Clinical Policy Title:	emicizumab-kxwh
Policy Number:	RxA.159
Drug(s) Applied:	Hemlibra®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
emicizumab-kxwh (Hemlibra®)	Routine prophylaxis of bleeding episodes	3 mg/kg subcutaneously (SC) once a week weekly for four weeks, followed by a maintenance dose of: 1.5 mg/kg SC once a week; or 3 mg/kg once every two weeks; or 6 mg/kg once every four weeks thereafter	3 mg/kg/week for the first 4 weeks, followed by 1.5 mg/kg/week thereafter

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the provisions of the pharmacy benefit administer by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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. 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
Commercial: 6 months
Medicaid: 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 has severe hemophilia A (severe defined as pre-treatment factor VIII level < 1%);
4. 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 contraindicated or clinically significant adverse effects are experienced;
   **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;
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. 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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Congenital Hemophilia A With or Without Inhibitors (must meet all):

1. Member is currently receiving the medication that has been authorized by RxAdvance or member has previously met initial approval criteria
2. Member is responding positively to therapy (see Appendix D);
3. Provider confirms that member will discontinue any use of bypassing agents (if member has inhibitors) or factor VIII products as prophylactic therapy while on Hemlibra®
4. 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
Commercial: 6 months
Medicaid: 6 months

APPENDIX A: Abbreviation/Acronym Key
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 fulfil 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

References

1. Hemlibra® Prescribing Information. South San Francisco, CA: Genentech, Inc.; June 2020. Available at: https://www.gene.com/download/pdf/hemlibra_prescribing.pdf.Accessed February 19, 2021.
2. WFH Guidelines for the Management of Hemophilia, 3rd edition. Srivastava A, Santagostino E et al. Available at WFH Guidelines for the Management of Hemophilia, 3rd edition - Srivastava - 2020 - Haemophilia - Wiley Online Library. Accessed March 29, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 2. In initial therapy and continued therapy: I.B - Added one Criteria- Member meets one of the following (a or b): a. Member has not received treatment with valoctocogene roxaparvovec; b. Request is for prophylaxis post-valoctocogene roxaparvovec gene therapy administration 3. Updated Approval Duration for initial therapy and continued therapy: I.B- Added 1 month approval duration for use post-valoctocogene gene therapy administration in hemophilia A. 4. Reference reviewed and updated.	06/16/2020	09/14/2020
Policy was reviewed: 1. Updated format of Approval Duration for initial therapy and continued therapy 2. Continued therapy criteria II.A.1 was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance..” 3. Reference reviewed and updated.	02/22/2021	06/10/2021