Clinical Policy: Emicizumab-kxwh (Hemlibra)

Reference Number: CP.PHAR.370
Effective Date: 03.01.18
Last Review Date: 05.22
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

Emicizumab-kxwh (Hemlibra®) is a bispecific factor IXa- and factor X-directed antibody.

FDA Approved Indication(s)

Hemlibra is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII 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 Hemlibra is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Prescribed for routine prophylaxis of bleeding episodes in patients with congenital hemophilia A (factor VIII deficiency);
2. Prescribed by or in consultation with a hematologist;
3. Member has inhibitor level ≥ 5 Bethesda units (BU);
4. Provider confirms that member will discontinue any use of bypassing agents or factor VIII products as prophylactic therapy while on Hemlibra (on-demand usage may be continued);
5. Documentation of member's current body weight (in kg);
6. Dose does not exceed 3 mg/kg per week during the first four weeks of therapy, followed by either 1.5 mg/kg per week, 3 mg/kg once every two weeks, or 6 mg/kg once every four weeks thereafter.

Approval duration: 6 months

B. Congenital Hemophilia A Without Inhibitors (must meet all)**:**

1. Prescribed for routine prophylaxis of bleeding episodes in patients with congenital hemophilia A (factor VIII deficiency);
2. Prescribed by or in consultation with a hematologist;
3. Member meets one of the following (a or b):
   a. Failure of a factor VIII product (e.g., Advate®, Adynovate®, Eloctate®) used for routine prophylaxis as assessed and documented by prescriber (*see Appendix D*),

unless clinically significant adverse effects are experienced or all are contraindicated;
**Prior authorization is required for factor VIII products*

b. Member has poor venous access, does not tolerate frequent venous access, or has central line or port placement;

4. For members who are new to Hemlibra therapy and have not previously used factor VIII products for routine prophylaxis: member meets one of the following (a or b):
   a. Member has severe hemophilia (defined as factor VIII level of < 1%);
   b. Member has experienced at least one life-threatening or serious spontaneous bleed (*see Appendix D*);
5. Provider confirms that member will discontinue any use of factor VIII products as prophylactic therapy while on Hemlibra (on-demand usage may be continued);
6. Documentation of member's current body weight (in kg);
7. Dose does not exceed 3 mg/kg per week during the first four weeks of therapy, followed by either 1.5 mg/kg per week, 3 mg/kg once every two weeks, or 6 mg/kg once every four weeks thereafter.

Approval duration: 6 months

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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 With or Without Inhibitors (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Provider confirms that member has discontinued any use of bypassing agents (if member has inhibitors) or factor VIII products as prophylactic therapy while on Hemlibra (on-demand usage may be continued);
4. Documentation of member's current body weight (in kg);
5. If request is for a dose increase, new dose does not exceed 3 mg/kg per week during the first four weeks of therapy, followed by either 1.5 mg/kg per week, 3 mg/kg once every two weeks or 6 mg/kg once every four weeks thereafter.

Approval duration: 6 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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

aPCC: activated prothrombin complex concentrate
BU: Bethesda unit
FDA: Food and Drug Administration
FEIBA: factor eight inhibitor bypassing activity

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): thrombotic microangiopathy and thromboembolism. 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 administered for 24 hours or more to patients receiving Hemlibra prophylaxis. Monitoring is recommended for the development of thrombotic microangiopathy and thrombotic events if aPCC is administered. Discontinuation of aPCC and suspended dosing of Hemlibra is also recommended if symptoms occur.

Appendix D: General Information

- The elimination half-life of Hemlibra is 27.8 ± 8.1 days. Therefore, the "on-demand" use of Hemlibra for the treatment of acute bleeding episodes is inappropriate.
- There is insufficient data to support the use of Hemlibra for the treatment of hemophilia B either with or without inhibitors.
- There is potential for thrombotic microangiopathy and thrombotic events when used concurrently with FEIBA > 100 U/kg/day for 24 hours or more. Additional monitoring is recommended with concomitant use of the two agents. Discontinuation of FEIBA and suspended dosing of Hemlibra is recommended if symptoms occur.
- The World Federation of Hemophilia recommends starting primary prophylaxis before the second clinically evident large joint bleed, and before 3 years of age, to prevent future bleeding episodes and the resulting complications.
- Examples of member responding positively to therapy may include: reduction in number of all bleeds over time, reduction in number of joint bleeds over time, or reduction in number of target joint bleeds over time.
- There are no strict criteria for failing factor VIII product 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 factor VIII 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.

- Examples of life-threatening bleeding episodes include, but are not limited to, bleeds in the following sites: intracranial, neck/throat, or gastrointestinal.
- Examples of serious bleeding episodes include bleeds in the following site: joints (hemarthrosis).
- A spontaneous bleed is defined as a bleeding episode that occurs without apparent cause and is not the result of trauma.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Routine prophylaxis of bleeding episodes	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 once every two weeks or 6 mg/kg once every four weeks	3 mg/kg/week for the first 4 weeks, followed by 1.5 mg/kg/week thereafter

VI. Product Availability

Single-dose vials for injection: 30 mg/mL, 60 mg/0.4 mL, 105 mg/0.7 mL, 150 mg/mL

VII. References

1. Hemlibra Prescribing Information. South San Francisco, CA: Genentech, Inc.; March 2021. Available at: https://www.gene.com/download/pdf/hemlibra_prescribing.pdf. Accessed November 23, 2021.

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
J7170	Injection, emicizumab-kxwh, 0.5 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.16.18	02.18
Criteria updated for new FDA indication: hemophilia A without inhibitors; references reviewed and updated.	11.20.18	02.19
Criteria updated to distinguish between hemophilia A with and without inhibitors; new approval criteria added for hemophilia A without inhibitors.	07.16.19	08.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2020 annual review: no significant changes; added HIM line of business from HIM-Medical Benefit; references reviewed and updated.	11.27.19	02.20
Added 1 month approval duration for use post-valoctocogene gene therapy administration in hemophilia A.	04.17.20	05.20
Added requirement for severe hemophilia classification or at least one life-threatening or serious spontaneous bleed for classification of non-severe hemophilia; added requirement for prescriber attestation of not partaking in contact sports.	05.27.20	08.20
Removed requirement for prescriber attestation of not partaking in contact sports.	10.01.20	11.20
1Q 2021 annual review: added requirement for documentation of member's body weight for calculation of appropriate dosage; removed references to valoctocogene as it was denied approval by the FDA and likely will not face FDA review again until at least late 2022; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	12.01.20	02.21
1Q 2022 annual review: no significant changes; updated the language on the continuation of therapy requirement that the member "will discontinue" to "has discontinued" use of bypassing agents or factor VIII products as routine prophylaxis while on Hemlibra therapy; references reviewed and updated.	11.23.21	02.22
For hemophilia A with inhibitors: removed the requirement for factor VIII activity level or documentation of bleed history since inhibitors would only be present after previous use of factor VIII products, and substantiation of severe disease is not necessary; for hemophilia A without inhibitors: clarified that the requirement for factor VIII activity level or documentation of bleed history only applies to requests for new starts to Hemlibra without previous factor VIII use for routine prophylaxis.	03.03.22	05.22

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.

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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.