Amsterdam, 25 June 2026
EMADOC-1700519818-3067534
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/0000340069

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	n/a
☒	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 TAK-577-5008: *Pediatric Post-hoc Analysis of The Cost of von Willebrand Disease Across Europe, a socioeconomic study (CVESS)* is a stand-alone study.

The MAH stated that 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 this analysis.

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.

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-577-5006: *Pediatric Post-hoc Analysis of The Cost of von Willebrand Disease Across Europe, a socioeconomic study (CVESS)*

Clinical study

TAK-577-5006: Paediatric Post-hoc Analysis of The Cost of von Willebrand Disease Across Europe, a socioeconomic study (CVESS)

Description

TAK-577-5006 was a post-hoc analysis of the CVESS (The Cost of von Willebrand Disease Across Europe, a socioeconomic study) dataset, which includes data for five paediatric patients who received VEYVONDI within the frame of a clinical trial.

CVESS was a descriptive, retrospective and cross-sectional, multi-site, bottom-up burden of illness study of adults and children with VWD in Europe consisting of two questionnaire forms:

- A physician reported case report forms (CRF), which captured information on the patient's demographics, clinical characteristics, clinical outcomes, treatment patterns, and health resource utilization over the 12 months prior to the index date (where applicable).
- A patient completed Patient and Public Involvement and Engagement questionnaire (PPIE), which captured information about direct non-medical and indirect costs via patient-reported resource use and outcomes, including Health-Related Quality of Life (HRQoL).

In the CVESS study, patients with VWD in France, Germany, Spain, Italy and the UK were recruited via their haematologists. Data was captured between August 2018 and December 2018.

The overarching goal of TAK-577-5006 was to understand the disease landscape for paediatric populations with VWD. Outcomes of interest were described for the following paediatric sub-cohorts:

- Age (≤2 years, 3-6 years, 7-12 years, 13-17 years)
- Sex (Male, Female)
- VWD Type (Type 1, Type 2, Type 3)

Treatment Strategy (CFC Episodic, CFC Intermittent Prophylaxis, CFC Continuous Prophylaxis, Clinical Trial (VEYVONDI), Not Used)

Methods

Study participants

Patients included in the CVESS dataset were eligible for the TAK-577-5006 analysis if they were aged under 18 years at the time of data collection (that is, aged 1 to 17 years).

To be eligible for the CVESS study, patients had to meet the following criteria:

Inclusion Criteria (CVESS):

- Age 1+ years
- Laboratory diagnosis of hereditary VWD
- Known VWD classification

Patients recruited to a clinical trial at the time of study recruitment could be included within the study, however limited treatment data was collected for these participants.

Exclusion Criteria (CVESS):

- Patients with acquired von Willebrand Syndrome

- Patients who cannot understand the questionnaire for issues such as language barriers

Those with a physical or mental condition that inhibits them from making a decision for themselves.

Treatments

TAK-577-5006 was a post-hoc analysis.

Objectives

To describe the patient characteristics and clinical outcomes of the paediatric VWD population in five European countries, exploring specific sub-cohorts of interest.

Specifically:

- Objective 1: To describe patient characteristics including sociodemographic and disease characteristics
- Objective 2: To describe clinical outcomes including bleed events, chronic pain and joint damage
- Objective 3: To describe treatment patterns, health resource utilization (HRU) and health related quality of life (HRQoL)

Outcomes/endpoints

The following variables were considered:

- *Patient characteristics:*

Age, Age group (<2 years, 3-6 years, 7-12 years, 13-17 years categorical), Sex (Male, Female), Height, Race (White, Non-White), Home circumstances (Lives with family/friends, Other, Unknown), Concomitant conditions by type (Diseases of the circulatory system, Diseases of the eye and adnexa, Mental and behavioural disorders, Diseases of the digestive system, Endocrine, nutritional and metabolic disease, Infectious and parasitic diseases, Diseases of the blood, Diseases of the musculoskeletal system and connective tissue, Diseases of the genitourinary system, Other disorders, No concomitant conditions), Country (Germany, Spain, France, Italy, UK), VWD type (Type 1, Type 2, Type 3), Family history of VWD (Yes, No), Physician Reported Severity (Mild, Moderate, Severe), Baseline laboratory parameters (VWF:RCo, VWF:GPIbR, VWF:GPIbM, VWF:Ab, VWF:Ag, VWF:CB, FVIII level), Age at diagnosis.

- *Clinical outcomes*

Age at diagnosis, Chronic pain level (No pain, Mild pain, Moderate pain, Severe pain), Number of bleeds for which medical attention was sought, overall and by type, Joints with limited range of motion (0 joints, 1 joint, 2+ joints), Number of joints with limit range of motion (Number of joints if one or more reported, Number of joints overall), Target joints (0 joints, 1 joint, 2+ joints), Number of target joints (Number of joints if one or more reported, Number of joints overall), Chronically damaged joints (0 joints, 1 joint, 2+ joints), Number of chronically damaged joints (Number of joints if one or more reported, Number of joints overall).

- *Treatment patterns*

Desmopressin use (Episodic, Intermittent prophylaxis, Continuous prophylaxis, Not used), Clotting Factor Concentrate (CFC) use (Episodic, Intermittent prophylaxis, Continuous prophylaxis, Not used, Clinical trial), Antifibrinolytic use (Episodic, Intermittent prophylaxis, Continuous prophylaxis, Not

used), Adherence to treatment regimen (Excellent [missing <10% of prescribed doses], Very good [missing 10 - 20% of prescribed does], Good [missing >20 - 30% of prescribed doses], Fair [missing >30 - 40% of prescribed doses], Poor/very poor [missing >40% of prescribed doses], Not applicable [not on regular treatment], Not applicable [patient is fully adherent]).

- *Health resource utilization*

Hospitalization for bleeding (Epistaxis, Oral cavity bleed, Bleeding post dental extraction, GI bleed, Muscle hematoma, Hemarthrosis, CNS bleed, Bleeding due to surgery/major trauma), Days in hospital/ICU for bleeding, Planned/routine visits, Unplanned/emergency visits, Outpatient consultations.

- *Health related quality of life*

EQ-5D Index Score, EQ-5D VAS

Sample size

The full paediatric sample size of the CVESS dataset was utilized for TAK-577-5006

Randomisation and blinding (masking)

Not applicable

Statistical Methods

Data was summarized for each sub-cohort using descriptive statistics. Continuous variables were presented as mean and standard deviation (numbers of missing values included where applicable). Categorical variables were presented as frequency and percentage. P-values for each variable were calculated using one-way ANOVA for continuous variables and chi-squared tests for categorical variables. Results were deemed statistically significant at p-values <0.05.

Results

Recruitment / Participant flow / Numbers analysed

The paediatric sample (i.e., patients aged ≥1 year to <18 years) within the CVESS dataset totals 266 patients, who contributed 266 CRFs and 39 PPIEs. The full paediatric sample size was utilized for TAK-577-5006. However, of the 266 paediatric patients, only 5 patients (1.88%) were identified as having received VEYVONDI within the frame of a clinical study, making them relevant to this Article 46 procedure.

Baseline data

In the subgroup of 5 patients who received VEYVONDI within the frame of a clinical trial, 4 were male, and the mean (SD) age was 15.00 (2.00), including 4 patients in the age range 13 to 17 years and 1 in the age range 7 to 12 years. The race reported was white for 4 patients and non-white for 1 patient. The mean (SD) age at diagnosis of VWD, available for 4 patients, was 14.75 (1.26) years. Three patients had type 1 VWD, and 2 patients had type 2 VWD. The majority (3 patients, 60.00%) had a family history of VWD. The physician reported the severity as mild for 2 patients, moderate for 2 patients, and severe for 1 patient. The only factor measured in all 5 patients was von Willebrand factor antigen, with a mean (SD) of 35.20 (43.68) IU/dL, and the only other factor measured in more than 2 patients was factor VIII, measured in 3 patients with a mean (SD) of 20.67 (34.08) IU/dL.

Of the 5 patients who received VEYVONDI in a clinical trial, 4 reported mild pain, and 1 reported moderate pain. In the 12 months prior to data collection, they had a mean (SD) of 2.60 (2.19) treated bleeds, most commonly epistaxis (1.00 [1.73]), oral cavity bleeding (0.80 [1.10]), gastrointestinal (GI) bleeding (0.40 [0.55]), hemarthrosis (0.20 [0.45]), and central nervous system (CNS) bleeding (0.20 [0.45]). The majority of patients (3, 60.00%) had no joints with a limited range of motion, and 2 patients had 2 or more joints with a limited range of motion, with a mean (SD) of 3.00 (1.41) affected joints. Two patients had 2 or more target joints, with a mean (SD) of 2.50 (0.71) target joints. Three patients had chronically damaged joints, including 1 patient with 1 damaged joint and 2 patients with 2 or more damaged joints, for a mean (SD) of 2.00 (1.00) in the affected patients.

None of the patients who received VEYVONDI in a clinical trial reported use of desmopressin or antifibrinolytics. Treatment adherence was reported as excellent (missing <10%) for 1 patient, very good (missing 10% to 20%) for 3 patients, and good (missing >20% to 30%) for 1 patient.

Of the 5 patients, 3 patients were hospitalized for bleeding, including 2 patients for GI bleeding and 1 patient each for CNS bleeding and epistaxis. For all bleeds, the mean (SD) days in the hospital was 3.80 (5.36), including 1.60 (3.58) days for CNS bleeding, 1.60 (2.30) days for GI bleeding, and 0.60 (1.34) days for epistaxis. This included a mean (SD) of 2.00 (3.08) days in the intensive care unit for any bleeding, including 1.00 (2.24) days for CNS bleeding, 0.40 (0.89) days for GI bleeding, and 0.60 (1.34) days for epistaxis. The 5 patients had a mean (SD) of 3.80 (1.79) planned/routine physician visits, 2.20 (1.09) planned/routine nurse specialist visits, 2.40 (1.95) unplanned/emergency physician visits, 0.80 (0.84) unplanned/emergency nurse specialist visits, and 5.80 (1.30) outpatient consultations with a specialist who was not their primary treating haematologist for reasons related to VWD.

Efficacy ans Safety results

Not applicable. The submitted post-hoc analysis did not assess the efficacy and/or safety of VEYVONDI. It was based on an existing dataset derived from a descriptive, retrospective and cross-sectional, multi-site, bottom-up burden of illness study and was conducted to characterize the disease landscape and assess the burden of illness among children with VWD in Europe.

Discussion on clinical aspects

In accordance with Article 46 of regulation (EC) No 1901/2006, the MAH submitted the report of TAK-577-5006 together with a short critical expert overview.

TAK-577-5006 was a post-hoc analysis of paediatric data captured between August 2018 and December 2018 in CVESS (The Cost of von Willebrand Disease Across Europe, a socioeconomic study), which was a descriptive, retrospective and cross-sectional, multi-site, bottom-up burden of illness study. CVESS was open to patients with hereditary VWD of all ages (irrespective of VWD type and treatment) and included a total of 266 paediatric patients (i.e., patients aged ≥1 year to <18 years). TAK-577-5006 utilized the full paediatric sample size of CVESS but included only 5 patients who received VEYVONDI within the frame of a clinical study, making them relevant to this Article 46 procedure. For the remaining patients, treatment information was limited to categorical descriptions of: (i) clotting factor concentrate use (with no further specification of the product used), (ii) desmopressin use, and (iii) antifibrinolytic use. Of note, the CVESS dataset does not contain any additional information regarding the clinical studies in which patients received treatment with VEYVONDI. However, considering the date of EU marketing authorisation (31 August 2018) and the CVESS data collection period (August 2018 to December 2018), it is considered likely that the data

from the 5 patients who received VEYVONDI in a then ongoing clinical trial had already been reported previously.

TAK-577-5006 evaluated various patient characteristics and clinical outcomes, with the aim of characterizing the disease landscape and assessing the burden of illness among children with VWD in Europe, irrespective of their underlying treatments. The analysis did not evaluate any efficacy and/or safety outcomes and, therefore, does not provide any relevant data regarding the benefit-risk balance of VEYVONDI for the treatment of VWD in children.

Consequently, it is agreed with the MAH that the newly submitted data do not change the currently established favourable benefit-risk profile of VEYVONDI in the treatment of children with VWD and do not warrant any changes to the EU product information of VEYVONDI.

3. Rapporteur's overall conclusion and recommendation

In summary, the results of the post-hoc analysis TAK-577-5006 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.