CARECONTINUUM™

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: 08/21/2024

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] Fibryga is also FDA-approved for fibrinogen supplementation in bleeding patients with **acquired fibrinogen deficiency**.[2] Both the Fibryga and RiaSTAP prescribing information note that these agents are not indicated for dysfibrinogenemia.[1,2]

Disease Overview

Congenital deficiencies in fibrinogen (also known as Factor I) can be quantitative or qualitative.[3-5] 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.[6,7] 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).

Guidelines

Guidelines are available from the British Committee for Standards in Haemotology (2014); the guideline was written prior to approval of Fibryga.[8] 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]

- **Acquired Fibrinogen Deficiency:** Additional doses of Fibryga may be required after initial administration based on plasma fibrinogen levels or thromboelastometry. Also, doses may need to be adjusted based on the bleeding severity, body weight of the patient, and clinical condition of the patient; multiple doses may be required. Dosing is provided for up to 10 doses per 28 days.

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 indications. 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

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

FDA-Approved Indication

1. Congenital Fibrinogen Deficiency (Factor I Deficiency), Including Afibrinogenemia and Hypofibrinogenemia. Approve for 1 year if the medication is prescribed by or in consultation with a hematologist.

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

II. Coverage of Fibryga is recommended in those who meet the following criteria:

FDA-Approved Indication

1. Acquired Fibrinogen Deficiency. Approve for 1 year if the medication is prescribed by or in consultation with a hematologist.

Dosing. Approve ONE of the following doses (A, B, or C):

A) Patients ≥ 18 years of age: Approve up to 40 g per 28 days given intravenously; OR

B) Patients < 18 years of age and ≥ 12 years of age: Approve up to 500 mg/kg per 28 days given intravenously; OR

C) Children < 12 years of age: Approve up to 700 mg/kg per 28 days given intravenously.

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 infusion [prescribing information]. Kankakee, IL: CSL Behring; June 2021.
2. Fibryga® intravenous infusion [prescribing information]. Paramus, NJ: Octapharma; July 2024.
3. May JE, Wolberg AS, Lim MY. Disorders of fibrinogen and fibrinolysis. *Hematol Oncol Clin North Am*. 2021;35(6):1197-1217.
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 August 19, 2024.
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 August 19, 2024.
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;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 August 14, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	11/08/2023
Early Annual Revision	**Congenital Fibrinogen Deficiency (Factor I Deficiency), Including Afibrinogenemia and Hypofibrinogenemia:** For both Fibryga and RiaSTAP, criteria were removed regarding the diagnosis be confirmed by laboratory testing. This includes the requirement that the patient has a prolonged activated partial thromboplastin time and prothrombin time at baseline (as defined by the laboratory reference values) AND the patient has lower than normal plasma functional and antigenic fibrinogen levels at baseline (as defined by the laboratory reference values). **Acquired Fibrinogen Deficiency:** This was added as a new approval indication for Fibryga only. Dosing was also added.	08/21/2024