25 April 2025
EMADOC-1700519818-1877468
Human Medicines Division

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

Firazyr

Icatibant

Procedure no: EMEA/H/C/000899/P46/01100/1

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	25 February 2025	25 February 2025
☐	CHMP Rapporteur AR	31 March 2025	24 March 2025
☐	CHMP comments	14 April 2025	n/a
☐	Updated CHMP Rapporteur AR	16 April 2025	n/a
☒	CHMP outcome	25 April 2025	25 April 2025

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1. Introduction

On 27 January 2025, the MAH submitted a completed paediatric study for Firazyr, 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 SHP667-401 ("The FIRAZYR Subcutaneous Injection 30 mg Syringe General Drug Use-Result Survey") is a stand-alone study.

2.2. Information on the pharmaceutical formulation used in the study

The study was performed in a post-marketing setting using commercial Firazyr.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

Study SHP667-401: *The FIRAZYR Subcutaneous Injection 30 mg Syringe General Drug Use-Result Survey*

2.3.2. Clinical study

Description

Study SHP667-401 ("FIRAZYR survey") was a survey study of patients with hereditary angioedema (HAE) in Japan who were administered or prescribed Firazyr (30 mg subcutaneous injection) for the first time.

This study was conducted as one of the conditions for approval in Japan, where there was a requirement to conduct a post-marketing drug use-results survey covering all patients treated with Firazyr in Japan. The survey was to be conducted until data from a certain number of patients had been accumulated in order to confirm the safety and efficacy of Firazyr.

Patients were to be observed for up to 3 months after treatment with Firazyr (observation period). However, reporting of attack and treatment status was either up to 3 months after the first attack, or until attack resolution after up to 5 treatments with Firazyr. Adverse events (AEs) that occurred after the end of the observation period were reported separately.

Paediatric use of Firazyr was approved in Japan on 24 August 2022, and since the FIRAZYR survey started on 20 November 2018, paediatric patients in this survey were treated off-label. Due to this off-label use, details on the treatment status for the paediatric patients were not presented in the FIRAZYR survey study report.

Methods

Study participants

Patients with a confirmed diagnosis of HAE (type I or II, or HAE with normal C1-inhibitor [HAE-nC1-INH], also called HAE III), regardless of age or sex, who were administered or prescribed this drug for the first time were included in this survey.

Patients with a history of administration prior to approval of this drug in a clinical trial were excluded from this survey.

Treatments

Typically, 30 mg of icatibant per dose was administered subcutaneously as an injection. If a response was insufficient or symptoms recurred, then additional doses of 30 mg could have been administered at least 6 hours apart, with no more than 3 doses in a 24-hour period.

Objective(s)

The main objectives of the FIRAZYR survey were:

- To monitor the occurrence of ADRs, including unknown ADRs.
- To understand factors thought to affect safety or effectiveness in patients with HAE who used Firazyr in the survey setting.
- To monitor other safety issues of interest, that is, serious hypersensitivity and severe injection site reactions, deterioration of cardiac function under ischemic conditions due to bradykinin antagonism, hypotensive effects, and immunogenicity

Statistical Methods

Only descriptive statistics applied.

Results

Participant flow

A total of 179 patients were enrolled from 93 sites. Of the 178 patients in which case report forms were collected, 155 patients were treated and included in the safety analysis set (SAS). Of the 155 patients in the SAS, 100 patients were included in the efficacy assessment set (EAS).

A total of 149 (96.13%) patients in the SAS completed the survey study; 6 (3.87%) patients discontinued, 2 of which were due to an AE.

The FIRAZYR survey included 11 patients aged <18 years.

Recruitment

All subjects were from Japan.

Baseline data paediatric population

The ages of the 11 paediatric patients ranged from 7 to 17 years.

The most common types of HAE diagnosis were Type III (5 patients) and Type I (4 patients). Nearly all patients had a family history of HAE (10 patients). The majority of patients had prior treatment with C1 inhibitor alone (7 patients); 3 patients had prior treatment with C1 inhibitor and tranexamic acid, and 1 patient received prior treatment with other.

Efficacy results

All paediatric patients were excluded from the Effectiveness analysis set

Safety results

In the safety analysis set, 11 (7 %) patients were aged <18 years with 3 (27%) patients experiencing an ADR: 2 patients had injection site reactions, and 1 patient had injection site urticaria.

None of these events were unknown or serious, and all were mild in severity. Both injection site reactions were reported as recovered, whilst the injection site urticaria was reported as recovering.

For the 3 paediatric patients experiencing an ADR, data on body weight were not available. Two of the 3 paediatric patients with an ADR had HAE Type III; the remaining patient had HAE Type I.

2.3.3. Discussion on clinical aspects

The FIRAZYR survey was an all-Japanese post-marketing drug use-results survey covering all patients treated with Firazyr in Japan.

Since this is a p46 procedure for a non-interventional study that is not part of the EU RMP, only the paediatric data are assessed.

Eleven subjects aged 7-17 years of age were included in the survey.

Since the FIRAZYR survey started before paediatric use of Firazyr was approved in Japan, paediatric patients in this survey were treated off-label. The paediatric population was therefore excluded from the Effectiveness analysis set and no effectiveness data was presented for this population.

Three paediatric subjects (27%) reported adverse events, all related to injection site reactions. Injection site reactions are labelled as very common for Firazyr in the EU SmPC.

3. Rapporteur's overall conclusion and recommendation

There was no effectiveness data for the paediatric population.

No new and unexpected safety issues in the paediatric population emerged from the FIRAZYR survey.

The benefit/risk ratio remains unchanged.

☒ **Fulfilled:**

No regulatory action required.