PreferredOne®

PRIOR AUTHORIZATION POLICY

POLICY: Hematology – Fibrinogen Products
- Fibryga® (fibrinogen [human] for intravenous use – Octapharma USA)
- RiaSTAP® (fibrinogen concentrate [human] for intravenous use – CSL Behring)

REVIEW DATE: 10/02/2019

OVERVIEW

Fibryga and RiaSTAP, human fibrinongen concentrates, are indicated for treatment of acute bleeding episodes in patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia.[1,2] Fibryga prescribing information notes that it is not indicated for dysfibrinogenemia.

Disease Overview

Congenital fibrinogen deficiencies are caused by mutations in the *FGA*, *FGB*, and *FGG* genes.[3,4] These genes are responsible for creating the polypeptide chains which form the functional fibrinogen (also known as Factor I) hexamer. Afibrinogenemia and hypofibrinogenemia are known as Type I or quantitative deficiencies due to low or absent circulating fibrinogen levels. Afibrinogenemia is very rare (estimated prevalence 1:1,000,000) and is caused by homozygous null mutations. It is often diagnosed in infancy with prolonged umbilical cord bleeding, although later age of onset is possible. Hypofibrinogenemia is caused by heterozygous null mutation and is therefore likely much more prevalent than afibrinogenemia, although the exact incidence is difficult to determine because many patients are asymptomatic.

Dysfibrinogenemia, also known as Type II or qualitative deficiency, is characterized by normal levels of fibrinogen but low functional activity.[3,4] It is caused by missense mutations. Clinical presentation is widely variable and can range from asymptomatic to bleeding or even thromboembolism. Increased thromboembolic risk may be explained by inability of defective fibrinogen to bind thrombin, leading to elevated circulating thrombin levels. Additionally, abnormal fibrinogen may form a fibrin clot that is resistant to plasmin degradation.

Diagnosis is made by routine coagulation tests in addition to fibrinogen assays.[5] An accurate diagnosis is crucial to distinguish between quantitative/type I and qualitative/type II disorders and guide appropriate treatment. Treatment of fibrinogen deficiency in 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] Fibrinogen concentrates are preferred over fresh frozen plasma or cryoprecipitate due to the ability for more precise dosing, less volume overload, and decreased risk of viral contamination.[3,6,7]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of fibrinogen products (Fibryga, RiaSTAP). 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.

RECOMMENDED AUTHORIZATION CRITERIA

PreferredOne®

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

FDA-Approved Indications

1. **Congenital Fibrinogen Deficiency (Factor I Deficiency), Including Afibrinogenemia and Hypofibrinogenemia.** Approve for 1 year if the patient meets the following criteria (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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Fibrinogen products have 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. **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] Prescribing information for Fibryga notes that it is not indicated in dysfibrinogenemia.[2] RiaSTAP should also not be used in these patients due to risk for thromboembolism.[4]

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® for intravenous use [prescribing information]. Kankakee, IL: CSL Behring; October 2017.
2. Fibryga® for intravenous use [prescribing information]. Hoboken, NJ: Octapharma USA; July 2017.
3. De Moerloose P, Casini A, Neerman-Arbez M. Congenital fibrinogen disorders: an update. *Semin Thromb Hemost*. 2013;39(6):585-595. Available at: https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0033-1349222#TB01978-1. Accessed on June 10, 2019.
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 June 10, 2019.
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). Available at: https://onlinelibrary.wiley.com/doi/full/10.1111/jth.14216. Accessed on June 11, 2019.
6. Congenital afibrinogenemia. National Organization for Rare Disorders. Updated 2018. Available at: https://rarediseases.org/rare-diseases/afibrinogenemia-congenital/. Accessed on June 10, 2019.
7. Palla R, Peyvandi F, Shapiro AD. Rare bleeding disorders: diagnosis and treatment. *Blood.* 2015;125(13):2052-2061.

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Fax: 763.847.4010
customerservice@preferredone.com

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You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

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U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
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