VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Hematology – Fibrinogen Products Utilization Management Medical Policy
- Fibryga® (fibrinogen [human] intravenous injection – Octapharma)
- RiaSTAP® (fibrinogen concentrate [human] intravenous injection – CSL Behring)

REVIEW DATE: 11/08/2023

OVERVIEW

Fibryga and RiaSTAP, human fibrinogen concentrates, are indicated for treatment of acute bleeding episodes in patients with **congenital fibrinogen deficiency**, including afibrinogenemia and hypofibrinogenemia.[1,2] Both the Fibryga and RiaSTAP prescribing information note that these agents are not indicated for dysfibrinogenemia.

Disease Overview

Congenital deficiencies in fibrinogen (also known as Factor I) can be quantitative or qualitative.[3,4] Quantitative disorders include afibrinogenemia (absence of circulating fibrinogen) and hypofibrinogenemia (low levels of circulating fibrinogen). By contrast, dysfibrinogenemia is a qualitative deficiency in which fibrinogen levels are adequate, but function is impaired. In all cases, clinical presentation is variable; however, bleeding and thromboembolism are possible.

Diagnosis is made by routine coagulation tests in addition to fibrinogen assays.[5] An accurate diagnosis is crucial to distinguish between quantitative and qualitative disorders and guide appropriate treatment. Treatment of fibrinogen deficiency is generally on-demand for acute bleeding episodes, although effective prophylaxis has been used in high-risk patients (e.g., secondary prevention after cerebral hemorrhage, primary prevention during pregnancy to prevent miscarriage).[6,7]

Guidelines

Guidelines are available from the British Committee for Standards in Haemotology (2014); the guideline was written prior to approval of Fibryga.[8] Regarding diagnosis, it is noted that afibrinogenemia and hypofibrinogenemia manifest as prolonged prothrombin time and activated partial thromboplastin time, as well as reduced fibrinogen activity and fibrinogen antigen. Fibrinogen concentrate (e.g., RiaSTAP) may be required to treat or prevent bleeding. Cryoprecipitate is noted to be similarly effective to fibrinogen concentrate but may be associated with transfusion reactions or volume overload.

Dosing Information

Dosing is highly individualized. Guidance specific to congenital fibrinogen deficiency is limited. The National Hemophilia Foundation Medical and Scientific Advisory Council (MASAC) provides recommendations regarding doses of clotting factor concentrate in the home (2016).[9] 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 clinician.

Dosing considerations for individual indications are as follows:

- **Congenital Fibrinogen Deficiency, Including Afibrinogenemia and Hypofibrinogenemia:** Doses of Fibryga and RiaSTAP are individualized based on patient-specific characteristics (e.g., extent of bleeding, clinical condition, laboratory values).[1,2] Treatment with fibrinogen products is repeated as needed to maintain target levels. Based on the product half-lives of approximately three days[1,2], it is not anticipated that dosing more frequent than once daily would typically be needed. On-demand doses up to 100 mg/kg are supported.[7] Prophylactic dosing is not well established; doses up to 100 mg/kg and intervals as frequent as once weekly have been reported.[7]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of fibrinogen products (Fibryga, RiaSTAP). Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. 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 fibrinogen products 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Fibryga and RiaSTAP is recommended in those who meet the following criteria:

FDA-Approved Indication

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1. **Congenital Fibrinogen Deficiency (Factor I Deficiency), Including Afibrinogenemia and Hypofibrinogenemia.** Approve for 1 year if the patient meets the following (A and B):
   - **A)** The diagnosis is confirmed by the following laboratory testing (i and ii):
     - **i.** Prolonged activated partial thromboplastin time and prothrombin time at baseline, as defined by the laboratory reference values; AND
     - **ii.** Lower than normal plasma functional and antigenic fibrinogen levels at baseline, as defined by the laboratory reference values; AND
   - **B)** The requested agent is prescribed by or in consultation with a hematologist.

   Dosing. Approve up to 700 mg/kg intravenously per 28 days.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Fibryga and RiaSTAP is not recommended in the following situations:

1. **Concomitant Use of Fibryga and RiaSTAP.** There are no data to support concomitant use of these products.

2. **Dysfibrinogenemia.** In dysfibrinogenemia, patients have adequate levels of fibrinogen but dysfunctional clotting.[3,4] Fibryga and RiaSTAP are not indicated for dysfibrinogenemia.[1,2]

3. 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. RiaSTAP® intravenous injection [prescribing information]. Kankakee, IL: CSL Behring; June 2021.
2. Fibryga® intravenous injection [prescribing information]. Hoboken, NJ: Octapharma; August 2022
3. De Moerloose P, Casini A, Neerman-Arbez M. Congenital fibrinogen disorders: an update. *Semin Thromb Hemost*. 2013;39(6):585-595.
4. Factor I (Fibrinogen) Deficiency. National Hemophilia Foundation. Available at: https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Other-Factor-Deficiencies/Factor-I. Accessed on November 5, 2023.
5. Casini A, Unda A, Palla R, et al. Diagnosis and classification of congenital fibrinogen disorders: communication from the SSC of the ISTH. *J Thromb Hemost.* 2018;16(9).
6. Congenital afibrinogenemia. National Organization for Rare Disorders. Updated 2018. Available at: https://rarediseases.org/rare-diseases/afibrinogenemia-congenital/. Accessed on November 5, 2023.
7. Palla R, Peyvandi F, Shapiro AD. Rare bleeding disorders: diagnosis and treatment. *Blood.* 2015;125(13):2052-2061.
8. Mumford AD, Ackroyd S, Alikhan R, et al.; BCSH Committee. Guideline for the diagnosis and management of the rare coagulation disorders: a United Kingdom Haemophilia Centre Doctors' Organization guideline on behalf of the British Committee for Standards in Haematology. *Br J Haematol*. 2014 Nov;167(3):304-26.
9. 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 November 5, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	11/02/2022
Annual Revision	No criteria changes.	11/08/2023