POLICY: Hemophilia – FEIBA® (anti-inhibitor coagulant complex for intravenous use – Takeda)

APPROVAL DATE: 10/02/2019

OVERVIEW

FEIBA, a human plasma fraction with Factor VIII bypassing activity, is indicated for use in hemophilia A and B patients with inhibitors for control and prevention of bleeding episodes, perioperative management, and routine prophylaxis to prevent or reduce the frequency of bleeding episodes.[1] It contains both activated and inactivated forms of Factors II, VII, IX, and X and is thus referred to as activated prothrombin complex concentrate.[1,2] FEIBA is produced from pooled human plasma.[1]

FEIBA is the only commercially available activated prothrombin complex concentrate. Prothrombin complex concentrates are commercially available, and each product has unique pharmacology and labeled use. Profilnine® SD (Factor IX complex for intravenous use) is a three-factor prothrombin complex concentrate containing Factors II, IX, and X, with minimal levels of Factor VII.[3] It is indicated only in hemophilia B. Kcentra® (prothrombin complex concentrate [human] for intravenous use) is a four-factor prothrombin complex concentrate containing inactivated forms of Factors II, VII, IX, and X.[4] Kcentra is labeled for urgent reversal of acquired coagulation factor deficiency induced by vitamin K antagonist (e.g, warfarin) therapy in adults with acute major bleeding or need for an urgent surgery or invasive procedure.

Disease Overview

Hemophilia A is an X-linked bleeding disorder caused by a deficiency in coagulation Factor VIII.[5] The birth prevalence of hemophilia A in the US is approximately 1:6,500 live male births. **Hemophilia B**, caused by deficiency in coagulation Factor IX, is clinically indistinguishable from hemophilia A and is also inherited in an X-linked manner.[6] The birth prevalence is approximately 1:30,000 live male births. Bleeding episodes are treated with plasma-derived or recombinant Factor VIII or Factor IX concentrates. These agents are also given prophylactically for individuals with severe disease.

Approximately 30% of patients with severe hemophilia A and 1 to 3% of patients with severe hemophilia B develop alloimmune inhibitors (antibodies) to Factor VIII or Factor IX concentrate.[5,6] Presence of inhibitors at high titers makes the factor replacement ineffective, and alternative "bypassing" agents are needed to promote hemostasis. FEIBA acts as a bypassing agent by multiple mechanisms which are not fully understood; one major mechanism is supplying activated Factor X, which is normally produced by activated Factors VIII and IX in healthy individuals.[7] Other bypassing agents include NovoSeven RT® (coagulation Factor VIIa [recombinant] for intravenous use) and Hemlibra® (emiczumab-kxwh for subcutaneous use). Hemlibra is a monoclonal antibody that mimics the action of Factor VIII and therefore is only indicated in hemophilia A.[8]

Guidelines

The National Hemophilia Foundation (NHF) Medical and Scientific Advisory Council (MASAC) has recommendations concerning products used for the treatment of hemophilia, as well as guidelines specific to treatment of hemophilia patients with inhibitors (2018 and 2013, respectively).[2,9] FEIBA is supported in these guidelines and noted to be indicated for use in hemophilia patients only when an inhibitor is present.

Dosing Information

Dosing of clotting factor concentrates is highly individualized. MASAC provides recommendations regarding doses of clotting factor concentrate in the home (2016).[10] The number of required doses varies

greatly and is dependent on the severity of the disorder and the prescribed regimen. Per MASAC guidance, patients on prophylaxis should also have a minimum of one major dose and two minor doses on hand for breakthrough episodes in addition to the prophylactic doses used monthly. The guidance also notes that an adequate supply of clotting factor concentrate is needed to accommodate weekends and holidays. Therefore, maximum doses in this policy allow for prophylactic dosing plus three days of acute episodes or perioperative management per 28 days. Doses exceeding this quantity will be reviewed on a case-by-case basis by a Scripts clinician.

Dosing considerations for individual indications are as follows:

- **Hemophilia A with Inhibitors** and **Hemophilia B with Inhibitors:** For routine prophylaxis, a dose of 85 units/kg every other day is recommended.[1] Dosing for acute episodes and perioperative management can range up to 100 units/kg every 6 hours (400 units/kg daily dose).

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of FEIBA. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). 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). All approvals are provided for the duration noted below.

Because of the specialized skills required for evaluation and diagnosis of patients treated with FEIBA as well as the monitoring required for adverse events and long-term efficacy, approval requires these agents to be prescribed by or in consultation with a physician who specializes in the condition being treated.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Hemophilia A with Inhibitors.** Approve for 1 year if FEIBA is prescribed by or in consultation with a hemophilia specialist.

   Dosing. Approve up to a maximum of 2,390 units/kg intravenously per 28 days.

2. **Hemophilia B with Inhibitors.** Approve for 1 year if FEIBA is prescribed by or in consultation with a hemophilia specialist.

   Dosing. Approve up to a maximum of 2,390 units/kg intravenously per 28 days.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

FEIBA 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. FEIBA® for intravenous use [prescribing information]. Lexington, MA: Shire/Takeda; December 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 23, 2018. Available at: https://www.hemophilia.org/sites/default/files/document/files/masac253.pdf. Accessed on July 8, 2019.
3. Profilnine® SD for intravenous use [prescribing information]. Los Angeles, CA: Grifols Biologicals; August 2010.
4. Kcentra® for intravenous use [prescribing information]. Kankakee, IL: CSL Behring LLC; October 2018.
5. Adam MP, Ardinger HH, Pagon RA, et al. GeneReviews®: Hemophilia A [Internet]. Updated June 22, 2017. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1404/. Accessed on June 6, 2019.
6. Konkle BA, Hutson J, Fletcher SN. GeneReviews®: Hemophilia B [Internet]. Updated June 15, 2017. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1495/. Accessed on June 6, 2019.
7. Hoffman M, Dargaud Y. Mechanisms and monitoring of bypassing agent therapy. *J Thromb Haemost.* 2012;10(8):1478-85.
8. Hemlibra® for subcutaneous use [prescribing information]. South San Francisco, CA: Genentech, Inc.: October 2018.
9. MASAC (Medical and Scientific Advisory Council) recommendation regarding prophylaxis with bypassing agents in patients with hemophilia and high titer inhibitors. MASAC Document #220. Adopted on October 6, 2013. Available at: https://www.hemophilia.org/sites/default/files/document/files/masac220.pdf. Accessed on June 6, 2019.
10. MASAC (Medical and Scientific Advisory Council) recommendations regarding doses of clotting factor concentrate in the home. MASAC Document #242. Adopted on June 7, 2016. Available at: https://www.hemophilia.org/sites/default/files/document/files/242.pdf. Accessed on July 22, 2019.

HISTORY

Type of Revision	Summary of Changes	Approval Date
New policy	--	10/02/2019