PRIOR AUTHORIZATION POLICY

POLICY: Hemophilia – Non-Factor Routine Prophylaxis Products – Alhemo Prior Authorization Policy
- Alhemo® (concizumab-mtci subcutaneous injection – NovoNordisk)

REVIEW DATE: 06/11/2025; selected revision 08/13/2025

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

Alhemo, a tissue factor pathway inhibitor antagonist, is indicated for **routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adults and pediatric patients ≥ 12 years of age** with 1) **hemophilia A** (congenital Factor VIII deficiency) **with or without Factor VIII inhibitors**, or 2) **hemophilia B** (congenital Factor IX deficiency) **with or without Factor IX inhibitors**.[1]

Alhemo is recommended to be given as a 1 mg/kg loading dose on Day 1 as a subcutaneous (SC) injection once daily (QD).[1] On Day 2, the maintenance dose of 0.2 mg/kg SC QD is recommended with individualized doses based on Alhemo concentrations obtained at 4 weeks following initiation of treatment. After proper training, Alhemo may be self-administered.

Disease Overview

Hemophilia A and B are genetic bleeding disorders caused by a dysfunction or a deficiency of coagulation Factor VIII and Factor IX, respectively.[2-7] Because hemophilia is an X-linked condition, males are primarily impacted. Patients who have these types of hemophilias 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. The main morbidity is hemophilic arthropathy, which limits mobility. It is estimated that 33,000 males are living with hemophilia in the US; hemophilia A accounts for around 80% of the cases (approximately 26,400 patients) and hemophilia B comprises 20% of cases (around 6,600 patients). Hemophilias are often classified as mild, moderate, or severe based on reduced Factor VIII or IX levels. Approximately 50% and 30% of patients with hemophilia A and hemophilia B, respectively, have severe disease. The formation of inhibitors (antibodies) to factor products is a challenging complication as it causes Factor VIII and Factor IX 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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Alhemo. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Alhemo as well as the monitoring required for adverse events and long-term efficacy, approval requires Alhemo to be prescribed by or in consultation with a hemophilia specialist.

- **Alhemo® (concizumab-mtci subcutaneous injection – NovoNordisk) 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, v, and vi):
     - **i.** Patient is ≥ 12 years of age; AND
     - **ii.** Patient is using Alhemo for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; AND
     - **iii.** 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

iv. 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 coagulation complex intravenous infusion).
v. Patient is not undergoing immune tolerance induction therapy; AND
vi. The medication is prescribed by or in consultation with a hemophilia specialist; OR

B) Patient is Currently Receiving Alhemo. Approve if the patient meets ALL of the following (i, ii, iii, iv, and v):
i. Patient is using Alhemo 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 Alhemo; 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 coagulation complex intravenous infusion).
iii. Patient is not undergoing immune tolerance induction therapy; AND
iv. According to the prescriber, patient experienced a beneficial response to therapy; AND
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.
v. The medication is prescribed by or in consultation with a hemophilia specialist.

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, v, and vi):
i. Patient is ≥ 12 years of age; AND
ii. Patient is using Alhemo for routine prophylaxis to prevent or reduce the frequency of bleeding episodes; AND
iii. Patient has moderately severe to severe hemophilia A as evidenced by a baseline (without Factor VIII replacement therapy) Factor VIII level of ≤ 2%; AND
iv. 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

v. According to the prescriber, prophylactic use of Factor VIII products will be discontinued before the initial Alhemo dose; AND
Note: Use of Factor VIII products for the treatment of breakthrough bleeding is permitted.

vi. The medication is prescribed by or in consultation with a hemophilia specialist; OR

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

i. Patient is using Alhemo 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 Alhemo; AND
Note: Use of Factor VIII products for the treatment of breakthrough bleeding is permitted.

iii. According to the prescriber, patient experienced a beneficial response to therapy; AND
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.

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

3. Hemophilia B with Factor IX 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 ≥ 12 years of age; AND

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

iii. Patient meets BOTH of the following (a and b):

a) Factor IX inhibitor titer testing has been performed within the past 30 days; AND

b) Patient has a positive test for Factor IX inhibitors of ≥ 0.6 Bethesda units/mL; AND

iv. 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 coagulation complex intravenous infusion).

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

vi. The medication is prescribed by or in consultation with a hemophilia specialist; OR

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

i. Patient is using Alhemo 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 Alhemo; 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 coagulation complex intravenous infusion).

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

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

v. The medication is prescribed by or in consultation with a hemophilia specialist.

4. Hemophilia B without Factor IX 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 ≥ 12 years of age; AND

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

iii. Patient has moderately severe to severe hemophilia B as evidenced by a baseline (without Factor IX replacement therapy) Factor IX level of ≤ 2%; AND

iv. Patient meets ONE of the following (a or b):

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

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

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

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

v. According to the prescriber, prophylactic use of Factor IX products will be discontinued before the initial Alhemo dose; AND
Note: Use of Factor IX products for the treatment of breakthrough bleeding is permitted.

vi. The medication is prescribed by or in consultation with a hemophilia specialist; OR

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

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

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

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

iii. According to the prescriber, patient experienced a beneficial response to therapy; AND
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.

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

CONDITIONS NOT COVERED

- **Alhemo® (concizumab-mtci subcutaneous injection – NovoNordisk) 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 new published data are available):**

1. **Concurrent Use with Hemlibra (emicizumab-kxwh 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/or B.[8-10] There is no evidence to support concomitant use of Alhemo with Hemlibra, Hympavzi, or Qfitlia.

REFERENCES

1. Alhemo® subcutaneous injection [prescribing information]. Plainsboro, NJ: Novo Nordisk; July 2025.
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. Croteau SE. Hemophilia A/B. *Hematol Oncol Clin North Am*. 2022;36(4):797-812.
5. Centers for Disease Control and Prevention. Data and statistics on hemophilia. Available at: https://www.cdc.gov/hemophilia/data-research/. Accessed on June 6, 2025.
6. National Bleeding Disorders Foundation. Hemophilia A: An overview of symptoms, genetics, and treatments to help you understand hemophilia A. Available at: https://www.bleeding.org/bleeding-disorders-a-z/types/hemophilia-a. Accessed on June 6, 2025.
7. National Hemophilia Foundation. Hemophilia B. An overview of symptoms, genetics, and treatments to help you understand hemophilia B. Available at: https://www.hemophilia.org/bleeding-disorders-a-z/types/hemophilia-b. Accessed on June 6, 2025.
8. Hemlibra® subcutaneous injection [prescribing information]. South San Francisco, CA and Tokyo, Japan: Genentech/Roche and Chugai; January 2024.
9. Hympavzi™ subcutaneous injection [prescribing information]. New York, NY: Pfizer; October 2024.
10. Qfitlia™ subcutaneous injection [prescribing information]. Cambridge, MA: Genzyme/Sanofi; March 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	01/29/2025

Early 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 and for a Patient Currently Receiving Alhemo, a requirement was added that according to the prescriber, prophylactic use of bypassing agents will be discontinued (for Initial Therapy) or will not occur while receiving Alhemo (for a Patient Currently Receiving Alhemo). A Note was added that use of bypassing agents for the treatment of breakthrough bleeding is permitted and examples of bypassing agents were listed in a Note. Previously, use of bypassing agents for routine prophylaxis was addressed in the Conditions Not Covered. Also, a requirement was added that the patient is not undergoing immune tolerance induction therapy. Previously, this was addressed in Conditions Not Covered. **Hemophilia B with Factor IX Inhibitors:** In Initial Therapy and for a Patient Currently Receiving Alhemo, a requirement was added that according to the prescriber, prophylactic use of bypassing agents will be discontinued (for Initial Therapy) or will not occur while receiving Alhemo (for a Patient Currently Receiving Alhemo). A Note was added that use of bypassing agents for the treatment of breakthrough bleeding is permitted and examples of bypassing agents were listed in a Note. Previously, use of bypassing agents for routine prophylaxis was addressed in the Conditions Not Covered. Also, a requirement was added that the patient is not undergoing immune tolerance induction therapy. Previously, this was addressed in Conditions Not Covered. **Conditions Not Covered:** Regarding Concurrent Use of Non-Factor Routine Prophylaxis Products, all agents are now listed together in one criterion, which now includes Qfitlia. The condition of Concurrent Use of Bypassing Agents for Routine Prophylaxis was removed as this is now addressed in the approval criteria. The condition of Patient Receiving Immune Tolerance Induction Therapy was removed as this is now addressed in the approval criteria.	06/11/2025
Selected Revision	**Hemophilia A without Factor VIII Inhibitors:** This condition and criteria for approval were added to the policy. **Hemophilia B without Factor IX Inhibitors:** This condition and criteria for approval were added to the policy.	08/13/2025