PHARMACY COVERAGE GUIDELINE

CORIFACT® [(factor XIII concentrate (human)]
TRETTEN® [(coagulation factor XIII A-subunit (recombinant)]
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Corifact [(factor XIII concentrate (human)], Tretten [(coagulation factor XIII A-subunit (recombinant)], and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Hematologist

  2. Individual has a confirmed diagnosis of **ONE** of the following:
     a. **For Corifact**: Routine prophylactic treatment and perioperative management of surgical bleeding in individual with congenital Factor XIII deficiency

     b. **For Tretten**: Prophylaxis of bleeding in individual with congenital Factor XIII-A subunit deficiency

3. Individual baseline Factor level is below the lower limit of the reference range or not detectable

4. Tretten is not for use in patients with congenital factor XIII-B subunit deficiency

5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

6. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Corifact [(factor XIII concentrate (human)], Tretten [(coagulation factor XIII A-subunit (recombinant)], and/or generic equivalent (if available) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Hematologist

2. Individual has a confirmed diagnosis of **ONE** of the following:
    a. **For Corifact**: Routine prophylactic treatment and perioperative management of surgical bleeding in individual with congenital Factor XIII deficiency
    b. **For Tretten**: Prophylaxis of bleeding in individual with congenital Factor XIII-A subunit deficiency

3. Individual's condition has responded while on therapy with response defined as the following:
    a. For Corifact: FXIII activity trough level is 5-20%
    b. For Tretten: FXIII activity trough level is at or above 10%

4. Tretten is not for use in patients with congenital factor XIII-B subunit deficiency

5. Individual has been adherent with the medication

6. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

7. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as:
    a. Hypersensitivity or allergic reaction
    b. Thrombosis

8. Individual is not currently taking any other drugs which cause severe adverse reactions or any significant drug interactions requiring discontinuation

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Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
2. **Off-Label Use of Cancer Medications**

Description:

Corifact [(factor XIII concentrate (human)] is indicated for adult and pediatric individuals with congenital Factor XIII (FXIII) deficiency for routine prophylactic treatment and peri-operative management of surgical bleeding. Tretten [(coagulation factor XIII A-subunit (recombinant)] is indicated for routine prophylaxis of bleeding in patients with congenital factor XIII A-subunit deficiency. Tretten is not for use in individuals with congenital factor XIII B-subunit deficiency.

FXIII is the terminal enzyme in the blood coagulation cascade. When activated by thrombin at the site of vessel wall injury, FXIII plays an important role in the maintenance of hemostasis through cross-linking of fibrin and other proteins in the fibrin clot.

The factor XIII enzyme is a heterotetramer consisting of two catalytic A subunits and two B subunits. Most reported cases of factor XIII deficiency are due to variants affecting the A subunit; rare cases due to variants affecting the B subunit have been reported.

The clinical symptoms of FXIII deficiency include delayed wound healing, recurrent miscarriage, bleeding of soft tissue, and life-threatening spontaneous CNS bleeding, which is the primary cause of death in affected individuals. Bleeding from Factor XIII deficiency can be treated with recombinant factor XIII A subunit or a plasma-derived factor XIII concentrate. If one of these is not available, a plasma product such as Fresh Frozen Plasma (FFP; solvent/detergent [S/D] treated if available) or cryoprecipitate may be used.

Factor XIII deficiency confers a risk of severe bleeding and early pregnancy loss. For factor XIII deficient patients with frequent bleeding or activity level ≤5 percent, monthly prophylaxis with recombinant factor XIII A subunit or factor XIII concentrate should be used. Individuals with B subunit deficiency (which is extremely rare) should receive the plasma-derived concentrate. Alternatives for those without access to these concentrates include FFP (S/D treated if available) or cryoprecipitate.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

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Resources:

Corifact [(factor XIII concentrate (human)] product information, revised by CSL Behring GmbH 09-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 17, 2024.

Tretten [(coagulation factor XIII A-subunit (recombinant)] product information, revised by Novo Nordisk 06-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 17, 2024.

Mannucci PM. Rare inherited coagulation disorders. In: UpToDate, Editor(s) (Ed), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through May 2024. Topic last updated February 02, 2024. Accessed June 15, 2024.

Menegatti M, Peyvandi F. Treatment of rare factor deficiencies other than hemophilia. Blood 2019;133(5):415-424. Accessed June 16, 2024.