Clinical Policy: Factor XIII A-Subunit, Recombinant (Tretten)

Reference Number: ERX.SPA.191
Effective Date: 01.11.17
Last Review Date: 05.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Factor XIII A-subunit, recombinant (Tretten®) is a recombinant factor XIII concentrate.

FDA Approved Indication(s)
Tretten is indicated for routine prophylaxis of bleeding in patients with congenital factor XIII A-subunit deficiency.

Limitation(s) of use: Tretten is not for use in patients with congenital factor XIII B-subunit deficiency.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Tretten is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Congenital Factor XIII A-Subunit Deficiency (must meet all)**:**

1. Diagnosis of congenital factor XIII A-subunit deficiency;
2. Prescribed by or in consultation with a hematologist;
3. Request is for routine prophylaxis to prevent or reduce the frequency of bleeding episodes;
4. For routine prophylaxis requests, member meets one of the following (a, b, or c):
   a. Member has previously used factor XIIIa for routine prophylaxis;
   b. Member has severe hemophilia (defined as factor level of < 1%);
   c. Member has experienced at least one life-threatening or serious spontaneous bleed (*see Appendix D*).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Congenital Factor XIII A-Subunit Deficiency (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;

B. Congenital factor XIII B-subunit deficiency.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): hypersensitivity to the active substance or to any of the excipients
- Boxed warning(s): none reported

Appendix D: General Information
- Life-threatening bleeding episodes include, but are not limited to, bleeds in the following sites: intracranial, neck/throat, or gastrointestinal.
- Serious bleeding episodes include bleeds in the following site: joints (hemarthrosis).
- Spontaneous bleed is defined as a bleeding episode that occurs without apparent cause and is not the result of trauma.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Routine bleeding prophylaxis	35 IU/kg IV once monthly to achieve a target trough level of Factor XIII activity ≥ 10%. Consider dose adjustment if adequate coverage is not achieved with the 35 IU/kg dose.	Individualized

VI. Product Availability

Powder for reconstitution in single-use vial: nominally 2,000 to 3,125 IU (*the actual amount of Tretten in international units is stated on each carton and vial; may vary for each vial*)

VII. References

1. Tretten Prescribing Information. Plainsboro, NJ: Novo Nordisk Inc.; June 2020. Available at: www.trettenpro.com. Accessed November 23, 2021.
2. Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al. Guidelines for the management of hemophilia. *Haemophilia.* Jan 2013; 19(1): e1-47.
3. Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation (NHF): Database of treatment guidelines. Available at https://www.hemophilia.org/Researchers-Healthcare-Providers/Medical-and-Scientific-Advisory-Council-MASAC/MASAC-Recommendations. Accessed December 1, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: Added efficacy statement to renewal criteria.	11.28.17	02.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2019 annual review: no significant changes; references reviewed and updated.	09.26.18	02.19
1Q 2020 annual review; no significant changes; references reviewed and updated.	11.28.19	02.20
Added routine prophylaxis-specific requirement for severe hemophilia classification or at least one life-threatening or serious spontaneous bleed for classification of non-severe hemophilia; added requirement for prescriber attestation of not partaking in contact sports.	05.27.20	08.20
Removed requirement for prescriber attestation of not partaking in contact sports.	10.01.20	11.20
1Q 2021 annual review: no significant changes; enhanced existing requirement for A-subunit disease by excluding coverage for B-subunit disease in section III; references reviewed and updated.	12.01.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.23.21	02.22
Clarified requirement for coverage of factor XIIIa for routine prophylaxis: the requirement for factor XIII activity level or documentation of bleed history only applies to requests for new starts to routine prophylactic therapy.	03.03.22	05.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.