Human Fibrinogen Concentrate Medical Drug Criteria with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
3/1/2023

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Fibryga® (fibrinogen concentrate [human]) Lyophilized powder for intravenous injection	• Treatment of acute bleeding episodes in adults and children with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia Fibryga is not indicated for dysfibrinogenemia		1
RiaSTAP® (fibrinogen concentrate [human]) Lyophilized powder for solution for intravenous injection	• Treatment of acute bleeding episodes in pediatric and adult patients with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia RiaSTAP is not indicated for dysfibrinogenemia		2

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Fibrinogen deficiency	Fibrinogen deficiency (Factor I deficiency) is a collective term for three rare inherited fibrinogen deficiencies (afibrinogenemia, hypofibrinogenemia, and dysfibrinogenemia). It affects men and women equally. Fibrinogen helps platelets stick together to form the initial "plug" after an injury. Fibrinogen deficiencies can be quantitative or qualitative, depending on whether the fibrinogen is deficient or defective.(3) Afibrinogenemia is an inherited autosomal recessive disease where fibrinogen is absent. Hypofibrinogenemia can be inherited in either an autosomal recessive or autosomal dominant fashion. In hypofibrinogenemia there is some protein with normal structure present but below levels needed for normal clotting. Dysfibrinogenemia is an inherited autosomal dominant disease in which normal amounts of fibrinogen are manufactured by the liver, but they don't clot properly.(3)

	Afibrinogenemia and hypofibrinogenemia are usually diagnosed in newborns who exhibit excessive bleeding from the umbilical cord and after circumcision. Easy bruising, nose and mouth bleeds, and soft tissue bleeds are common. Joint and muscle bleeds can also occur. Women with afibrinogenemia typically have menorrhagia and difficulties carrying a baby to term because fibrinogen plays a role in embryo implantation. People with dysfibrinogenemia experience prolonged wound healing and are at increased risk of blood clots in the veins.(3) Tests to diagnose factor I deficiency measure the amount of fibrinogen in the blood and the time it takes for the blood to clot during the prothrombin time (PT) test, activated partial thromboplastin time (aPTT) test and thrombin clotting time (TCT) test.(3) Fibrinogen concentrate cannot be used in patients with dysfibrinogenemia because of the risk of blood clots. For patients with dysfibrinogenemia fresh frozen plasma or cryoprecipitate is recommended.(3,4) The National Hemophilia Foundation Medical and Scientific Advisory Council (MASAC) recommends that patients who use on-demand therapy or who infrequently infuse have doses of product available at home to allow for safe patient care; this will provide care in an emergency, as local healthcare facilities cannot be relied upon to stock the appropriate replacement products for these patients. Patients and family members are encouraged to track expiration dates of product on a monthly basis, and doses that are about to expire should be utilized first to prevent waste.(5)
Pain	People with bleeding disorders experience both acute and chronic pain associated with bleeding. Bleeding into soft tissues and joints, whether spontaneous or associated with trauma, often causes acute pain. Repeated bleeding events over time can lead to long-term changes in affected tissues, particularly joints. Chronic arthropathy causes disability and reduces quality of life due to chronic pain.(6) Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain in patients with bleeding disorders. Non-steroidal anti-inflammatory drugs (NSAIDs) should typically be avoided in patients with bleeding disorders, particularly higher doses over extended durations, due to risks of potential short-term interference with platelet function and of GI ulcer formation. Selective COX-2 inhibitors (e.g., celecoxib) appear to be associated with decreased risk of anti-platelet effects and ulcer formation when compared to NSAIDs and may be considered.(6)
Efficacy(1-2)	Fibryga [fibrinogen concentrate (human)] is a human plasma-derived, sterile, purified, virus-inactivated and nanofiltered fibrinogen concentrate. The pharmacodynamics and pharmacokinetics of Fibryga were evaluated in an open-label, prospective, randomized, controlled, two-arm, cross-over study in 22 patients with congenital fibrinogen deficiency (afibrinogenemia). Each subject received a single intravenous 70 mg/kg dose of Fibryga and the comparator product. For each subject, maximum clot firmness (MCF) was determined before (baseline) and one hour after the single dose administration of Fibryga. The results of the study demonstrated that

	the MCF values were significantly higher after administration of Fibryga than at baseline. RiaSTAP [fibrinogen concentrate (human)] is a sterile, heat-treated, lyophilized fibrinogen (coagulation factor I) concentrate powder manufactured from pooled human plasma. Administration of RiaSTAP to patients with congenital fibrinogen deficiency replaces missing or low levels of coagulation factor. Normal levels are in the range of 200 to 450 mg/dL. The efficacy of RiaSTAP is based on maximum clot firmness, a measure of clot structural integrity that reflects the underlying effectiveness of the fibrinogen present to form a fibrin clot. A pharmacokinetic study evaluated single dose PK and maximum clot firmness in subjects with afibrinogenemia. Maximum clot firmness was determined by thromboelastometry testing and was used to demonstrate functional activity of replacement fibrinogen when a fixed dose of RiaSTAP is administered. Clot firmness is a functional parameter that depends on activation of coagulation, fibrinogen content of the sample and polymerization/crosslinking of the fibrin network. Thromboelastometry has been shown to be a functional marker for assessment of fibrinogen content and for effects of fibrinogen supplementation on clinical efficacy. Maximum clot firmness was determined in 13 patients before and one hour after single dose administration of RiaSTAP. RiaSTAP was found to be effective in increasing clot firmness in subjects with congenital fibrinogen deficiency as measured by thromboelastometry. The study results demonstrated that maximum clot firmness values were significantly higher after administration of RiaSTAP that at baseline.
Safety(1-2)	Fibryga is contraindicated in patients with anaphylactic or severe reactions to Fibryga or its components RiaSTAP is contraindicated in patients with known anaphylactic or severe systemic reactions to human plasma-derived products.

REFERENCES

Number	Reference
1	Fibryga Prescribing Information. Octapharma USA Inc. December 2020.
2	RiaSTAP Prescribing Information. CSL Behring LLC. June 2021.
3	National Hemophilia Foundation. Bleeding disorders, types of bleeding disorders, other factor deficiencies, Factor I. Accessed at https://www.hemophilia.org/Bleeding-Disorders/Types-of-Bleeding-Disorders/Other-Factor-Deficiencies/Factor-I.
4	Medical and Scientific Advisory Council (MASAC). MASAC Document 263 Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders. September 2020.
5	Medical and Scientific Advisory Council (MASAC). MASAC Document 242 Recommendations Regarding Doses of Clotting Factor Concentrate in the Home. June 2016.

Number	Reference
6	Medical and Scientific Advisory Committee. MASC Document 260 – Management of Chronic Pain in Persons with Bleeding Disorders: Guidance for Practical Application of The Centers for Disease Control's Opioid Prescribing Guidelines. March 2020.

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Preferred Status	Effective Date
J7177 ; J7178	Fibryga	fibrinogen conc (human) inj approximately	0	M ; N ; O ; Y	N		
J7177 ; J7178	Riastap	fibrinogen conc (human) inj approximately	0	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Days Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
Fibryga	fibrinogen conc (human) inj approximately	0	0.0		0		70 mg/kg per dose		68982-0347-01 ; 68982-0348-01	
Riastap	fibrinogen conc (human) inj approximately	0	0.0		0		70 mg/kg per dose		63833-0891-51 ; 63833-0891-90	

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Fibryga	fibrinogen conc (human) inj approximately	0	Commercial ; HIM ; ResultsRx
Riastap	fibrinogen conc (human) inj approximately	0	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Fibryga	fibrinogen conc (human) inj approximately	0	Commercial ; HIM ; ResultsRx
Riastap	fibrinogen conc (human) inj approximately	0	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has a diagnosis of fibrinogen deficiency (factor I deficiency) AND ONE of the following: A. The patient is currently experiencing a bleed AND BOTH of the following: 1. The patient is out of medication **AND**

Module	Clinical Criteria for Approval
	2. The patient needs to receive a ONE TIME emergency supply of medication **OR** B. ALL of the following: 1. The patient has a fibrinogen level of less than 150 mg/dL **AND** 2. The patient does NOT have dysfibrinogenemia **AND** 3. The requested agent will be used as on-demand treatment to control acute bleeding episodes **AND** 4. The prescriber has communicated with the patient (via any means) and has verified that the patient does NOT have more than 5 on-demand doses on hand AND 2. The prescriber is a specialist (e.g. hematologist) in the area of the patient's diagnosis or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 3. The patient will NOT be using the requested agent in combination with nonsteroidal anti-inflammatory agents (NSAIDs) (e.g., aspirin, ibuprofen) **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 5. ONE of the following: A. The prescriber communicated with the patient (via any means) and has verified that the patient does not have greater than 5 on demand doses **OR** B. The prescriber has provided information in support of the patient having more than 5 on-demand doses on hand **AND** 6. ONE of the following: A. The requested quantity (dose) does NOT exceed the program quantity limit defined by BOTH of the following: 1. The requested dose is within the FDA labeled dosing **AND** 2. The requested quantity (number of doses) is appropriate based on intended use (e.g., on-demand) **OR** B. The prescriber has provided clinical reasoning for exceeding the defined program quantity limit (dose and/or number of doses) **Length of Approval:** One time emergency use: 1 time On-demand treatment: 3 months