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

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I. Length of Authorization

Perioperative management of bleeding:

- Initial: Prior authorization validity will be provided initially for 1 month (30 days).
- Renewal: Prior authorization validity may NOT be renewed.

On-demand treatment and control of bleeding episodes:

- Initial: Prior authorization validity will be provided initially for 3 months (90 days).
- Renewal: Prior authorization validity may be renewed every 6 months (180 days) thereafter.

Routine prophylaxis:

- Initial: Prior authorization validity will be provided initially for 3 months (90 days).
- Renewal: Prior authorization validity be renewed every 12 months (365 days) thereafter.

Note: The cumulative amount of medication the member 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.

II. Dosing Limits

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

- 36,800 billable units per 90 day supply

III. Initial Approval Criteria [1,2,8,10-12]

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.

Prior authorization validity is provided in the following conditions:

- Member is at least 1 year of age, unless otherwise specified; **AND**

Von Willebrand Disease (vWD) † Φ

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- Diagnosis of von Willebrand disease has been confirmed by blood coagulation and von Willebrand factor testing; **AND**
  - Used as treatment in at least one of the following:
    - On-demand treatment and control of bleeding episodes; **AND**
      - Member has severe vWD; **OR**
      - Member has mild or moderate vWD and the use of desmopressin is known or suspected to be ineffective or contraindicated; **OR**
    - Perioperative management of bleeding; **OR**
    - Routine prophylaxis to reduce the frequency of bleeding episodes; **AND**
      - Member is at least 18 years of age

Hemophilia Management Program
For minimally treated members (< 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 members, semi-annually for the severe members)

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

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

- Prescriptions cannot be filled without an expressed need from the member, 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 member clinical history (including member 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 member has on-hand should be taken into account when dispensing factor product. Members should not have more than 5 extra doses on-hand for the treatment of acute bleeding episodes.
- Dispensing requirements for rendering 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.

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V. Renewal Criteria [1,2,8,10]

Prior authorization validity may be renewed based upon the following criteria:

- Member continues to meet the indication-specific relevant criteria identified in section III; **AND**
- Duration of authorization has not been exceeded *(refer to Section I)*; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: hypersensitivity and infusion-related reactions (including anaphylactic shock, generalized urticaria, angioedema, chest tightness, hypotension, shock, lethargy, nausea, vomiting, paresthesia, pruritus, restlessness, blurred vision, wheezing and/or acute respiratory distress), thromboembolic events (including disseminated intravascular coagulation [DIC], venous thrombosis, pulmonary embolism, myocardial infarction, and stroke), development of neutralizing antibodies, 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 member is fully adherent to therapy, etc.); **AND**
- The cumulative amount of medication(s) the member 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**

Routine prophylaxis to reduce the frequency of bleeding episodes

- Member has demonstrated a beneficial response to therapy (i.e., the frequency of bleeding episodes has decreased from pre-treatment baseline)

VI. Dosage/Administration [1]

Indication	Dose
On-demand treatment and control of bleeding episodes VWD	• For each bleeding episode, administer the first dose of Vonvendi with an approved recombinant (non-von Willebrand factor containing) factor VIII (rFVIII) if factor VIII baseline levels are below 40% or are unknown. • If rFVIII is required, the rFVIII dose should be calculated according to the difference between the member's baseline plasma FVIII:C level, and the desired peak FVIII:C level to achieve an appropriate plasma FVIII:C level based on the approximate mean recovery of 2 (IU/dL)/(IU/kg). • Administer the complete dose of Vonvendi followed by rFVIII within 10 minutes. <u>Minor (e.g., readily managed epistaxis, oral bleeding, menorrhagia)</u>: • Loading dose: 40-50 IU/kg • Maintenance dose: 40-50 IU/kg every 8-24 hours as clinically required <u>Major (e.g., severe or refractory epistaxis, menorrhagia, GI bleeding, CNS trauma, hemarthrosis, or traumatic hemorrhage)</u>: • Loading dose: 50-80 IU/kg

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Indication	Dose
	• Maintenance dose: 40-60 IU/kg every 8-24 hours for approximately 2 to 3 days as clinically required
Perioperative management of bleeding VWD	Elective Surgical Procedure A preoperative dose may be administered 12-24 hours 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 Vonvendi, with or without rFVIII. • 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 rFVIII within 10 minutes to raise VWF:RCo and FVIII:C. • Assess baseline plasma VWF:RCo activity level within 3 hours prior to administration of the 12- 24 hour preoperative dose of Vonvendi. If no dose is administered 12-24 hours preoperatively, it's recommended to use the VWF:RCo levels 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. – Use the following formula to calculate IR: IR= [Plasma VWF:RCo at 30 minutes (IU/dL) – Plasma VWF:RCo at baseline (IU/dL)]/Dose(IU/kg). Emergency Surgery • A 12-24 hour preoperative dose may not be feasible in members requiring emergency surgery. Baseline VWF:RCo and FVIII:C levels should be assessed within 3 hours prior to initiating the surgical procedure if it is feasible. If baseline VWF:RCo and FVIII:C are available, 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 are not available, as a general guidance a loading dose (1 hour preoperative dose) of Vonvendi, 40 to 60 IU/kg VWF:RCo, should be administered. Additionally, rFVIII at a dose of 30 to 45 IU/kg may be infused sequentially, preferably within 10 minutes after the Vonvendi infusion in members 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.

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Indication	Dose
	Note: *refer to the package insert for recommended VWF:RCo and FVIII:C target peak plasma levels and dosing guidelines for perioperative management of bleeding.*
Routine prophylaxis to reduce the frequency of bleeding episodes in members with VWD	• For initiation of prophylactic treatment, administer 40 to 60 IU/kg twice weekly. **Treat breakthrough bleeding as per the dosing guidelines for minor and major bleeding.*

VII. Billing Code/Availability Information

HCPCS Code & NDC(s):

Drug	Manufacturer	HCPCS Code	1 Billable Unit Equiv.	Vial Size	NDC
Vonvendi	Takeda Pharmaceuticals USA, Inc.	J7179	1 IU VWF:RCO	450-850 IU	00944-7551-xx
				900-1700 IU	00944-7553-xx

VIII. References

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Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	No: PA not a priority
Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D68.01	Von Willebrand disease, type 1
D68.020	Von Willebrand disease, type 2A
D68.021	Von Willebrand disease, type 2B
D68.022	Von Willebrand disease, type 2M
D68.023	Von Willebrand disease, type 2N
D68.03	Von Willebrand disease, type 3
D68.04	Acquired von Willebrand disease
D68.09	Other von Willebrand disease

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

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes		
Jurisdiction	**NCD/LCA/LCD Document (s)**	**Contractor**
J,M	A56065	Palmetto GBA

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
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA

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Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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

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