# concizumab-mtci (Alhemo®)

**Medicare Advantage Medical Policy # MA-113**
Original Effective Date: 08/01/2025
Current Effective Date: 08/01/2025

*Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

# When Services May Be Eligible for Coverage

*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Health Plan may consider concizumab-mtci (Alhemo®)‡ for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in patients with hemophilia A or B to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for concizumab-mtci (Alhemo) will be considered when the following criteria are met:

**Initial**

- Patient is ≥ 12 years of age or older; AND
- Patient has a diagnosis of congenital factor VIII deficiency (hemophilia A) or congenital factor IX deficiency (hemophilia B); AND
- Patient has a history of FVIII or FIX inhibitors based on results of the Nijmegen-Bethesda assay (e.g., ≥ 0.6 Bethesda units/mL); AND
- Patient has required treatment with bypassing agents (e.g., anti-inhibitor coagulant complex [FEIBA®], coagulation factor via [NovoSeven®, Sevenfact®])‡ in the past; AND
- Documentation of the patient's current weight is submitted; AND
- According to the prescriber, prophylactic use of factor VIII or IX products, bypassing agents, marstacimab-hncq (Hympavzi™)‡, or emicizumab (Hemlibra®)‡ will not occur while using Alhemo. Note that the use of bypassing agents or factor products for the treatment of breakthrough bleeding is permitted; AND
- Dose will be less than or equal to 0.25 mg/kg/day following an initial loading dose of 1mg/kg.

**Continuation**

- Patient has received an initial authorization for Alhemo from the plan OR has provided documentation of authorization from previous Medicare Advantage plan; AND
- Prescriber attests that the patient has responded to Alhemo as evidenced by a decrease in bleeding episodes or bleeding time; AND
- Dose will be less than or equal to 0.25 mg/kg/day

# When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of concizumab-mtci (Alhemo) when the patient has not required treatment with a bypassing agent or has not submitted documentation of current weight to be **not medically necessary.****

Based on review of available data, the Health Plan considers the continued use of concizumab-mtci (Alhemo) when the patient has not responded to treatment with Alhemo to be **not medically necessary.****

# When Services Are Considered Investigational

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Health Plan considers the use of concizumab-mtci (Alhemo) when the patient selection criteria are not met (with the exception of those denoted above as **not medically necessary****) to be **investigational.***

# Background/Overview

Alhemo is an anti-tissue factor pathway inhibitor (anti-TFPI) approved for the prophylactic treatment of patients 12 years of age and older with hemophilia A or B with inhibitors. It is an alternative to the bypassing agents used for the treatment of hemophilia with inhibitors and has the potential advantage of subcutaneous dosing. Alhemo should be dosed via a weight based dose once daily that is optimized using measurements of drug plasma concentration after 4 weeks of treatment. The maximum dose approved by the FDA is 0.25 mg/kg/day following an initial loading dose of 1 mg/kg. Alhemo is thought to work by reducing the amount of naturally occurring TFPI. This increases the amount of thrombin that is generated, which is expected to reduce the frequency of or prevent bleeding episodes.

Hemophilia is a bleeding disorder that is caused by a deficiency or dysfunction in one of the clotting factors that enables blood to clot. Hemophilia A is caused by a deficiency in factor VIII (FVIII) and hemophilia B is caused by a deficiency in factor IX (FIX). Because the disorder is transmitted on the X-chromosome, it primarily affects males. The incidence of hemophilia is one in every 5,000 males born in the United States, approximately 80% of whom have hemophilia A. 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). The bleeding manifestations can lead to substantial morbidity, as well as mortality, if not properly treated.

Disease severity is usually defined by plasma levels of factor VIII or IX (depending on hemophilia type) and has been classified as follows:

- Severe: levels less than 1% of normal

- Moderate: levels 1-5% of normal
- Mild: levels > 5 to 40% of normal

The main treatment strategy for both types of hemophilia is factor replacement therapy in which administration of the deficient clotting factor is given to achieve adequate hemostasis. Depending on individual patient characteristics such as disease severity and number of bleeds, patients may receive prophylactic factor replacement therapy or only receive treatment in response to a bleed ("on demand therapy"). Many different factor VIII and IX replacement therapies are FDA approved. An alternative to factor prophylaxis in patients with hemophilia A is emicizumab (Hemlibra), a bispecific factor IXa and factor X-directed antibody that is administered subcutaneously.

After administration of factor replacement therapies, some patients may develop an immune response known as a factor inhibitor. These inhibitors are antibodies directed against the deficient factor and are more common among patients with more severe disease. Inhibitors occur in approximately 30% of patients with hemophilia A, usually after the first 20 to 30 days of exposure to factor VIII replacement. The inhibitor interferes with the efficacy of the replacement products and can lead to bleeding, morbidity, decreased quality of life, and mortality. An inhibitor should be suspected if a bleeding event is not efficiently controlled by usual doses of factor replacement therapy or if breakthrough bleeding increases while receiving routine prophylaxis. Inhibitors are generally classified as high-titer ($\geq$ 5 Bethesda units) or low titer (< 5 Bethesda units). Low-titer inhibitors can usually be overcome by using supratherapeutic doses of factor replacement therapy and are usually transient. High-titer inhibitors can be permanent if not eradicated. Bleeding episodes in patients with high-titer inhibitors are often managed with bypassing agents (such as FEIBA and NovoSeven) which generate thrombin by bypassing the specific missing coagulation factor. Immune tolerance therapy may also be used to eradicate inhibitors via frequent and regular exposure to high doses of factor concentrates over several months to years. Successful immune tolerance therapy allows the patient to resume the use of standard factor therapies for prophylaxis and management of bleeding.

# FDA or Other Governmental Regulatory Approval

**U.S. Food and Drug Administration (FDA)**

Alhemo was approved in December 2024 for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients 12 years of age and older with:

- Hemophilia A (congenital factor VIII deficiency) with FVIII inhibitors
- Hemophilia B (congenital factor IX deficiency) with FIX inhibitors

# Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical

practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Alhemo in patients with hemophilia A and B with inhibitors was evaluated in the explorer7 trial, a multi-national, multi-center, open-label, phase 3 trial that investigated the safety and efficacy of Alhemo for routine prophylaxis in 91 adults (58 with hemophilia A with inhibitors and 33 with hemophilia B with inhibitors) and 42 adolescent (22 with hemophilia A with inhibitors and 20 with hemophilia B with inhibitors) male patients with hemophilia A or B with inhibitors who have been prescribed, or are in need of, treatment with bypassing agents. Patients were excluded if they had a history, current signs or symptoms, or at high risk of thromboembolic events, ongoing or planned immune tolerance induction treatment, or planned major surgery.

The trial was comprised of 4 arms, two randomized arms and two non-randomized arms:

- Arms 1 and 2: 52 patients, previously treated on-demand, were randomized 1:2 to no prophylaxis (arm 1: on demand treatment with bypassing agents) or Alhemo prophylaxis (arm 2), with stratification by hemophilia type and prior 24-week bleeding rate
- Arms 3 and 4: 81 additional patients treated with Alhemo prophylaxis

Treatment with Alhemo included a loading dose of 1 mg/kg on the first day and a once-daily dose of 0.20 mg/kg starting on the second day. The dose was individualized to 0.25 mg/kg or 0.15 mg/kg if Alhemo plasma concentration measured once after 4 weeks of treatment was < 200 ng/mL or > 4000 ng/mL, respectively. Measurement of concizumab-mtci plasma concentration after 4 weeks was used to optimize the daily maintenance dose. In the trial, a total of 108 patients received their individualized dose, 1 patient on 0.15 mg/kg, 79 patients on 0.25 mg/kg, and 28 patients on 0.25 mg/kg.

Efficacy was evaluated in hemophilia A and B patients with inhibitors when all patients in arms 1 and 2 had completed at least 24 or at least 32 weeks, by comparing the number of treated bleeding episodes between Alhemo prophylaxis (arm 2) and no prophylaxis (arm 1). Using a negative binomial model, a ratio of the annualized bleeding rates (ABR) was estimated to 0.14 ($p < 0.001$), corresponding to a reduction in ABR of 86% for subjects on Alhemo prophylaxis compared to no prophylaxis. The estimated mean ABR was 1.7 for patients on Alhemo prophylaxis and 11.8 for patients on no prophylaxis.

# References

1. Alhemo [package insert]. Novo Nordisk. Plainsboro, NJ. Updated December 2024.
2. Inhibitors in hemophilia: Mechanisms, prevalence, diagnosis, and eradication. UpToDate. Updated January 2025.
3. Alhemo (concizumab-mtci) New Drug Review. IPD Analytics. Updated February 2025.

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# Policy History

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Current Effective Date: 08/01/2025
05/20/2025 UM Committee review. New policy
Next Scheduled Review Date: 05/2026

# Coding

*The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.*

*The responsibility for the content of the Health Plan Medical Policy Coverage Guidelines is with the Health Plan and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in the Health Plan Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of the Health Plan Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.*

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

| Code Type | Code |
|---|---|
| CPT | No codes |
| HCPCS | C9399, J3590 |
| ICD-10 Diagnosis | All related diagnoses |

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

**NOTICE:** If the Patient's health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

**NOTICE:** Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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**NOTICE:** Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

## Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.