Clinical Policy: Concizumab-mtci (Alhemo)

Reference Number: CP.PHAR.625
Effective Date: 12.20.24
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Concizumab-mtci (Alhemo®) is a tissue factor pathway inhibitor (TFPI) antagonist.

FDA Approved Indication(s)

Concizumab-mtci is indicated 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 [FVIII] deficiency) with FVIII inhibitors
- Hemophilia B (congenital factor IX [FIX] deficiency) with FIX inhibitors

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Alhemo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Congenital Hemophilia A or B With Inhibitors (must meet all)**:**

1. Prescribed for routine prophylaxis of bleeding episodes in members with one of the following diagnoses (a or b):
   a. Congenital hemophilia A (FVIII deficiency);
   b. Congenital hemophilia B (FIX deficiency);
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 12 years;
4. Member has inhibitor level ≥ 5 Bethesda units (BU);
5. Provider confirms that member will discontinue any use of Hemlibra®, bypassing agents, FVIII products, or FIX products as prophylactic therapy while on Alhemo (on-demand usage may be continued);
6. For hemophilia A: Failure of Hemlibra as assessed and documented by prescriber, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix D*);*
   **Prior authorization may be required for Hemlibra*
7. Provider attestation that Concizumab Enzyme-Linked Immunosorbent Assay (ELISA) will be completed 4 weeks post-Alhemo initiation for subsequent dosing by week 8;
8. Documentation of member's current body weight (in kg);

9. Dose does not exceed both of the following (a and b):
    a. One loading dose of 1 mg/kg;
    b. Maintenance dose of 0.25 mg/kg per day.

Approval duration: 2 months ***(12 months for HIM Texas)***

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
    a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
    b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Congenital Hemophilia A or B With Inhibitors (must meet all)**:**

1. Member meets one of the following (a or b):
    a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
    b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy (e.g., reduction in number of all bleeds, joint bleeds, and/or target joint bleeds over time);
3. Documentation of member's current body weight (in kg);
4. One of the following (a or b):
    a. For members who have received ≤ 8 weeks of treatment: Documentation of Alhemo plasma concentration by Concizumab ELISA completed 4 weeks post-Alhemo initiation;
    b. For members who have received > 8 weeks of treatment: Attestation that Alhemo plasma concentration by Concizumab ELISA is being monitored routinely;
5. Member has not had 2 consecutive Alhemo plasma concentrations < 200 ng/mL (*see Appendix D*);
6. New dose does not exceed the following per Alhemo plasma concentration (a, b, or c):
    a. < 200 ng/mL: 0.25 mg/kg per day;
    b. 200 to 4,000 ng/mL: 0.2 mg/kg per day;

c. > 4,000 ng/mL: 0.15 mg/kg per day.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BU: Bethesda unit
FDA: Food and Drug Administration
FVIII: factor VIII
FIX: factor IX
ELISA: enzyme-linked immunosorbent assay
TFPI: tissue factor pathway inhibitor

Appendix B: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Hemlibra® (emicizumab-kxwh)	Loading dose of 3 mg/kg SC weekly for four weeks, followed by a maintenance dose of 1.5 mg/kg SC weekly, or 3 mg/kg SC once every two weeks, or 6 mg/kg SC once every four weeks	Refer to dosing regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): history of known serious hypersensitivity to Alhemo or its components or the inactive ingredients
- Boxed warning(s): none reported

Appendix D: General Information

- There are no strict criteria for failing Hemlibra for routine prophylaxis; however, the following reasons are acceptable to fulfill the criteria:
  - Prescriber has documented clinical criteria which support his or her assessment that the member has failed Hemlibra therapy;
  - Clinically significant bleeding, hemarthroses, life-threatening bleeding episodes, joint swelling, upcoming surgery/procedure not responding to current therapy, or other clinical assessment as determined by prescriber.
- The Concizumab ELISA should be used to measure the Alhemo plasma concentration at four weeks after Alhemo initiation, prior to the administration of the next scheduled dose. Subsequently, the maintenance dose of Alhemo should be individualized ≤ 8 weeks post-Alhemo initiation. Additional measurements of Alhemo plasma concentration should be taken at routine clinical follow-ups provided the member has been on the same maintenance dose for 8 weeks of treatment to ensure steady-state plasma concentration. An FDA-authorized test for the measurement of Alhemo concentration in plasma is not currently available.
  - Per the prescribing information, maintenance of Alhemo plasma concentration above 200 ng/mL is important to decrease the risk of bleeding episodes. If Alhemo plasma concentration remains below 200 ng/mL at two consecutive measurements, the benefits of continued Alhemo treatment should be evaluated versus the potential risk of bleeding events, and alternative therapies if available should be considered.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Routine prophylaxis of bleeding episodes in hemophilia A or B with inhibitors	Loading dose of 1 mg/kg SC one time, followed by a maintenance dose of 0.2 mg/kg SC once daily <u>4 weeks after initiation of treatment</u>: For dose optimization, measure Alhemo plasma concentration by Concizumab ELISA prior to administration of next scheduled dose. Individualize the maintenance dose of Alhemo ≤ 8 weeks after treatment initiation per the following plasma concentrations: • ≤ 200 ng/mL: 0.25 mg/kg SC once daily • 200 to 4,000 ng/mL: 0.2 mg/kg SC once daily • > 4,000 ng/mL: 0.15 mg/kg once daily	1 mg/kg loading dose, followed by 0.25 mg/kg/day

VI. Product Availability

Single-use prefilled pens: 60 mg/1.5 mL (40 mg/mL), 60 mg/1.5 mL (100 mg/mL), 300 mg/3 mL (100 mg/mL)

VII. References

1. Alhemo Prescribing Information. Plainsboro, NJ: Novo Nordisk; December 2024. Available at: https://www.novo-pi.com/alhemo.pdf. Accessed February 24, 2025.
2. Matsushita T, Shapiro A, Abraham A, et al. Phase 3 trial of concizumab in hemophilia with inhibitors. N Engl J Med. 2023;389(9):783-794.
3. Srivastava A, Santagostino E, Dougall A, et al. WFH guidelines for the management of hemophilia. Haemophilia. 2020;26(suppl 6):1-158.
4. Medical and Scientific Advisory Council (MASAC) of the National Bleeding Disorders Foundation (formerly National Hemophilia Foundation): Database of treatment guidelines. Available at https://www.hemophilia.org/healthcare-professionals/guidelines-on-care/masac-documents. Accessed February 24, 2025.
5. Rezende SM, Neumann I, Angchaisuksiri P, et al. International Society on Thrombosis and Haemostasis clinical practice guideline for treatment of congenital hemophilia A and B based on the Grading of Recommendations Assessment, Development, and Evaluation methodology. J Thromb Haemost. 2024;22(9):2629-2652.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3590	Unclassified biologics

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	04.11.23	05.23
2Q 2024 annual review: no significant changes as drug is not yet FDA-approved; references reviewed and updated.	01.12.24	05.24
Drug is now FDA-approved – criteria updated per FDA labeling: maximum dosing revised; for initial request, added requirement for provider attestation that Concizumab ELISA will be completed 4 weeks post-Alhemo initiation; added Hemlibra to list of prophylactic therapies requiring discontinuation confirmation by provider; initial approval duration revised to 2 months; continued approval duration for Medicaid/HIM lines of business revised to 12 months; continued approval duration for Commercial line of business revised to "6 months or to the member's renewal date, whichever is longer;" for continued therapy, added requirements	01.06.25	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
for documentation of Alhemo plasma concentration by Concizumab ELISA within 4-8 weeks of initiation, attestation of routine clinical monitoring of Alhemo concentration thereafter, and exclusion for 2 consecutive Alhemo plasma concentrations < 200 ng/mL; references reviewed and updated.		
2Q 2025 annual review: added Hemlibra redirection for hemophilia A with inhibitors indication; moved Appendix D examples of positive response to therapy into continued therapy criteria section; references reviewed and updated.	02.24.25	05.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.