

Tretten (Coagulation Factor XIII A-Subunit (Recombinant))

STRENGTH	DOSAGE FORM	ROUTE	HICL
2500 IU vial	injectable	intravenous	40839

MANUFACTURER

Novo Nordisk, Inc

INDICATION(S)

Tretten, Coagulation Factor XIII A-Subunit (Recombinant), is indicated for routine prophylaxis for bleeding in patients with congenital factor XIII A-subunit deficiency.

Limitations of use:

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

DRUG CLASS

HEMATOLOGICAL DISORDERS; FACTOR XIII PREPARATIONS

PLACE IN THERAPY

Tretten is the second FDA approved agent indicated as prophylaxis for bleeding in patients with congenital factor XIII (FXIII) A-subunit deficiency. Congenital FXIII deficiency is a rare bleeding disorder that is seen in approximately 1 out of 2 million individuals. Factor XIII is the protein responsible for stabilizing the formation of a blood clot. Clots will still form with FXIII deficiency but bleeding is prolonged and recurrent. Bleeding associated with the FXIII deficiency include umbilical stump bleeding during the first few days of life, postoperative bleeding, and intracranial hemorrhage in severe patients. Prophylaxis with replacement therapy is very effective but to date only plasma-derived sources of FXIII have been available including: fresh frozen plasma, cryoprecipitate and plasma derived, virally inactivated FXIII concentrate.

Corifact (derived from human plasma), the other FDA approved product, is indicated for routine prophylactic treatment and perioperative management of surgical bleeding in adult and pediatric patients with congenital FXIII deficiency. Tretten is the first recombinant Factor XIII A-subunit agent available. Although Tretten is only indicated in patients with the A-subunit deficiency, the majority of patients with the FXIII deficiency have the A-subunit type. Because Tretten is not derived from human plasma it may have the following advantages: it does not carry the risk of transmitting infectious agents, viruses or pathogens and is not dependent on plasma donor availability. It has been estimated that in the United States there are roughly 120 patients with congenital FXIII deficiency. The utilization of these agents should be limited but there cost is substantial.

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EFFICACY

The efficacy of Tretten was evaluated in one 52-week, multi-center, open-label, non-controlled trial in 41 patients. Patients with congenital FXIII A-subunit deficiency confirmed by genotyping were included and were ≥ 6 years of age. The primary efficacy parameter was the annualized frequency of bleeding events requiring treatment with FXIII-containing products during the rFXIII prophylaxis treatment period versus the historical bleeding rate in patients with congenital FXIII deficiency treated on demand. Overall, the estimated bleeding rate (bleeds/subject/year) 0.138 was lower and statistically significant as compared to the historical control bleeding rate of 1.68 (bleeds/subject/year). The bleed rates for patients < 18 years old were higher (0.362) than patients ≥ 18 years old (0.040) but both were lower than historical control groups (2.00 and 1.59; respectively).

SAFETY

The most common adverse events of Tretten observed in clinical trials ($\geq 1\%$) were headache, pain in the extremities, injection site pain, and D dimer increase. Adverse reactions were seen more frequently in pediatric patients. Of the 41 patients studied 27 were less than 18 years old. No dose adjustments are required for pediatric patients.

Contraindications for Tretten include hypersensitivity to the active substance or to any of the excipients. Warning and precautions of Tretten include: hypersensitivity reactions, thromboembolic complications and the presence of inhibitory antibodies.

Tretten may not be administered concomitantly with factor VIIa due to risk of thrombosis.

Tretten is pregnancy category C. There have been no clinical studies in women who were pregnant or nursing.

DOSAGE

The treatment should be initiated under the supervision of a physician experienced in the treatment of rare bleeding disorders. The recommended prophylaxis dose is 35 international units (IU) per kilogram body weight once monthly and should target a trough level of FXIII activity at or above 10% using a validated assay. Dosing adjustments can be made if patients do not achieve targets at the recommended 35 IU/kg dose. After Tretten is reconstituted it must be used within three hours of reconstitution. It is for intravenous use only and the rate should not exceed 1-2 mL per minute.

COST

Drug	Cost/unit	Cost per 28 days [#]
Tretten [Coagulation Factor XIII A-Subunit (Recombinant)] 2500 IU vial	AWP=\$15.96 per unit \$39,900 per vial	\$39,900- \$78,000
Corifact [Factor XIII Concentrate (human)] 1000-1600 IU vial	AWP=\$9.83 per unit \$9,830- \$15,728 per vial	\$29,490- \$31,456

= Dose dependent on weight; cost is calculated using 80 kg

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FORMULARY PLACEMENT RECOMMENDATIONS

Based on this initial assessment of available clinical and financial information, consider NOT ADDING Tretten to the formulary pending complete review by the appropriate oversight committee for the plan.

REFERENCES

- Tretten [Prescribing Information]. Plainsboro, NJ: Novo Nordisk, Inc.; Accessed on March 17th, 2014 <http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/UCM379763.pdf>
- Inbal, A., et.al. Recombinant factor XIII: a safe and novel treatment for congenital factor XIII deficiency, *Blood*. 2012;119(22): 5111-511716
- National Hemophilia Foundation. Factor XIII Deficiency. Accessed on March 18th, 2014 <http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=190&contentid=58&rptname=bleeding>
- Corifact [Prescribing Information]. Kankakee, IL: CSL Behring LLC; Accessed on March 19th, 2014 <http://www.corifact.com/docs/Corifact-Prescribing-Information.pdf>