VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

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

TAC APPROVAL DATE: 10/10/2018

OVERVIEW

Hemlibra is a bispecific factor IXa- and factor X-directed antibody 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.

Clinical Efficacy

The efficacy of Hemlibra for routine prophylaxis in patients with hemophilia A without factor VIII inhibitors was assessed in two clinical trials (HAVEN 3 and HAVEN 4 [adult and adolescent studies]).[1,2] HAVEN 3 was a randomized, multicenter, open-label trial involving 152 male patients ≥ 12 years of age (and ≥ 40 kg) with hemophilia A without Factor VIII inhibitors.[1] Patients had previously received either episodic (on demand) or prophylactic therapy with Factor VIII. Patients received Hemlibra prophylaxis at a dose of 3 mg/kg QW for the first 4 weeks, followed by either 1.5 mg/kg QW or 3 mg/kg once every 2 weeks, or no prophylaxis. Patients receiving prophylaxis could switching to Hemlibra therapy (3 mg/kg once every 2 weeks) after completing at least 24 weeks of prophylaxis and up-titration to 3 mg/kg QW was permitted after 24 weeks for patients on Hemlibra who experienced two or more qualified bleeds. The efficacy of Hemlibra prophylaxis was also compared with patients previously given prophylactic Factor VIII prior to enrollment in a non-interventional study. The annualized bleeding rate for treatment bleeds among patients given Hemlibra 1.5 mg QW (n = 36), Hemlibra 3 mg/kg (n = 35) once every 2 weeks, and no prophylaxis (n = 18) was 1.5, 1.3 and 38.2, respectively; the percentage of patients with zero bleeds was 55.6%, 60%, and 0%, respectively. In the HAVEN 3 intra-patient analysis, use of Hemlibra prophylaxis led to a 68% reduction in the bleed rate for treatment bleeds compared with previous prophylaxis collected in the non-interventional study prior to enrollment ($P < 0.0001$).

The efficacy of Hemlibra for routine prophylaxis in patients with hemophilia A <u>with</u> factor VIII inhibitors was assessed in three clinical trials (HAVEN 1 and HAVEN 4 [adults and adolescents] and HAVEN-2 [pediatric]).[1,3] HAVEN-1 was a randomized, multicenter, open-label clinical trial that investigated the effects of Hemlibra in 109 adult and adolescent male patients (aged 12 to 75 years and > 40 kg) with hemophilia A with factor VIII inhibitors who previously received either episodic (on-demand) or prophylactic treatment with bypassing agents.[1] Patients received weekly Hemlibra prophylaxis 3 mg/kg QW for the first 4 weeks followed by 1.5 mg/kg QW thereafter, or no prophylaxis. Dose up-titration was permitted in some circumstances. The annualized bleeding rate (ABR) for patients who received Hemlibra prophylaxis (n = 35) was 2.9 treated bleeding episodes per year compared with 23.3 treated bleeding episodes per year for patients who did not receive prophylaxis (n = 18). This represents an 87% reduction in the rate of treated bleeds ($P < 0.0001$). Statistically significant differences favoring the Hemlibra group were also noted regarding all bleeds, treated spontaneous bleeds, treated joint bleeds, and treated target joint bleeds. HAVEN-2 was a single-arm, multicenter, open-label clinical trial that assessed Hemlibra in pediatric males (aged < 12 years or 12 to 17 years who weigh < 40 kg) with hemophilia A with factor VIII inhibitors. Patients were given Hemlibra prophylaxis at 3 mg/kg QW for the first 4 weeks followed by 1.5 mg/kg QW thereafter. At the time of the interim analysis, efficacy was assessed in

59 ~~23~~ pediatric patients who were < 12 years old and had been receiving Hemlibra prophylaxis QW for at least 12 weeks. The ABR was 0.3 and 87% of patients receiving Hemlibra did not experience a bleeding episode that required treatment.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Hemlibra. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Hemlibra has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. 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. Mahlangu J, Oldenburg J, Paz-Priel I, et al. Emicizumab prophylaxis in patients who have hemophilia A without inhibitors. *N Engl J Med*. 2018;379(9):811-822.
3. Oldenburg J, Mahlangu JN, Kim B et al. Emicizumab prophylaxis in hemophilia A with inhibitors. *N Engl J Med*. 2017;377(9):809-818.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
New Policy	-	11/16/2017
Early annual revision	Added to the criteria that patients with hemophilia A can also receive approval for the agent if they have a history of factor VIII inhibitors.	01/24/2018
Early annual revision	Based on the new indication for Hemlibra, removed the criteria that the patients has factor VIII inhibitors or a history of factor VIII inhibitors. The criterion were added that Hemlibra is being utilized for routine prophylaxis.	10/10/2018

* For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; TAC – Therapeutic Assessment Committee.