

POLICY: Hematology – Tretten® (coagulation Factor XIII A-Subunit [recombinant] injection for intravenous use – NovoNordisk)

APPROVAL DATE: 09/11/2019

OVERVIEW

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

Disease Overview

Congenital Factor XIII deficiency is caused by defects in both Factor XIII A and Factor XIII B genes.^{2,3} 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 injection for intravenous use), or Tretten.

Guidelines

The National Hemophilia Foundation Medical and Scientific Advisory Council has guidelines for the treatment of hemophilia and other bleeding disorders (revised April 2018).⁴ 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).⁵ 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.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage Tretten. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). 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.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Tretten is recommended for patients who meet criteria:

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. Approve up to 140 IU/kg intravenously no more frequently than once every 28 days.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

1. **Congenital Factor XIII B-Subunit Deficiency.** Tretten will not work in patients who only lack Factor XIII-B subunit.^{1,2}
2. **Other Indications.** Coverage is not recommended for circumstances not listed in the Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Tretten® injection for intravenous use [prescribing information]. Plainsboro, NJ: Novo Nordisk; November 2016.
2. Menegatti M, Peyvandi F. Treatment of rare factor deficiencies other than hemophilia. *Blood*. 2019;133(5):415-424.
3. Palla R, Peyvandi F, Shapiro AD. Rare bleeding disorders: diagnosis and treatment. *Blood*. 2015;125(13):2052-2061.
4. National Hemophilia Foundation. MASAC (Medical and Scientific Advisory Council) recommendations concerning products licensed for the treatment of hemophilia and other bleeding disorders (Revised April 2018). MASAC Document #253. Adopted on April 19, 2018. Available at: <https://www.hemophilia.org/node/3675>. Accessed on September 9, 2019.
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 September 9, 2019.

HISTORY

Type of Revision	Summary of Changes	Approval Date
New policy	--	09/11/2019