25 June 2026
EMADOC-1700519818-3067566
Human Medicines Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Veyvondi

Vonicog alfa

Procedure no: EMA/PAM/0000340074

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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Status of this report and steps taken for the assessment			
Current step[1]	**Description**	**Planned date**	**Actual Date**
☐	Start date	27 April 2026	27 April 2026
☐	CHMP Rapporteur AR	1 June 2026	1 June 2026
☐	CHMP comments	15 June 2026	n/a
☐	Updated CHMP Rapporteur AR	18 June 2026	17 June 2026
☒	CHMP outcome	25 June 2026	25 June 2026

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1. Introduction

On 31 March 2026, the MAH submitted a completed paediatric study for VEYVONDI, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

A short critical expert overview has also been provided**.**

2. Scientific discussion

2.1. Information on the development program

The MAH stated that study TAK-577-5008: *Real-world treatment patterns and outcomes among patients with type 1 and 2 von Willebrand disease (VWD) treated prophylactically with Vonvendi: A panel-based chart review study* is a stand-alone study.

The MAH stated that study TAK-577-5008 is not part of the PIP or the clinical development program of VEYVONDI.

No changes are proposed to the product information of VEYVONDI based on the results of the study.

2.2. Information on the pharmaceutical formulation used in the study

VEYVONDI (vonicog alfa) is a purified rVWF, in the drug class of blood coagulation factors, and the Anatomical Therapeutic Chemical System classification code is B02BD10.

Vonicog alfa is a purified recombinant human von Willebrand factor (rVWF). It is manufactured by recombinant DNA (rDNA) technology in the Chinese Hamster Ovary (CHO) cell line without the addition of any exogenous human-or animal-derived protein in the cell culture process, purification or final formulation. The only proteins present in the final container product, other than vonicog alfa, are trace quantities of murine IgG from the immunoaffinity purification process, host cell (CHO) protein, and rFurin. The registered tradename in the US is Vonvendi, whereas in European Union (EU) it is VEYVONDI.

In the EU, VEYVONDI is currently authorized for: Prevention and treatment of haemorrhage or surgical bleeding in adults (aged 18 years and older) with von Willebrand disease (VWD), when desmopressin (DDAVP) treatment alone is ineffective or contraindicated and for treatment of haemorrhage in children (aged less than 18 years) with von Willebrand disease (VWD), when desmopressin (DDAVP) treatment alone is ineffective or contraindicated. VEYVONDI should not be used in the treatment of haemophilia A.

2.3. Clinical aspects

Introduction

The MAH submitted a final report for:

- TAK-577-5008: *Real-world treatment patterns and outcomes among patients with type 1 and 2 von Willebrand disease (VWD) treated prophylactically with Vonvendi: A panel-based chart review study*

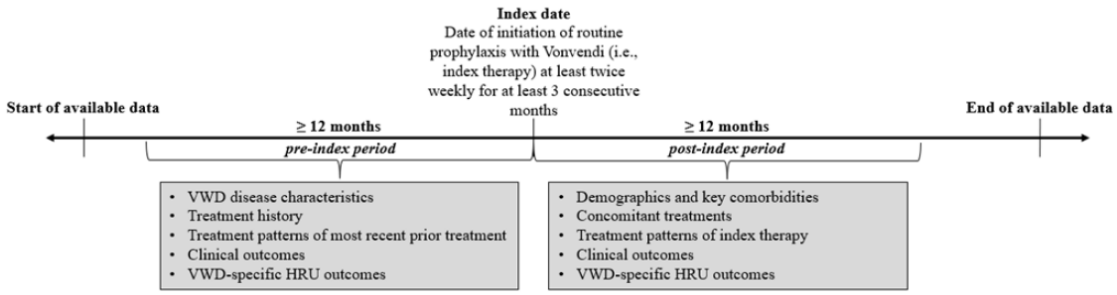
Clinical study

TAK-577-5008: Real-world treatment patterns and outcomes among patients with type 1 and 2 von Willebrand disease (VWD) treated prophylactically with Vonvendi: A panel-based chart review study

Description

Study TAK-577-5008 was a panel-based, non-interventional, retrospective cohort study using chart review. The study population included patients with type 1 or 2 VWD who were initiated on prophylactic treatment with vonicog alfa in the US. US-based haematologists and/or oncologists belonging to a physician-based panel were selected for participation from a panel vendor and recruited to participate in the study if they had initiated at least one patient with type 1 or 2 VWD on prophylactic treatment with vonicog alfa. The study design is shown in Figure 1 below. The index date was defined as the date of initiation of first routine prophylaxis treatment with vonicog alfa. Routine prophylaxis was defined as receiving vonicog alfa at least twice weekly for at least three consecutive months.

Figure 1: Study design



Source. Figure 4-2_tak-577-5008-noninterventionalreport.pdf

The physicians performed one-time data abstraction from patient charts using an electronic case report form (eCRF). The eCRF included a physician screener to confirm eligibility criteria for the physician, a patient screener to confirm patient eligibility, followed by sections for the medical chart data abstraction. The panel vendor managed the data collection process. Patient data was collected for 12 or more months prior to and following the index date. The study was conducted between February 2024 and December 2024

Methods

Study participants

Criteria for Selection of Eligible Physicians

1. Practice located in the US
2. Primary specialty in haematology and/or oncology
3. Had initiated at least one patient on prophylactic treatment with Vonvendi for type 1 or 2 VWD
4. Physician has access to medical records/patient charts including patient characteristics, prescribed treatments, clinical outcomes, and HRU (Healthcare resource utilization) for patients with type 1 or 2 VWD

Criteria for Selection of Eligible Patients

Inclusion Criteria

1. Confirmed physician diagnosis of type 1 or 2 VWD
2. Initiated on first ever routine prophylaxis with Vonvendi (at least twice weekly for at least three consecutive months) for the prophylactic treatment of type 1 or 2 VWD at the index date
3. Age at least 6 years at the index date
4. Had medical records available for at least 12 months prior to the index date
5. Had medical records available for at least 12 months after the index date, except in the case of death

Exclusion Criteria

1. On-study participants in phase 1-3 clinical trials and data from patients while on any phase 1-3 VWD clinical trial
2. Acquired von Willebrand syndrome (VWS)
3. Any other bleeding disorder than VWD

Treatments

The study was non-interventional

Objectives

The primary objectives of TAK-577-5008 were:

1. To describe the demographic and clinical characteristics of patients with type 1 and 2 VWD initiated on prophylactic treatment with Vonvendi
2. To describe the treatment patterns of patients with type 1 and 2 VWD
3. To describe the clinical outcomes of patients with type 1 and 2 VWD initiated on prophylactic treatment with Vonvendi
4. To describe the HRU of patients with type 1 and 2 VWD initiated on prophylactic treatment with Vonvendi

Outcomes/endpoints

- Clinical outcomes (assessed during the 12-month period prior to the index date and up to the earliest of discontinuation date of Vonvendi or end of data availability or death):
    - Number and type of bleeding episodes (treated and untreated) - used to calculate annualized bleeding rate (ABR)
    - For treated bleeding episodes only:
        - Location of bleed
        - Severity of bleed

        - Time to bleed resolution in days
        - On-demand treatment(s) used to resolve the bleeding episode
- VWD-specific HRU outcomes (assessed during the 12-month period prior to the index date and up to the earliest of 12 months after the index date or end of data availability or death):
    - Number of hospitalizations and admission and discharge dates (used to calculate duration of hospitalization)
    - Number of emergency room (ER) visits
    - Number of outpatient (OP) visits

Sample size

The study targeted to collect 50 eligible patient charts from 25 haematologists and/or oncologists. The sample size was based on expected feasible patient counts and was not based on statistical considerations.

Randomisation and blinding (masking)

Not applicable

Statistical Methods

Physician characteristics, and patient demographics, clinical, and treatment characteristics were summarized descriptively. Means, standard deviations (SD), medians, and ranges were provided for continuous variables; counts and percentages were provided for categorical variables. Clinical outcomes were described during the pre-index and post-index periods. ABR was calculated as the number of bleeding episodes divided by the number of months in the pre- or post-index period and multiplied by 12. ABR was calculated for all bleeding episodes, and for treated and untreated bleeding episodes separately. ABR was reported overall (i.e., among all patients), and among patients with at least one bleeding episode. HRU outcomes were described during the pre-index and post-index periods. The number and proportion of patients with at least one visit was summarized for hospitalizations, ER, and OP visits. Additionally, duration of hospitalization (days) was summarized. To adjust for variable follow-up durations, number of hospitalizations, OP visits, and ER visits were assessed as per patient per year (PPPY), among patients with at least one visit of that type. Patient demographic and clinical characteristics, treatment patterns, clinical outcomes, and HRU outcomes were also assessed among the following three subgroups:

- VWD sub-type (type 1 and type 2)
- VWD severity (mild, moderate, and severe)
- Age (less than 18 years and 18 years and older)

Results

Recruitment / Participant flow / Numbers analysed

Patient charts were provided by a sample of 26 physicians. The study included 91 patients with type 1 or type 2 VWD, of whom 29 (31.9%) were aged <18 years.

Baseline data

Across all patients, the mean (SD) age at Vonvendi initiation was 25.8 (13.6) years, with 29 (31.9%) patients being less than 18 years of age (paediatric) at index. Paediatric patients began Vonvendi prophylaxis at a mean (SD) age of 13.6 (2.7) years (range, 8.0 to 17.8 years).

The interval from VWD diagnosis to initiation of Vonvendi prophylaxis was shorter in paediatric patients (3.1 [3.5] years) than in adults (7.5 [9.2] years). In both age groups, the majority of patients were male (65.5% of paediatric and 53.2% of adult patients).

Type 1 VWD was the most common type in both age groups, including a majority (51.7%) of paediatric patients and 38.7% of adult patients, while type 2 subtypes collectively accounted for a substantial proportion, particularly type 2B (31.0% of paediatric and 24.2% of adult patients) and type 2A (13.8% of paediatric and 27.4% adult patients). VWD severity at diagnosis was mild and moderate in equal percentages (44.8%) of paediatric patients, with a small percentage (10.3%) of severe disease, while the majority (56.5%) of adult patients had moderate VWD, with nearly equal percentages of adult patients having mild (22.6%) and severe (21.0%) VWD.

The majority of paediatric patients did not receive prior on-demand treatment (62.1%) or prophylactic treatment (86.2%) but did receive other prior treatment (55.2%), while, among adult patients, 45.2% did not receive prior on-demand therapy, 79.0% did not receive prior prophylaxis, and 74.2% did receive other prior treatment.

The most commonly recorded prior on-demand treatment in both age groups was plasma-derived VWF concentrates with FVIII (17.2% of paediatric and 30.6% of adult patients), followed by antifibrinolytic drugs (17.2% of paediatric and 21.0% of adult patients), and desmopressin acetate injection (6.9% of paediatric and 11.3% of adult patients) or nasal spray (3.4% of paediatric and 9.7% of adult patients).

Other prophylactic treatments that were more commonly used by both paediatric (6.9%) and adult (12.9%) patients included antifibrinolytic drugs, desmopressin acetate injection or nasal spray, and emicizumab. No paediatric patient and 4.8% of adult patients used pdVWF concentrates with FVIII for prior prophylaxis. The most recent prior prophylactic treatments in paediatric patients were antifibrinolytic drugs (3.4%) and emicizumab (3.4%).

The most common prior treatments in the category "other" were painkillers (31.0%), iron therapy/iron deficiency replacement (27.6%), hormonal therapy (10.3%), and antidepressants (10.3%) in paediatric patients and iron therapy/iron deficiency replacement (46.8%), hormonal therapy (24.2%), and painkillers (16.1%) in adult patients.

Efficacy results

Post-index Vonvendi treatment patterns

Paediatric patients and adult patients had similar mean (SD) treatment durations (18.2 [13.4] and 18.5 [14.5] months), number of infusions per week for the overall treatment schedule (2.1 [0.3] and 2.4 [0.7]), initial doses per infusion (44.0 [5.1] and 47.1 [7.0] IU/kg), and initial numbers of infusions per week (2.0 [0.2] and 2.5 [0.6]).

Reasons for initiating Vonvendi were attributed to efficacy reasons for the majority of both paediatric (69.0%) and adult patients (83.9%). Caregiver preference (58.6%) and access to treatment (58.6%) were also cited for the majority of paediatric patients; these were lower for adult patients (24.2% and 21.0%, respectively). The other reasons for initiating treatment were patient preference (41.4% of paediatric and 33.9% of adult patients), safety reasons (6.9% and 25.8%, respectively), and switching from another treatment (6.9% and 11.3%, respectively).

A similar proportion of paediatric (44.8%) and adult patients (48.4%) discontinued treatment. Among reasons for discontinuation, improvement in signs/symptoms was the most common reason for both paediatric (37.9%) and adult patients (25.8%); other reasons cited by >10% of patients were patient preference (24.1% of paediatric and 12.9% of adult patients), and availability of other treatment options (only cited by adult patients, in 12.9%).

Pre- and post-index bleeding outcomes

The annualized bleeding rate (ABR) for all bleeding episodes (treated and untreated) is summarized both before and after the start of Vonvendi prophylaxis for the 2 age groups in Table 1 below.

Table 1: Bleeding episodes (treated and untreated) by age

	Age <18 years: Pre-index period N = 29	Age <18 years: Post-index period N = 29	Age ≥18 years: Pre-index period N = 62	Age ≥18 years: Post-index period N = 62
Period duration				
Period duration (months)				
Mean ± SD	12.0 ± 0.0	18.2 ± 13.4	12.0 ± 0.0	18.5 ± 14.5
Median	12.0	17.1	12.0	13.5
IQR	(12.0, 12.0)	(5.6, 26.3)	(12.0, 12.0)	(7.8, 24.6)
Range	(12.0, 12.0)	(3.9, 45.8)	(12.0, 12.0)	(3.4, 75.7)
All bleeding episodes (treated and untreated)				
Number of bleeds, n (%)				
0 bleeds	14 (48.3%)	22 (75.9%)	22 (35.5%)	47 (75.8%)
1 bleed	10 (34.5%)	6 (20.7%)	6 (9.7%)	9 (14.5%)
2 bleeds	2 (6.9%)	1 (3.4%)	14 (22.6%)	5 (8.1%)
≥3 bleeds	3 (10.3%)	0 (0.0%)	17 (27.4%)	0 (0.0%)
Unknown	0 (0.0%)	0 (0.0%)	3 (4.8%)	1 (1.6%)
Number of patients with ≥1 bleeding episode, n (%)	15 (51.7%)	7 (24.1%)	37 (59.7%)	14 (22.6%)
ABR (among all patients)[2,3]				
Total number of patients with reported data on bleeds, n (%)	29 (100.0%)	29 (100.0%)	59 (95.2%)	61 (98.4%)
ABR - overall				
Mean ± SD	0.8 ± 1.0	0.1 ± 0.2	2.2 ± 3.4	0.2 ± 0.4
Median	1.0	0.0	2.0	0.0
IQR	(0.0, 1.0)	(0.0, 0.0)	(0.0, 3.0)	(0.0, 0.0)
Range	(0.0, 3.0)	(0.0, 0.6)	(0.0, 19.0)	(0.0, 1.9)

Source: Extract from Table 20A_tak-577-5008-noninterventionalreportalltables.pdf

Before the start of Vonvendi prophylaxis, fewer than half of paediatric (48.3%) and adult (35.5%) patients had 0 bleeds. After the index date, the majority of patients in both groups (75.9% paediatric and 75.8% adult patients) had 0 bleeds, and no patients in either group had ≥3 bleeds. The ABR among all patients decreased in both groups, from mean (SD) 0.8 (1.0) to 0.1 (0.2) in paediatric patients and from 2.2 (3.4) to 0.2 (0.4) in adult patients. Similar reductions were seen for treated bleeding episodes. In paediatric patients, the percentage of patients with treated epistaxis decreased from 24.1% to 6.9%, and no treated heavy menstrual bleed, muscle bleed, gastrointestinal bleed, joint bleed, or nasopharyngeal bleed was reported after the start of Vonvendi prophylaxis. However, treated mouth and oral cavity bleeds were reported in a small percentage (6.9%) of paediatric patients only after the start of Vonvendi prophylaxis. The percentage of paediatric patients with treated spontaneous

bleeds decreased from 24.1% to 10.3%, and with treated traumatic bleeds decreased from 6.9% to 0. The percentage of paediatric patients with treated minor bleeds decreased from 31.0% to 13.8%, and the percentage with treated major bleeds decreased from 17.2% to 0.

The mean (SD) time to the resolution of treated bleeds decreased after the start of Vonvendi prophylaxis in both age groups, from 3.3 (1.9) to 1.7 (0.6) days for paediatric and 3.6 (2.1) to 2.7 (1.2) days for adult patients. Blood transfusions, used by about 3% of both paediatric and adult patients before the start of Vonvendi prophylaxis, were not reported afterwards.

HRU outcomes

The percentage of patients with hospitalizations decreased from 6.9% to 0 for paediatric and from 16.1% to 3.2% for adult patients, and the percentage with ER visits from 27.6% to 3.4% for paediatric and 29.0% to 17.7% for adult patients. The majority of patients had ≥1 VWD-specific outpatient visit both before and after the initiation of Vonvendi prophylaxis, including 96.6% and 93.1% of paediatric patients and 71.0% and 75.8% of adult patients. The mean (SD) number of outpatient visits was 7.5 (3.9) per patient per year (PPPY) before and 6.6 (2.0) PPPY after Vonvendi treatment for paediatric patients and 5.8 (4.9) PPPY before and 5.6 (3.0) PPPY after Vonvendi treatment for adult patients.

Safety results

Not applicable. The submitted study did not include assessments of safety.

Discussion on clinical aspects

In accordance with Article 46 of regulation (EC) No 1901/2006, the MAH submitted the final report of TAK-577-5008 together with a short critical expert overview.

TAK-577-5008 was a panel-based, non-interventional, retrospective cohort study using chart review that was designed to examine the prophylactic use of Vonvendi (registered tradename of vonicog alfa in the US) among patients with type 1 and type 2 VWD in US real-world settings, including real-world treatment patterns, clinical outcomes, and health resource use.

Patient data was collected for 12 or more months prior to and following the index date, which was defined as the date of initiation of first routine prophylaxis treatment with vonicog alfa. Routine prophylaxis was defined as receiving vonicog alfa at least twice weekly for at least three consecutive months.

The study included a total 91 patients with medical charts provided by a sample of 26 physician. Of these, 29 (31.9%) were paediatric patients (aged <18 years), who began Vonvendi prophylaxis at a mean (SD) age of 13.6 (2.7) years (range, 8.0 to 17.8 years).

Of note, in the EU, vonicog alfa (VEYVONDI) is currently authorised in children only for the treatment of haemorrhage. Therefore, its prophylactic use in children, as analysed in TAK-577-5008, falls outside the current EU authorisation for VEYVONDI.

TAK-577-5008 adds to the limited evidence on real-world prophylactic use of vonicog alfa among patients with type 1 and 2 VWD. In essence, results of this study suggest that prophylactic treatment improves bleeding outcomes and VWD-related hospitalizations and ER visits, irrespective of patients' age. However, interpretation of the reported clinical outcomes is hampered by the inherent methodological limitations of retrospective, observational real-world studies, including the lack of randomisation and uncertainties regarding potential selection bias and incomplete data. Furthermore, given the formal exclusion of patients with type 3 VWD (i.e. the most severe type of VWD), the

generalisability of study results remains uncertain and the study did not include an any assessments of safety.

Therefore, the newly submitted data do not allow for drawing any meaningful conclusions regarding the benefit–risk balance of VEYVONDI for prophylactic treatment of VWD in children.

Consequently, it is agreed with the MAH that the results of study TAK-577-5008 do not warrant any changes to the currently approved EU product information of VEYVONDI.

3. Rapporteur's overall conclusion and recommendation

In summary, the results of study TAK-577-5008 do not change the favourable benefit risk profile of VEYVONDI in its approved indication. The submitted data do not warrant any update of the EU product information of VEYVONDI and no regulatory actions are required

☒ **Fulfilled:**

No regulatory action required.

4. Request for supplementary information

None

MAH responses to Request for supplementary information

Not applicable

Annex. Line listing of all the studies included in the development program

Not applicable. Submitted study is not part of the clinical development program of VEYVONDI.