Emicizumab-kxwh (Hemlilbra ®)-Hemophilia A
EOCCO POLICY

Policy Type: PA/ SP Pharmacy Coverage Policy: EOCCO022

Description
Emicizumab-kxwh (Hemlibra) is a monoclonal antibody used for routine prophylaxis to prevent or decrease the frequency of bleeding episodes for patients with hemophilia A with or without inhibitors.

Length of Authorization
- Initial: 6 months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit*‡
Hemlibra, emicizumab-kxwh	30 mg	Routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ages newborn and older with hemophilia A with or without factor VIII inhibitors	Up to 690 mg every 28 days
	60 mg		
	105 mg		
	150 mg		

* Max dose based on 115kg person

‡ Members must be dosed at a frequency that will produce the least wastage per dose based on available vial sizes

Initial Evaluation

I. Emicizumab-kxwh (Hemlibra) may be considered medically necessary when the following criteria below are met:
   A. Member has a confirmed diagnosis of **hemophilia A *with* inhibitors** and the following are met:
      1. Treatment is prescribed by or in consultation with a hematologist; **AND**
      2. Clinical documentation confirming of a history of inhibitors [i.e. high anti-FVIII titer (≥ 5 Bethesda units)]; **AND**
      3. Emicizumab-kxwh (Hemlibra) will be used as routine prophylaxis to reduce the frequency of bleeding episodes; **AND**
      4. Emicizumab-kxwh (Hemlibra) will not be used in combination with Immune Tolerance Induction (ITI); **AND**
      5. At least one of the following is met:
         i. Member has at least two documented episodes of spontaneous bleeding into joints; **OR**
         ii. Member has had an inadequate response to ITI; **OR**
         iii. Member is currently on, or has had an inadequate response to routine prophylaxis with a bypassing agent (e.g. NovoSeven, FEIBA); **OR**
   B. Member has a confirmed diagnosis of **hemophilia A *without* inhibitors** and the following are met:

1. Treatment is prescribed by or in consultation with a hematologist; **AND**
2. Clinical documentation confirming that the member does not have a history of inhibitors [i.e. high anti-FVIII titer (≥ 5 Bethesda units); **AND**
3. Emicizumab-kxwh (Hemlibra) will be used as routine prophylaxis to reduce the frequency of bleeding episodes when one of the following is met:
   i. Member has severe hemophilia A (defined as factor VIII level of <1%); **OR**
   ii. Member has had more than one documented episode of spontaneous bleeding; **AND**
4. Clinical documentation that prior prophylaxis with factor VIII was ineffective for the prevention of bleeding episodes

II. Emicizumab-kxwh (Hemlibra) is considered investigational when used for all other conditions.

Renewal Evaluation

I. Documentation of clinical benefit, including decreased incidence of bleeding episodes or stability of bleeding episodes relative to baseline

Supporting Evidence

I. Hemophilia A (factor VIII deficiency) is an X-linked inherited coagulation factor deficiency that results in lifelong bleeding disorders. The availability of factor replacement products has dramatically improved care for those with hemophilia A. Emicizumab-kxwh (Hemlibra) represents a new mechanism of action for the management of hemophilia A with and without inhibitors.

II. There are varying severities of hemophilia A depending on the level of factor produced by the patient. Hemophilia A is divided into the following categories based on severity:
   i. **Severe**: <1% factor activity (<0.01 IU/mL)
   ii. **Moderate**: Factor activity level ≥ 1% of normal and ≤ 5% of normal (≥ 0.01 and ≤ 0.05 IU/mL)
   iii. **Mild**: Factor activity level >5% of normal and < 40% of normal (> 0.05 and < 0.40 IU/mL

III. There are three general approaches to bleeding management in those with hemophilia A:
   - Episodic ("on demand") treatment that is given at the time of clinically evident bleeding
   - Perioperative management of bleeding for those undergoing elective surgery/procedures
   - Routine prophylaxis is administered in the absence of bleeding to reduce bleeding and long-term complications of bleeding (e.g. arthropathy)

II. The current standard of care for hemophilia A is to replace the deficient coagulation factor either through episodic ("on demand") treatment given at the time of bleeding, or through continuous prophylaxis to prevent bleeding. Recombinant factor VIII products are the treatment

of choice for hemophilia A as recommended by The National Hemophilia Foundation's Medical and Scientific Advisory Council (MASAC).

III. MASAC recommends that prophylaxis be considered optimal therapy for individuals age one and older with severe hemophilia A. Therapy should be initiated early with the goal of keeping the trough factor VIII level above 1% between doses.

IV. For individuals who have had more than one bleeding episode (e.g. two or more bleeds into a target joint, evidence of joint disease by physical exam or radiography), prophylaxis may be appropriate to prevent further morbidity, regardless of factor activity level.

V. People with hemophilia A can develop antibodies to the factor replacement product that can interfere with the ability to treat bleeding and achieve adequate homeostasis. These antibodies, called inhibitors, develop in about 23-30% of people with Hemophilia A. Inhibitors often develop during childhood, especially during the first 50 exposure days to factor, with the greatest risk occurring between the first ten to 20 treatments.

VI. Treatment options for people who develop inhibitors are limited. Immune tolerance induction (ITI) is the main method for inhibitor eradication. It involves the administration of repeated doses of factor to tolerize the individual's immune system to the factor and reduce antibody production.

VII. Other options to treat bleeding in patients with inhibitors include bypassing products [e.g. recombinant activated factor VII (NovoSeven®), factor eight inhibitor bypassing agent (FEIBA®)], plasmapheresis, and high-dose factor infusion. Emicizumab-kxwh (Hemlibra) is indicated for prophylaxis in patients with hemophilia A and inhibitors. Choice of therapy is individualized and dependent on many factors.

VIII. The safety and efficacy of emicizumab-kxwh (Hemlibra) in adult and pediatric patients with inhibitors was established in two Phase 3 trials (HAVEN 1 and HAVEN 2). Patients treated with emicizumab-kxwh (Hemlibra) experienced significantly fewer bleeds compared to patients who received no prophylaxis.

IX. The safety and efficacy of emicizumab-kxwh (Hemlibra) in patients without inhibitors was established in two Phase 3 trials (HAVEN 3 and HAVEN 4). Prophylaxis with emicizumab-kxwh (Hemlibra) resulted in a reduction in bleeding compared to those who received no prophylaxis.

X. Emicizumab-kxwh (Hemlibra) prophylaxis has not been compared to any other treatment option (e.g. bypassing agent, factor VIII replacement); therefore, the comparative safety and efficacy is unknown.

Investigational or Not Medically Necessary Uses

There is no evidence to support the use of emicizumab-kxwh (Hemlibra) in any other condition.

References

1. Hemlibra [Prescribing Information]. South San Francisco, CA: Genentech October 2018

2. National Hemophilia Foundation. Hemophilia A. Available from: https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Hemophilia-A. Accessed July 5, 2019.
3. National Hemophilia Foundation. MASAC Recommendations Concerning products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders. Available from: https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations. Accessed July 5, 2019.
4. Recommendation on the Use and Management of Emicizumab-kxwh (Hemlibra®) for Hemophilia A with and without Inhibitors. Available from: https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations/Recommendation-on-the-Use-and-Management-of-Emicizumab-kxwh-Hemlibra-for-Hemophilia-A-with-and-without-Inhibitors Accessed August 19, 2019
5. UpToDate, Inc. Hemophilia A and B: Routine management including prophylaxis. UpToDate [database online]. Last updated February 11, 2019.

Policy Implementation/Update:

Date Created	August 2019
Date Effective	August 2019
Last Updated	August 2019
Last Reviewed	08/2019

Action and Summary of Changes	Date
New policy created for emicizumab-kxwh (Hemlibra)	08/2019