks; AND

B) Patient is receiving ONE of the following maintenance doses (i, ii, or iii):

i. 1.5 mg/kg by subcutaneous injection once every week, OR

ii. 3 mg/kg by subcutaneous injection once every 2 weeks; OR

iii. 6 mg/kg by subcutaneous injection once every 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Hemlibra is not recommended in the following situations:

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.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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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.
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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 requirement was deleted that 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; 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, it was added 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 units/mL or the patient has not received Factor VIII therapy in the past. The 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 was removed that the prescriber attests that prophylactic use of bypassing agents will not occur while using Hemlibra (along with the related Note). 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	06/11/2025

	Note regarding examples of a beneficial response, the phrase "to therapy" was added and "spontaneous bleeding events" was changed to "spontaneous bleeds." **Conditions Not Recommended for Approval:** It was added that Concurrent Use of Alhemo, Hympavzi, or Qfitlia is not permitted.	