

Hemophilia Products – Coagulation Factor XIII A-subunit: Tretten® (Intravenous)

Effective date: 10/1/2019

Review date: 1/29/2020, 7/15/2021

Revision date: 1/29/2020, 7/15/2021

Scope: Medicaid*, Commercial*, Medicare-Medicaid Plan (MMP)

*(Medication only available on the Medical Benefit)

I. Length of Authorization

Unless otherwise specified*, the initial authorization will be provided for 3 months and may be renewed for a period of 12 months.

Note: The cumulative amount of medication the patient has on-hand will be taken into account for authorizations. Up to 5 'on-hand' doses for the treatment of acute bleeding episodes will be permitted at the time of the authorization request.

** Initial and renewal authorization periods may vary by specific covered indication*

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

N/A

B. Max Units (per dose and over time) [Medical Benefit]:

– 4,025 billable units per 28 day supply

III. Initial Approval Criteria

Hemophilia Management Program

Requirements for half-life study and inhibitor tests are a part of the hemophilia management program. This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide.

A. Tretten

Coverage is provided in the following conditions:

- MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

Congenital Factor XIII A-subunit deficiency † Φ Diagnosis of congenital factor XIII A-subunit deficiency has been confirmed by blood coagulation testing; **AND**

- Used for routine prophylaxis of bleeding

Hemophilia Management Program

- If the request is for routine prophylaxis and the requested dose exceeds dosing limits under part II, a half-life study should be performed to determine the appropriate dose and dosing interval.
- For members with a BMI ≥ 30 , a half-life study should be performed to determine the appropriate dose and dosing interval.
- For minimally treated patients (< 50 exposure days to factor products) previously receiving a different factor product, inhibitor testing is required at baseline, then at every comprehensive care visit (yearly for the mild and moderate patients, semi-annually for the severe patients).

† FDA Approved Indication(s) Φ Orphan Drug

IV. Dispensing Requirements for Rendering Providers (Hemophilia Management Program)

- Prescriptions cannot be filled without an expressed need from the patient, caregiver or prescribing practitioner. Auto-filling is not allowed.
- Monthly, rendering provider must submit for authorization of dispensing quantity before delivering factor product. Information submitted must include:
 - Original prescription information, requested amount to be dispensed, vial sizes available to be ordered from the manufacturer, and patient clinical history (including patient product inventory and bleed history)
 - Factor dose should not exceed +1% of the prescribed dose and a maximum of three vials may be dispensed per dose. If unable to provide factor dosing within the required threshold, below the required threshold, the lowest possible dose able to be achieved above +1% should be dispensed. Prescribed dose should not be increased to meet assay management requirements.
- The cumulative amount of medication(s) the patient has on-hand should be taken into account when dispensing factor product. Patients should not have more than 5 extra doses on-hand for the treatment of acute bleeding episodes.
- Dispensing requirements for renderings providers are a part of the hemophilia management program. This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide.

V. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Patient continues to meet criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: symptoms of allergic-anaphylactic reactions (anaphylaxis, dyspnea, rash, etc.), thromboembolic events (thromboembolism, pulmonary embolism), development of neutralizing antibodies (inhibitors), etc.; **AND**
- Any increases in dose must be supported by an acceptable clinical rationale (i.e., weight gain, half-life study results, increase in breakthrough bleeding when patient is fully adherent to therapy, etc.); **AND**

- The cumulative amount of medication(s) the patient has on-hand will be taken into account when authorizing. The authorization will allow up to 5 doses on-hand for the treatment of acute bleeding episodes as needed for the duration of the authorization; **AND**

Prevention of acute bleeding episodes/Routine prophylaxis to prevent or reduce the frequency of bleeding episode

- Renewals will be approved for a 12 month authorization period; AND
- Patient has demonstrated a beneficial response to therapy (i.e., the frequency of bleeding episodes has decreased from pre-treatment baseline)

VI. Dosage/Administration

Indication	Dose
Routine prophylaxis for bleeding Congenital factor XIII A-subunit deficiency	35 international units (IU) per kilogram body weight once monthly to achieve a target trough level of FXIII activity at or above 10% using a validated assay.

VII. Billing Code/Availability Information

HCPCS & NDC:

Drug	Manufacturer	J-Code	1 Billable Unit Equiv.	Vial Size	NDC
Tretten	Novo Nordisk	J7181	1 IU	Unassigned size	00169-7013

VIII. References

1. Tretten [package insert]. Bagsvaerd, Denmark; Novo Nordisk; June 2020. Accessed April 2021.
2. MASAC RECOMMENDATIONS CONCERNING PRODUCTS LICENSED FOR THE TREATMENT OF HEMOPHILIA AND OTHER BLEEDING DISORDERS. 2016 National Hemophilia Foundation. MASAC Document #249; October 2016. Available at: <http://www.hemophilia.org>. Accessed January 2019.
3. Guidelines for the Management of Hemophilia. 2nd Edition. World Federation of Hemophilia. 2013. Available at: <https://www1.wfh.org/publication/files/pdf-1472.pdf>. Accessed January 2019.
4. Annual Review of Factor Replacement Products. Oklahoma Health Care Authority Review Board. Updated April 2016. Access January 2019.
5. Graham A1, Jaworski K. Pharmacokinetic analysis of anti-hemophilic factor in the obese patient. Haemophilia. 2014 Mar;20(2):226-9.
6. Croteau SE1, Neufeld EJ. Transition considerations for extended half-life factor products. Haemophilia. 2015 May;21(3):285-8.

7. Mingot-Castellano, et al. Application of Pharmacokinetics Programs in Optimization of Haemostatic Treatment in Severe Hemophilia a Patients: Changes in Consumption, Clinical Outcomes and Quality of Life. Blood. 2014 December; 124 (21).
8. MASAC RECOMMENDATION CONCERNING PROPHYLAXIS. 2016 National Hemophilia Foundation. MASAC Document #241; February 2016. Available at: <http://www.hemophilia.org>. Accessed January 2019.
9. First Coast Service Options, Inc. Local Coverage Determination (LCD): Hemophilia Clotting Factors (L33684). Centers for Medicare & Medicaid Services, Inc. Updated on 01/04/2019 with effective date 01/01/2019. Accessed January 2019.
10. Novitas Solutions, Inc. Local Coverage Determination (LCD): Hemophilia Clotting Factors (L35111). Centers for Medicare & Medicaid Services, Inc. Updated on 01/19/2018 with effective date 01/01/2018. Accessed January 2019.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D68.2	Hereditary deficiency of other clotting factors

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

Jurisdiction(s): H,L	NCD/LCD Document (s): L35111
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L35111&bc=gAAAAAAAAAAAAAAAAA ==	
Jurisdiction(s): N	NCD/LCD Document (s): L33684
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L33684&bc=gAAAAAAAAAAAAAAAAA ==	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC