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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

SIMBRINZA

brinzolamide / brimonidine

Procedure no: EMEA/H/C/003698/P46/002

Note

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

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Amsterdam, 24 February 2022
EMA/CHMP/66626/2022
Committee for Medicinal Products for Human Use (CHMP)

Assessment report for pediatric studies submitted in accordance with article 46 of regulation (EC) No 1901/2006, as amended

SIMBRINZA

International non-proprietary name: Brimonidine tartrate, brinzolamide

Procedure no.: EMA/H/C/003698/P46/002

Marketing authorisation holder (MAH): Novartis Europharm Limited

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1. Introduction

On December 2021, the MAH submitted a completed paediatric study for Simbrinza®, eye drops, suspension, 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 the study CQVJ499A2001, "Post-marketing surveillance to observe the safety and efficacy of Simbrinza Eye Drops®" is a stand alone study.

The study is not conducted in compliance with any agreed paediatric investigation plan.

The MAH does not propose an update to the product information based on the results of this study.

2.2. Information on the pharmaceutical formulation used in the study

Commercial formulation of Simbrinza®, eye drops, suspension (Brinzolamide 10 mg/mL/ Brimonidine tartrate 2 mg/mL) was used in this study.

As per Company Core Data Sheet and Korea prescription information, Simbrinza is indicated for the reduction of elevated intraocular pressure (IOP) in adult patients with open angle glaucoma or ocular hypertension.

Simbrinza is administered in adults as one drop in the affected eye(s) two or three times daily. Simbrinza is contraindicated in children less than 2 years of age and not recommended in children or adolescents aged 2 to 17 years because of the potential for CNS depression due to the brimonidine tartrate component.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for study CQVJ499A2001: "Post-marketing surveillance to observe the safety and efficacy of Simbrinza Eye Drops®"

2.3.2. Clinical study CQVJ499A2001

Description

This was a multicenter, prospective, observational, post-marketing surveillance study to evaluate the safety and efficacy of Simbrinza in Korean patients with open angle glaucoma or ocular hypertension.

Surveillance data from total of 693 patients were collected during the study period (from June 10, 2015 to June 9, 2021) and the study was completed on 09-Jun-2021.

This post-marketing surveillance will collect and evaluate the safety/ efficacy data in Korean patients while using Simbrinza Eye Drops or related information as a condition for approval of the new drug.

Methods

Objective

This post-marketing surveillance (PMS) aims to collect and evaluate the following events or relevant information during the use of Simbrinza Eye Drops on condition of new drug approval.

- Serious adverse events/adverse drug reactions
- Unexpected adverse events/ adverse drug reactions
- Known adverse drug reactions
- Mild adverse events
- Other safety information
- Efficacy (effects on IOP)

Study design

This study was designed as a prospective, observational, multicenter, non-interventional, post-marketing surveillance (PMS) study. The method used to obtain the safety and effectiveness data of Simbrinza Eye Drops was a total surveillance method, where the investigators included all patients, without exception, who received Simbrinza Eye Drops until the number of patients reached the requested number and completed Case Report Forms (CRF) for all patients included.

Study population /Sample size

This PMS aims to recruit at least 600 patients diagnosed with open-angle glaucoma or ocular hypertension who

- Confirmed incomplete decrease in IOP with monotherapy
- Have been prescribed Simbrinza for the first time in the study eye

Treatments

Simbrinza was treated based on local approved label. The recommended dose is one drop of Simbrinza in the affected eye(s) two times daily.

Outcomes/endpoints

- Safety endpoint: Incidence rates of adverse events after Visit 1
- Efficacy endpoint: IOP at Week 12 and Week 24 or additional visits after 24 weeks

Statistical Methods

In this study, data was collected using CRF as per data collection schedule defined in protocol.

Results

Recruitment/ Number analysed/ Baseline data

The analysis of baseline characteristics of the 679 patients who received Simbrinza eye drops and were assessed for safety during this study period, revealed that their age (mean ± SD) was 61.72 ± 13.09 years. There was only one patient (0.15%) of age < 18 years old.

This overview provides details on this one pediatric patient. This patient had ocular hypertension. The patient had no past medical history/ history of present illness at the time of enrolment. The patient received a daily dosage of Simbrinza between 2019 and 2020 (treatment period was 9 months). The patient continued the treatment of Simbrinza at the end of study and the IOP was evaluated as improved. No AE was reported during the study period.

The patient was included in both safety and efficacy analysis sets.

Table 1 Demographic characteristics of pediatric patient

Subject ID	Age	Sex	Date of onset	Height (cm)	Weight (kg)	Medical history
			-2019			Ocular Hypertension (Diagnosis: -2019)

Table 2 Simbrinza administration status in pediatric patient

Subject ID	Visit	Visit date	eye	IOP
	Baseline	2019	Left eye	21mmHg
	Visit 2 Week 12 (± 4 Weeks)	2020	Left eye	16mmHg
	Visit 3 Week 24 (± 4 Weeks)	2020	Left eye	18mmHg

Efficacy results

IOP reduction from baseline was 23.8% in the pediatric patient at week 12. It was interpreted as 'improved' and categorized as 'effective' based on the protocol definition.

Safety results

No adverse event was reported in the pediatric patient.

2.3.3. Discussion on clinical aspects

The study was conducted to evaluate the safety and efficacy of Simbrinza in patients with open angle glaucoma or ocular hypertension. The study enrolled only one paediatric patient. There are insufficient data to allow any discussion on paediatric aspects.

3. CHMP overall conclusion and recommendation

No efficacy or safety conclusion can be made from the single paediatric patient enrolled in this observational study. The result of this study does not change the favourable benefit-risk profile of Simbrinza.

☒ Fulfilled:

No regulatory action required.