

Hemophilia Products – von Willebrand Factor: Vonvendi® (Intravenous)

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I. Length of Authorization

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

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) [NDC Unit]:

- Vonvendi 450-850 units: 82 vials per 90-day supply
- Vonvendi 900-1700 units: 41 vials per 90-day supply

B. Max Units (per dose and over time) [HCPCS Unit]:

- 36,800 billable units per 90 day supply

III. Initial Approval Criteria ^{1,2,3}

Hemophilia Management Program

Requirements for 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.

Coverage is provided in the following conditions:

Universal Criteria

- Patient is 18 years or older; **AND**

Von Willebrand Disease (vWD) †

- Diagnosis of von Willebrand disease has been confirmed by blood coagulation and von Willebrand factor testing; **AND**
 - Used as treatment of spontaneous and trauma-induced bleeding episodes in at least one of the following:
 - Patients with severe vWD; **OR**
 - Patients mild or moderate vWD in whom the use of desmopressin is known or suspected to be ineffective or contraindicated; **OR**
 - Perioperative management (*Note: Authorizations valid for 1 month*); **AND**
- Is NOT being used for routine prophylactic treatment of spontaneous bleeding episodes

Hemophilia Management Program

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)

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 ^{1,2,3}

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. 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); thromboembolic events (thromboembolism, pulmonary embolism); and development of neutralizing antibodies (inhibitors); **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**

Treatment of acute bleeding episodes/Treatment of Spontaneous and trauma-induced bleeding episodes/On-demand treatment of bleeding episodes

- Renewals will be approved for a 6 month authorization period

VI. Dosage/Administration¹⁻³

Indication	Dose
Control of bleeding episodes VWD	<ul style="list-style-type: none"> • For each bleeding episode, administer the first dose of VONVENDI with an approved recombinant (non-von Willebrand factor containing) factor VIII if factor VIII baseline levels are below 40% or are unknown. • If recombinant factor VIII is required, give recombinant factor VIII within 10 minutes of completing VONVENDI infusion at a ratio of 1.3:1 (i.e., 30% more VONVENDI than recombinant factor VIII, based on the approximate mean recoveries of 1.5 and 2 IU/dL for VONVENDI and recombinant factor VIII, respectively). <p><u>Minor:</u> Loading dose: 40-50 IU/kg; Maintenance dose: 40-50 IU/kg every 8-24 hours as clinically required</p> <p><u>Major:</u> Loading dose: 50-80 IU/kg; Maintenance dose: 40-60 IU/kg every 8-24 hours for approximately 2 to 3 days as clinically required</p>
Perioperative management of Bleeding VWD	<p><u>Elective Surgical Procedure</u></p> <p>A preoperative dose may be administered 12-24 hrs prior to surgery to allow the endogenous factor VIII levels to increase to at least 30 IU/dL (minor surgery) or 60 IU/dL (major surgery) before the loading dose (1 hour preoperative dose) of rVWF, with or without recombinant factor VIII, is administered.</p>

Indication	Dose
	<ul style="list-style-type: none"> Ensure baseline FVIII:C level is available prior to determining the need for 12-24 hr preoperative dose. FVIII:C level should also be assessed within 3 hours prior to initiating the surgical procedure. If the level is at the recommended minimum target levels (30 IU/dL for minor surgery and 60 IU/dL for major surgery), administer a dose of Vonvendi alone (without factor VIII treatment) within 1 hour prior to the procedure. If the FVIII:C level is below the recommended minimum target level, administer complete dose of Vonvendi followed by recombinant factor VIII within 10 minutes to raise VWF:RCo and FVIII:C. Assess baseline VWF:RCo levels within 3 hours of administration of the 12-24 hr preoperative dose. If the 12-24 hour preoperative dose is not administered, then assess baseline level VWF:RCo prior to surgery. When possible, measure incremental recovery (IR) for Vonvendi before surgery. For calculation of IR, measure baseline plasma VWF:RCo. Then infuse a dose of 50 IU/kg of Vonvendi. Measure VWF:RCo, 30 minutes after infusion of Vonvendi. <ul style="list-style-type: none"> Use the following formula to calculate IR: $IR = \frac{[\text{Plasma VWF:RCo at 30 minutes (IU/dL)} - \text{Plasma VWF:RCo at baseline (IU/dL)}]}{\text{Dose (IU/kg)}}$. <p><u>Emergency Surgical Procedure</u></p> <ul style="list-style-type: none"> A 12-24 hr preoperative dose may not be feasible in subjects requiring emergency surgery. Baseline VWF:RCo and FVIII:C levels should be assessed within 3 hrs prior to initiating the surgical procedure if it is feasible. The loading dose (1 hour preoperative dose) can be calculated as the difference in the target peak and baseline plasma VWF:RCo levels divided by the IR. If the IR is not available, assume an IR of 2.0 IU/dL per IU/kg. If baseline VWF:RCo and FVIII:C is not available, as a general guidance a loading dose (1 hour preoperative dose), 40 to 60 IU/kg VWF:RCo, should be administered. Additionally, recombinant factor VIII at a dose of 30 to 45 IU/kg may be infused sequentially, preferably within 10 minutes after the Vonvendi infusion in patients whose factor VIII plasma levels already are (or are highly likely to be) less than 40 to 50 IU/dL for minor surgery or 80 to 100 IU/dL for major surgery. <p>Note: refer to the package insert recommended VWF:RCo and FVIII:C target peak plasma levels and dosing guidelines for perioperative management of bleeding.</p>

VII. Billing Code/Availability Information

HCPCS & NDC:

Drug	Manufacturer	J-Code	1 Billable Unit Equiv.	Vial Size	NDC
Vonvendi	Baxalta US Inc	J7179	1 IU	450-850 units	00944-7551
				900-1700 units	00944-7553

VIII. References

1. Vonvendi [package insert]. Westlake Village, CA; Baxalta US Inc.; February 2019. Accessed January 2020.
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 Article: Hemophilia Clotting Factors (A56482). Centers for Medicare & Medicaid Services Inc. Updated on 12/06/2019 with effective date 07/01/2019. Accessed January 2020.
10. Palmetto GBA. Local Coverage Article: Billing and Coding: Guidance for Anti-Inhibitor Coagulant Complex (AICC) National Coverage Determination (NCD) 110.3 (A56065). Centers for Medicare & Medicaid Services Inc. Updated on 10/24/2019 with effective date 10/31/2019. Accessed January 2020.
11. Novitas Solutions, Inc. Local Coverage Article: Billing and Coding: Hemophilia Factor Products (A56433). Centers for Medicare & Medicaid Services Inc. Updated on 11/08/2019 with effective date 11/14/2019. Accessed January 2020.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D68.0	Von Willebrand's disease

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): N	NCD/LCD Document (s): A56482
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56482&bc=gAAAAAAAAAAAA	

Jurisdiction(s): J,M	NCD/LCD Document (s): A56065
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56065&bc=gAAAAAAAAAAAA	

Jurisdiction(s): H,L	NCD/LCD Document (s): A56433
https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56433&bc=gAAAAAAAAAAAA	

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)
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