

POLICY: Hemophilia – Hemlibra® (emicizumab-kxwh injection for subcutaneous use – Genentech)

APPROVAL DATE: 10/02/2019

OVERVIEW

Hemlibra, a bispecific Factor IXa- and Factor X-directed antibody, 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.¹ The recommended dose 3 mg/kg by subcutaneous injection once weekly (QW) for the first 4 weeks, followed by a maintenance dose of 1.5 mg/kg QW; 3 mg/kg once every 2 weeks; or 6 mg/kg once every 4 weeks. Hemlibra bridges activated Factor IX and Factor X to restore the function of missing activated Factor VIII that is required for effective hemostasis.

Disease Overview

Hemophilia A is an X-linked bleeding disorder caused by a deficiency in Factor VIII.²⁻⁴ In the US, the incidence of hemophilia A in males is 1:5,000 with an estimated 20,000 people in the US living with hemophilia A. Sometimes the disorder is caused by a spontaneous genetic mutation. Males primarily have the disorder and most times females are asymptomatic carriers. 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). Hemarthrosis is the main sign of hemophilia in older children and adults. In newborns and toddlers, bleeding in the head (intracranial hemorrhage and extracranial hemorrhage), bleeding from circumcision, and in the oral cavity are more common. The bleeding manifestations can lead to substantial morbidity, as well as mortality, if not properly treated. Disease severity is usually defined by the plasma levels of Factor VIII and have been classified as follows: severe (levels less than 1% of normal [normal plasma levels are 50 to 100 U/dL]), moderate (levels 1% to 5% of normal), and mild (levels > 5%); phenotypic expression may also vary. Approximately 25% to 30% of patients with hemophilia A have severe deficiency whereas 3% to 13% of patients have moderate to mild deficiency. Diagnoses can be substantially delayed, especially in patients with mild disease, as bleeding may not clinically occur. Higher doses than that typically used for these uses of standard half-life products can be given if the patient develops an inhibitor, which develop in approximately 25% of patients.⁵ Products that contains Factor VIII, which are given intravenously, are utilized as well as agents such as Hemlibra.²⁻⁴

Guidelines

The National Hemophilia Foundation Medical and Scientific Advisory Committee (MASAC) [updated April 2018] states that Hemlibra prevents or reduces bleeding in patients with hemophilia A and inhibitors.² MASAC also published a document regarding the recommendations on the use and management of emicizumab-kxwh (Hemlibra) for hemophilia A with and without inhibitors.⁶ Patients both with and without inhibitors should consider Hemlibra therapy. However, based on the clinical trial data, any patient with hemophilia A with an inhibitor who is having frequent bleeding episodes and is on either episodic therapy or bypassing agent prophylaxis will likely derive significant benefit from Hemlibra. Patients receiving bypassing agent prophylaxis with a few bleeding episodes could considered switching to Hemlibra due to factors such as a reduced burden of administration. Infants should be considered for prophylaxis with Hemlibra at any time after birth given the increased risk of intracranial hemorrhage prior to initiation of Factor VIII prophylaxis. It should be noted, however, that data are limited in patients < 6 months of age and the pharmacokinetic exposure is likely to be lower compared with older infants and children.

Safety

Hemlibra has a Boxed Warning regarding thrombotic microangiopathy and thromboembolism.¹ Cases of thrombotic microangiopathy are thrombotic events were reported when on average a cumulative amount of > 100 U/kg/24 hours of activated prothrombin complex concentrate (aPCC) was given for 24 hours or more to patients receiving Hemlibra prophylaxis. Monitor for the development of thrombotic microangiopathy and thrombotic events in aPCC is given.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Hemlibra. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed for the duration noted below if the patient continues to meet the criteria and dosing for the indication provided. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). Because of the specialized skills required for evaluation and diagnosis of patients treated with Hemlibra as well as the monitoring required for adverse events and long-term efficacy, approval requires Hemlibra to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Hemlibra is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. Hemophilia A. Approve for 1 year if the patient meets the following criteria (A and B):

- A) The agent is prescribed by or in consultation with a hemophilia specialist; **AND**
- B) The patient is using Hemlibra for routine prophylaxis.

Dosing. Approve the following dosing regimens:

- A) Loading dose is 3 mg/kg for subcutaneous (SC) injection once weekly for the first 4 weeks;
- B) The patient is receiving one of the following maintenance doses (i, ii or iii):
 - i. 1.5 mg/kg SC once every week, **OR**
 - ii. 3 mg/kg SC once every 2 weeks; **OR**
 - iii. 6 mg/kg SC once every 4 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

1. Other Indications. Coverage is not recommended for circumstances not listed in the Authorization Criteria (FDA-approved indications and Other Uses with Supportive Evidence). Criteria will be updated as new published data are available.

REFERENCES

1. Hemlibra[®] injection for subcutaneous use [prescribing information]. South San Francisco, CA and Tokyo, Japan: Genentech/Roche and Chugai Pharmaceutical; October 2018.
 2. MASAC (Medical and Scientific Advisory Council) recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders (Revised April 2018). MASAC Document #253. Adopted on April 19, 2018. Available at: <https://www.hemophilia.org/node/3675>. Accessed on October 1, 2019.
 3. Peyvandi F, Garagiola I, Young G. The past and future of haemophilia: diagnosis, treatments and its complications. *Lancet*. 2016;388(10040):187-197.
 4. Berntorp E, Shapiro. Modern haemophilia care. *Lancet*. 2012;379:1447-1456.
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5. Valentino LA, Kempton CL, Kruse-Jarres R, et al, on behalf of the International Immune Tolerance Induction Study Investigators. US guidelines for immune tolerance induction in patients with haemophilia a and inhibitors. *Haemophilia*. 2015;21(5):559-567.
6. MASAC (Medical and Scientific Advisory Council) recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders (Revised December 2018). MASAC Document #255. Adopted on December 6, 2018. Available at: <https://www.hemophilia.org/sites/default/files/document/files/masac253.pdf>. Accessed on October 1, 2019.

HISTORY

Type of Revision	Summary of Changes	Approval Date
New policy	--	01/30/2019
Early annual revision	No criteria changes.	10/02/2019