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SCIENCE MEDICINES HEALTH

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Human Medicines Division

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

TAKHZYRO

Lanadelumab

Procedure no: EMA/PAM/0000285505

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 of Procedure	21 July 2025	21 July 2025
☐	CHMP Rapporteur AR	25 August 2025	22 August 2025
☐	CHMP comments	8 September 2025	n/a
☐	Updated CHMP Rapporteur AR	11 September 2025	n/a
☒	CHMP outcome	18 September 2025	18 September 2025

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1. Introduction

On 02 October 2023, the MAH submitted data from Interim Analysis 3 for SHP643-403 (the *EMPOWER* Study), a Phase 4 observational non-interventional study of lanadelumab that includes paediatric subjects under 18 years of age. Interim data were based on a data cut-off date of 01 Mar 2022. These interim data were assessed in procedure TAKHZYRO EMEA/H/C/004806/P46/006.

On 7 July 2025, the MAH submitted the final report for the same study in accordance with Article 46 of Regulation (EC) No1901/2006, as amended. The current procedure concerns the final paediatric data from Study SHP643-403.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

Study SHP643-403 (EMPOWER) is a stand-alone study.

SHP643-403 (EMPOWER) is Phase 4 non-interventional study (observational) of lanadelumab (SHP643) that includes paediatric subjects under 18 years of age. The study is not part of the EU RMP.

2.2. Information on the pharmaceutical formulation used in the study

Commercial Takhzyro was used.

2.3. Clinical aspects

2.3.1. Clinical study

Clinical study number and title

SHP643-403*: An observational, non-interventional, study of patients with Hereditary Angioedema in the United States and Canada (EMPOWER Study)*

Description

Methods

Please refer to procedure TAKHZYRO EMEA/H/C/004806/P46/006.

In summary, Study SHP643-403 was a self-controlled prospective, observational cohort study of patients with a diagnosis of hereditary angioedema (HAE) Type I or II.

All the patients who were enrolled in this prospective observational study have been categorized into one of two groups: the prevalent lanadelumab users and the new lanadelumab users. The prevalent lanadelumab users are defined as those patients who a) had received at least 4 lanadelumab doses prior to enrolment and b) were receiving lanadelumab at enrolment or received the last dose <70 days prior to enrolment. The new lanadelumab users had not started lanadelumab at the time of enrolment or already started lanadelumab prior to enrolment and had received <4 lanadelumab doses prior to enrolment date.

Results

Participant flow

In total, 16 subjects aged 12-17 years were enrolled in the study.

Of these, 14 subjects are included in the safety set, i.e., took at least 1 dose of lanadelumab after enrolment or if their last dose was within 70 days prior to enrolment.
Twelve subjects were included in the Full Analysis Set had at least 1 postbaseline effectiveness outcome (endpoint) assessment.

Baseline data

In the paediatric FAS, the mean (SD) age at enrolment was 15.0 (2.13) years. Seven (58.3%) participants were female, and all 12 (100.0%) participants were White and were of Not Hispanic or Latino ethnicity. All paediatric subjects were enrolled in the US.

Efficacy results

The monthly HAE attack rate during treatment in comparison to pre-enrolment for new lanadelumab users (paediatric participants) (n=5) is presented in Table 1

Table 1. Observed Attack-Rate Comparison to Pre-enrollment for New Lanadelumab Users – Pediatric Participant (truncated by Assessor)

	Full Analysis Set (N=12) [a]			
	Prelanadelumab	Postlanadelumab		
		Early [b]	Steady [c]	Cumulative [d]
All new lanadelumab users Attack rate (attacks/months) [f]				
Mean rate	1.27	0.35	0.06	0.09
95% CI	(-1.53, 4.08)	(-0.10, 0.80)	(-0.04, 0.15)	(-0.03, 0.21)

b Early state defined as the first 69 days after lanadelumab initiation. Defined only for new lanadelumab users.
c Steady state defined as the period of lanadelumab exposure starting at day 70 after lanadelumab initiation. Not all participants continued treatment until achievement of steady state at day 69. Defined only for new lanadelumab users.
d Cumulative state defined as a summary of the 2 states of postlanadelumab treatment that consisted of "early" and "steady". Defined only for new lanadelumab users.

The monthly HAE attack rate during treatment for prevalent lanadelumab users (paediatric participants) (n=7) is presented in Table 2.

Table 2. Observed Attack-Rate for Prevalent Lanadelumab Users – Pediatric Participants (truncated by Assessor)

	Full Analysis Set [a] (N=12)
	Overall Study Period [b]
Prevalent lanadelumab users [c]	
Attack rate (attacks/per month) [e]	
Attacks/months	0.04
95% CI	(0.01, 0.07)

Safety results

Nine paediatric participants in the safety set experienced a total of 16 lanadelumab TEAEs.

There were 9 (56.3%) events assessed as mild and 7 (43.8%) events assessed as moderate in severity. Half (50.0%) of the events were considered related to HAE treatment.

There were no deaths, TEAEs related to lanadelumab, serious TEAEs, or TEAEs which resulted in study discontinuation in the paediatric population

Lanadelumab TEAEs (excluding HAE attacks) reported in the paediatric population are summarized by SOC and PT in Table 3. The most common TEAEs by SOC were infections and infestations (n=6, 66.7%), with COVID-19 infections representing the most common PT (6 events in 6 participants).

Table 3. Treatment-emergent Adverse Events (Excluding HAE Attack Reported Adverse Events) Reported by Pediatric Participants – Safety Set

	Safety Set [a] (N=14)	
System Organ Class Preferred Term	**Participants [b] (N=9)**	**Events [c] (N=16)**
	n (%)	
Any lanadelumab TEAE	9 (100.0)	16 (100.0)
General disorders and administration site conditions	1 (11.1)	3 (18.8)
Peripheral swelling	1 (11.1)	3 (18.8)
Infections and infestations	6 (66.7)	6 (37.5)
COVID-19	6 (66.7)	6 (37.5)
Injury, poisoning and procedural complications	1 (11.1)	1 (6.3)
Foreign body	1 (11.1)	1 (6.3)
Musculoskeletal and connective tissue disorders	1 (11.1)	1 (6.3)
Knee impingement syndrome	1 (11.1)	1 (6.3)
Nervous system disorders	1 (11.1)	1 (6.3)
Bell's palsy	1 (11.1)	1 (6.3)
Psychiatric disorders	1 (11.1)	2 (12.5)
Anxiety	1 (11.1)	1 (6.3)
Depression	1 (11.1)	1 (6.3)
Respiratory, thoracic, and mediastinal disorders	2 (22.2)	2 (12.5)
Asthma	1 (11.1)	1 (6.3)
Wheezing	1 (11.1)	1 (6.3)

2.3.2. Discussion on clinical aspects

SHP643-403 (EMPOWER) is Phase 4 non-interventional observational study of lanadelumab that includes paediatric subjects under 18 years of age. Since this is a p46 procedure and the study was not part of the EU RMP, only the paediatric data are assessed.

Paediatric data from Interim Analysis 3 of the study (cut-off date 01 Mar 2022) was assessed in procedure TAKHZYRO EMEA/H/C/004806/P46/006.

The current procedure presents the final paediatric data from the study.

Sixteen patients under the age of 18 years (12-17 years) were enrolled in the study. Of these, 12 subjects were part of the Full Analysis Set. Five of the subjects were new users, seven prevalent users.

For the paediatric subpopulation, only the primary endpoint has been presented separately. The eligibility criteria did not include any minimum required HAE attack rate at baseline. The mean HAE attack rate/ month at baseline was therefore lower than in the pivotal clinical studies. A decrease in mean HAE attack rate/month on treatment from 1.27 to 0.09 was observed in new paediatric lanadelumab users (n=5). In prevalent paediatric lanadelumab users (n=7), the mean HAE attack rate/month during the observation period was 0.04. This is largely in line with the previous experience of lanadelumab.

In total, 16 treatment emerging adverse event (TEAE) were reported by nine subjects in the paediatric subpopulation. No SAE was reported. There were no fatal event or discontinuation due to TEAE reported in the paediatric subpopulation. The only event reported by more than one subject was COVID-19.

In summary, no new and unexpected safety issues emerged from the paediatric study population.

3. Rapporteur's overall conclusion and recommendation

The conclusions based on the study paediatric interim data assessed in procedure TAKHZYRO EMEA/H/C/004806/P46/006 remain.

The effectiveness of lanadelumab in the paediatric subpopulation of study SHP643-403 is largely in line with the previous experience of lanadelumab. The safety seems to be in line with the known safety profile of lanadelumab.

No additional actions are considered warranted based on the data in the paediatric subpopulation of the study.

The benefit/risk ratio for Takhzyro remains unchanged.

☒ **Fulfilled:**

No regulatory action required.