11 December 2025
EMADOC-1700519818-2906839
Human Medicines Division

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

HyQvia

Human normal immunoglobulin

Procedure no: EMA/PAM/0000302076

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**	**Need for discussion[2]**
☐	Start of procedure	13 October 2025	13 October 2025	☐
☐	CHMP Rapporteur Assessment Report	17 November 2025	17 November 2025	☐
☐	CHMP members comments	01 December 2025	n/a	☐
☐	Updated CHMP Rapporteur Assessment Report	04 December 2025	n/a	☐
☒	CHMP adoption of conclusions:	11 December 2025	11 December 2025	☐

Table of contents

1. Introduction

On 25 September 2025, the MAH submitted a completed paediatric study for HyQvia, 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-771-3004 ("A Phase 3, Open-label, Non-controlled Study to Evaluate the Pharmacokinetics, Safety and Tolerability, and Efficacy of TAK-771 in Japanese Subjects with Primary Immunodeficiency Diseases (PID)") is a stand alone study.

2.2. Information on the pharmaceutical formulation used in the study

Commercial HyQvia

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

- Study TAK-771-3004: A Phase 3, Open-label, Non-controlled Study to Evaluate the Pharmacokinetics, Safety and Tolerability, and Efficacy of TAK-771 in Japanese Subjects with Primary Immunodeficiency Diseases (PID)

2.3.2. Clinical study

TAK-771-3004: A Phase 3, Open-label, Non-controlled Study to Evaluate the Pharmacokinetics, Safety and Tolerability, and Efficacy of TAK-771 in Japanese Subjects with Primary Immunodeficiency Diseases (PID)

Description

TAK-771-3004, an open-label, non-controlled, multidose, multicenter study was conducted to evaluate the pharmacokinetics, safety, tolerability and efficacy of HyQvia in Japanese subjects with primary immunodeficiency diseases. The study was completed on 28th August 2023 ("last patient out").

Methods

Study participants

A total of 16 participants with a documented diagnosis of a form of primary humoral immunodeficiency involving antibody formation and requiring gammaglobulin replacement were enrolled from 12 sites in Japan.

Of those, 5 subjects were aged <18 years.

Treatments

The trial consisted of signing informed (e)Consent, a screening period (up to 13 weeks), a treatment period (Epoch 1: 3 to 6 weeks of dose ramp-up period, Epoch 2: 12 weeks of dose adjustment period and 12 weeks of trough evaluation period), and an EOS/early termination visit.

Epoch 1: For all participants, administration of HyQvia started with the ramp-up infusion (3 to 6 weeks).

Epoch 2: HyQvia was administered SC at 3- or 4-week dosing intervals after the ramp-up (Epoch 1).

The IgG dosing regimen for TAK-771 was the same as the subject's previous monthly equivalent IVIG dose or SCIG when administered at a dosing frequency of every 3 or 4 weeks.

Objective(s)

The primary objective of the trial was to assess serum trough levels of total IgG when using HyQvia as maintenance therapy in Japanese participants with PID.

The secondary objectives of this trial were:

- To characterize the PK profiles of HyQvia in Japanese participants with PID following HyQvia administration.
- To evaluate the safety and tolerability of HyQvia in Japanese participants with PID.
- To evaluate the efficacy of HyQvia in Japanese participants with PID.
- To assess disease activity and HRQoL in Japanese participants with PID following HyQvia administration.

Outcomes/endpoints

Primary endpoint: The serum trough levels of total IgG (total serum trough IgG antibodies) measured during the trough evaluation period of Epoch 2 (administration of TAK-771)

Secondary endpoints:

- PK parameters for total serum levels of IgG and for IgG subclasses in PK assessment period in Epoch 2 (in a subset of 5 to 7 subjects aged 12 years or older), which included but not limited to the following: Cmax, Tmax, AUC, half-life, CL/F, Vz/F, and Cmin
- Serum trough levels of IgG subclasses in the trough evaluation period of Epoch 2
- Trough levels of specific antibodies to clinically relevant pathogens (Clostridium tetani toxoid, HIB, and HBV) in Epoch 1 and 2
- Safety & tolerability, immunogenicity to rHuPH20
- Annual rate of validated ASBIs per subject in Epoch 1 and 2
- Annual rate of all infections per subject in Epoch 1 and 2
- Health resource utilization in Epoch 1 and 2
- Days not able to attend school/work or to perform normal daily activities due to illness/infection
- Days on antibiotics
- Number of hospitalizations due to illness/infection and length of stay (in days)
- Number of acute (urgent or unscheduled) physician visits due to illness/infection
- Infusion parameters in Epoch 2, including but not limited to: number of infusions per month, number of infusion sites per infusion, number of infusion sites per month, duration of individual infusions, maximum infusion rate/site, and infusion volume/site
- QoL: PEDS-QL, EQ-5D-3L Health Questionnaire
- Treatment satisfaction (TSQM-9)

- treatment preference at EOS/Early termination

Statistical Methods

Only descriptive analysis for paediatric patients

Results

Participant flow

All 5 paediatric subjects completed the study.

Baseline data

Subject Number / Age (years), Sex, Race [a]	Ethnicity	Height (cm)	Weight (kg)	BMI (kg/m2)	Dosing Frequency Per Interval	Prior Treatment at Consent	Primary Immunodeficiency Diagnosis
[redacted] 5/M/A(J)	Not Hispanic/Latino	105.5	15.9	14.3	Every 3 Weeks	IVIG	Ataxia Telangiectasia
12/F/A(J)	Not Hispanic/Latino	149.2	37	16.6	Every 4 Weeks	cSCIG	Common Variable Deficiency
9/M/A(J)	Not Hispanic/Latino	93.3	18.4	21.1	Every 4 Weeks	IVIG	Common Variable Deficiency
7/M/A(J)	Not Hispanic/Latino	119.4	24.3	17.0	Every 4 Weeks	IVIG	Congenital Agamma - XLA
8/M/A(J)	Not Hispanic/Latino	119.8	24.3	16.9	Every 4 Weeks	cSCIG	Common Variable Deficiency

Number analysed

All 5 paediatric subjects were included in all analysis sets.

Efficacy results

Primary endpoint:

The serum total IgG levels before starting TAK-771 dose (at 2 pre-doses) and after receiving TAK-771 over 6 months (at last 3 doses) were comparable, with Geo mean of 9.624 g/L (95% CI of Geo mean: 8.421-11.00, median: 9.68) and 9.494 g/L (95% CI of Geo mean: 8.286-10.88, median: 9.24), respectively. Additionally, the serum total IgG levels before starting TAK-771 dose and after receiving TAK-771 over 6 months by age were also comparable, with Geo mean of 7.804 g/L (95% CI of Geo mean: 6.224-9.786, median: 8.23) and 8.822 g/L (95% CI of Geo mean: 5.236-14.87, median: 8.56) for subjects aged <12 years old, and 10.32 g/L (95% CI of Geo mean: 8.846-12.04, median: 10.1) and 9.686 g/L (95% CI of Geo mean: 8.201-11.44, median: 9.32) for subjects aged >12 years old, respectively.

Summary of secondary endpoints:

There were no validated ASBIs reported in this study. The annual rate of all infections in the overall treatment period in the FAS was 2.74 (95% CI: 1.40-4.74).

The analyses of efficacy results in this trial indicated that HyQvia is effective and favoured for the treatment of Japanese participants with PID aged 2 years or older, in terms of infection rates, patient-related outcomes, treatment satisfaction, and treatment preference.

Safety results

Of the 16 participants, 5 were paediatric (aged ≤17 years). TEAEs were reported in all 5 (100.0%) paediatric participants in the overall treatment period and in Epoch 1 and Epoch 2. Related TEAEs occurred in 4 (80.0%) paediatric participants in the overall treatment period; 3 (60.0%) participants in Epoch 1 and 4 (80.0%) participants in Epoch 2. Infusion-associated TEAEs were reported in 2 (40.0%) paediatric participants in the overall treatment period and in Epoch 1 and in Epoch 2. The reported

TEAEs were comparable between the age groups ≤17 years and ≥18 years. One paediatric participant experienced 2 unrelated SAEs of gastroenteritis and adrenal insufficiency in Epoch 1; no serious TEAE was reported in Epoch 2.

Narratives for all 5 paediatric participants are presented.

Table 1: Summary of TEAEs reported in the age group of ≤17 years (SAS)

	Epoch 1 (N=5)		Epoch 2 (N=5)		Overall (N=5)	
Category	Number (%) of participants	Number of events	Number (%) of participants	Number of events	Number (%) of participants	Number of events
Any TEAE	5 (100.0)	20	5 (100.0)	53	5 (100.0)	73
Any TEAE related to IP	3 (60.0)	10	4 (80.0)	24	4 (80.0)	34
Any TEAE nonrelated to IP	4 (80.0)	10	5 (100.0)	29	5 (100.0)	39
Any serious TEAE	1 (20.0)	2	0	0	1 (20.0)	2
Any serious TEAE related to IP	0	0	0	0	0	0
Any severe TEAE	0	0	0	0	0	0
Any severe TEAE related to IP	0	0	0	0	0	0
Any local TEAE	3 (60.0)	9	3 (60.0)	25	3 (60.0)	34
Any local TEAE related to IP	2 (40.0)	7	3 (60.0)	19	3 (60.0)	26
Any systemic TEAE	5 (100.0)	11	5 (100.0)	28	5 (100.0)	39
Any systemic TEAE related to IP	2 (40.0)	3	1 (20.0)	5	2 (40.0)	8
Any infusion-associated TEAE	2 (40.0)	3	2 (40.0)	13	2 (40.0)	16
Any TEAE leading to trial discontinuation	0	0	0	0	0	0
Any TEAE leading to death	0	0	0	0	0	0

Source: TAK-771-3004 CSR Table 32.

2.3.3. Discussion on clinical aspects

As part of this procedure, the MAH submitted the final results of the Study TAK-771-3004, an open-label, non-controlled, multidose, multicenter study was conducted to evaluate the pharmacokinetics, safety, tolerability and efficacy of HyQvia in Japanese subjects with primary immunodeficiency diseases.

A total of five paediatric patients were enrolled in the study of which all completed the study. Prior to the study, all subjects received IVIg or SCIg and then switched to maintenance treatment with HyQvia.

The primary endpoint was met: Serum trough levels of total IgG remained above 5 g/L at all study visits for all paediatric subjects. The secondary endpoints supported the primary analysis in terms of infection rates, patient-related outcomes, treatment satisfaction, and treatment preference in patients with PID. No acute serious bacterial infections were observed during the study.

All 5 paediatric subjects had TEAEs, of which 34 events in 4 patients were IP-related. Narratives for each paediatric patient was provided. Only 2 serious TEAEs were reported in one patient, both events were considered unrelated. No unexpected findings with regard to safety were observed.

Overall, the presented data support the use of HyQvia in paediatric patients with PID.

3. CHMP overall conclusion and recommendation

Efficacy of HyQvia was confirmed in the selected paediatric study population with PID in study TAK-771-3004. The safety findings were consistent with the established safety profile of HyQvia. No new safety issues were identified.

Overall, the risk-benefit balance remains the same for paediatric patients with PID. It is agreed that no changes to the product information are required.

☒ **Fulfilled:**

No regulatory action required.