



## Drug Coverage Policy

Effective Date.....3/1/2026

Coverage Policy Number ..... IP0553

Policy Title.....Tretten

# Hematology – Tretten

- Tretten® (coagulation Factor XIII A-Subunit [recombinant] intravenous infusion – NovoNordisk)

### **INSTRUCTIONS FOR USE**

*The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.*

Tretten, a coagulation Factor XIII A-subunit, is indicated for routine prophylaxis of bleeding in congenital factor XIII A-subunit deficiency.<sup>1</sup> The agent is not indicated for use in patients with congenital Factor XIII B-subunit deficiency.

## OVERVIEW

### Disease Overview

Congenital Factor XIII deficiency is caused by defects in both Factor XIII A and Factor XIII B genes.<sup>2,3</sup> However, most cases are due to genetic alterations on the Factor XIII A gene. The estimated prevalence of Factor XIII A deficiency is one case in 1 to 2 million people. Clinical symptoms include delayed wound healing, bleeding of soft and subcutaneous tissue, recurrent spontaneous miscarriage, and central nervous system (CNS) bleeding, which may be life-threatening. If patients have severe Factor XIII deficiency, early manifestations include bleeding from the umbilical cord or CNS. Prospective data showed that a level of 30% Factor XIII clotting activity is an adequate therapeutic target for most patients. Treatment of Factor XIII deficiency involves use of fresh frozen plasma, cryoprecipitate, Corifact® (Factor XIII concentration intravenous infusion), or Tretten.

### Guidelines

The National Bleeding Disorders Foundation Medical and Scientific Advisory Council (MASAC) has guidelines for the treatment of hemophilia and other bleeding disorders (revised October 2024).<sup>4</sup> Tretten is recommended in patients who have factor XIII deficiency who lack the factor XIII-A subunit. It will not work in patients who only lack factor XIII-B subunit.

### Dosing Considerations

Dosing of clotting factor concentrates is highly individualized. MASAC provides recommendations regarding doses of clotting factor concentrate in the home (2016).<sup>5</sup> 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 bleeding 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 bleeding or perioperative management per 28 days. Doses exceeding this quantity will be reviewed on a case-by-case basis by a clinician.

## Coverage Policy

### POLICY STATEMENT

Prior Authorization is required for benefit coverage Tretten. Approval is required for those who meet the **Criteria** and **Dosing** for the listed indication. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. 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). Because of the specialized skills required for evaluation and diagnosis of patients treated with Tretten, as well as the monitoring required for adverse events and long-term efficacy, the agent is required to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Tretten is considered medically necessary when the following criteria are met:**

### FDA-Approved Indication

1. **Congenital Factor XIII A-Subunit Deficiency.** Approve for 1 year if the agent is prescribed by or in consultation with a hematologist.

**Dosing.** Up to 140 IU/kg intravenously no more frequently than once every 28 days.

## Conditions Not Covered

**Tretten for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):**

- 1. Congenital Factor XIII B-Subunit Deficiency.** Tretten will not work in patients who only lack Factor XIII-B subunit.<sup>1,2</sup>

## Coding Information

**Note:** 1) This list of codes may not be all-inclusive.  
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

**Considered Medically Necessary when criteria in the applicable policy statements listed above are met:**

HCPCS Codes	Description
J7181	Injection, Factor XIII A-subunit, (recombinant), per IU

## References

1. Tretten® intravenous infusion [prescribing information]. Plainsboro, NJ: Novo Nordisk; June 2020.
2. Mangla A, Hamad H, Killeen RB, et al. Factor XIII Deficiency. [Updated 2024 Feb 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK557467/>. Accessed on December 7, 2025.
3. Dorgalaleh A, Jozdani S, Zadeh MK. Factor XIII deficiency: laboratory, molecular, and clinical aspects. *Semin Thromb Hemost.* 2025;51(2):155-169.
4. National Bleeding Disorders Foundation. MASAC (Medical and Scientific Advisory Council) recommendations concerning products licensed for the treatment of hemophilia and selected disorders of the coagulation system (October 2024). MASAC Document #290. Available at: <https://www.hemophilia.org/sites/default/files/document/files/MASAC-Products-Licensed.pdf>. Accessed on December 7, 2025.
5. National Hemophilia Foundation. MASAC (Medical and Scientific Advisory Council) recommendations regarding doses of clotting factor concentrate in the home (Revised June 7, 2016). MASAC Document #242. Adopted on June 7, 2016. Available at: <https://www.hemophilia.org/sites/default/files/document/files/242.pdf>. Accessed on December 7, 2025.

## Revision Details

Type of Revision	Summary of Changes	Date
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Annual Revision	No criteria changes	5/1/2024
Annual Revision	No criteria changes.	3/1/2025
Annual Revision	<b>Congenital Factor XIII A-Subunit Deficiency. Removed</b> ONE of the following conditions is met: Peri-operative management of bleeding; Routine prophylaxis to reduce the frequency of bleeding episodes; Treatment of bleeding episodes	3/1/2026

The policy effective date is in force until updated or retired.

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