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

Effective date: 01/01/2020
Review date: 10/02/2019, 12/13/2019, 1/22/2020, 7/15/2021, 12/02/2021, 4/14/2022, 7/7/2022, 6/22/2023, 12/07/2023, 01/04/2024, 05/15/2024, 08/14/2024
Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

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) [Pharmacy Benefit]:

- 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) [Medical Benefit]:

- 36,800 billable units per 90-day supply

III. Initial Approval Criteria

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.

A. Vonvendi

Coverage is provided in the following conditions:

Von Willebrand Disease (vWD) †

- Patient is at least 18 years of age; **AND**
- 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
  - Patient has severe vWD; **OR**
  - Patient has mild or moderate vWD and the use of desmopressin is known or suspected to be ineffective or contraindicated; **OR**
- Perioperative management of bleeding *(Note: Authorizations valid for 1 month);* **OR**
- Routine prophylaxis to reduce the frequency of bleeding episodes; **AND**
  - Patient has severe Type 3 vWD and is receiving on-demand therapy

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) ‡ 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 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 the indication specific relevant criteria identified in section IV; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include:

- hypersensitivity 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 reactions (including disseminated intravascular coagulation [DIC], thromboembolism, venous thrombosis, pulmonary embolism, myocardial infarction, and stroke), 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**

On-demand treatment and control of bleeding episodes

- Renewals will be approved for a 6-month authorization period

Perioperative management of surgical bleeding

- Coverage may NOT be renewed

Routine prophylaxis to reduce the frequency of bleeding episodes

- Renewals will be approved for a 6-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
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 recombinant factor VIII is required, the rFVIII dose should be calculated according to the difference between the patient'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. • • Minor(e.g., readily managed epistaxis, oral bleeding, menorrhagia):

Indication	Dose
	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; Maintenance dose: 40-60 IU/kg every 8-24 hours for approximately 2 to 3 days (as clinically required)
Perioperative management of bleeding VWD	<u>Elective Surgical Procedure</u> 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 rVWF, with or without recombinant factor VIII, is administered. • 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. • 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). <u>Emergency Surgery</u> • 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 hours 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) of Vonvendi, 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. ***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.***

Indication	Dose
Routine prophylaxis to reduce the frequency of bleeding episodes in patients with sever Type 3 VWD	• For initiation of prophylactic treatment, administer 40 to 60 IU/kg twice weekly. – Adjust prophylaxis dose up to 60 IU/kg twice weekly if breakthrough bleeding* occurs in joints or if severe bleeding occurs. **Treat breakthrough bleeding as per the dosing guidelines for minor and major bleeding.*

VII. Billing Code/Availability Information

HCPCS & NDC:

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

VIII. References

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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