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Human Medicines Evaluation Division

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

Opatanol

olopatadine

Procedure no: EMEA/H/C/000407/P46/017

Note

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

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1. Introduction

On 23rd March 2018, the MAH submitted a completed paediatric study for for Opatanol 1 Mg/Ml Eye Drops Solution, 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 a Phase III, multi-centre, randomized, double-masked, vehicle-controlled, parallel-group study to evaluate the safety of olopatadine hydrochloride 0.77% ophthalmic solution in patients with asymptomatic eyes, when administered once daily in both eyes for up to 6 weeks. Study C-12-028 is a stand alone study.

2.2. Information on the pharmaceutical formulation used in the study

Olopatadine hydrochloride 0.77% ophthalmic solution

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for:

Study C-12-028 was a Phase III, multi-centre, randomized, double-masked, vehicle-controlled, parallel-group study to evaluate the safety of olopatadine hydrochloride 0.77% ophthalmic solution in patients with asymptomatic eyes, when administered once daily in both eyes for up to 6 weeks. The study was conducted in 15 study centres in the United States.

2.3.2. Clinical study

Clinical study number and title

Study C-12-028 was a Phase III, multi-centre, randomized, double-masked, vehicle-controlled, parallel-group study to evaluate the safety of olopatadine hydrochloride 0.77% ophthalmic solution in patients with asymptomatic eyes, when administered once daily in both eyes for up to 6 weeks.

Description

The purpose of study C-12-028 was to assess the safety of olopatadine hydrochloride 0.77% ophthalmic solution after topical ocular administration. The estimated target sample size was 495 patients.

Methods

Objective

The objective of this study was to evaluate the **ocular safety** of olopatadine hydrochloride 0.77% ophthalmic solution compared to vehicle in patients 2 years of age or older with **asymptomatic eyes,** when administered once daily in both eyes for up to 6 weeks.

Study design

Phase III, multi-centre, randomized, double-masked, vehicle-controlled, parallel-group study. The expected duration of patient participation in this study was 7 weeks, with 4 office visits (Baseline and Weeks 1, 3, and 6) and 4 telephone contacts (Weeks 2, 4, 5, and 7). At the Baseline Visit (Day 0), patients whose eligibility was confirmed were randomized in a 2:1 ratio to receive olopatadine hydrochloride 0.77% ophthalmic solution or vehicle (placebo) respectively.

Patients < 6 years of age were randomized from 1 randomization schedule and patients ≥ 6 years of age were randomized from another randomization schedule. All randomized patients were to receive 1 drop of either olopatadine hydrochloride 0.77% ophthalmic solution or vehicle once daily in both eyes for 6 weeks.

Study population /Sample size

All patients who completed screening were randomized (500 patients; 100%) at Baseline (Visit 1, Day 0); of these, 331 patients were randomized to receive olopatadine hydrochloride 0.77%, while 169 patients were randomized to receive vehicle.

The mean age of the overall patient population was 32.1 (± 16.6) years, and ranged from 2 to 74 years. Most of the patients (424 patients; 85.0%) were ≥ 18 years of age**, while a total of 75 patients (15.0%) were < 18 years of age, i.e. paediatric patients. Most paediatric patients were 2 to 11 years of age (68 patients; 13.6%); of these, 56 patients (11.2%) were < 6 years of age. The remainder (7 patients; 1.4%) were 12 to 17 years of age.** The majority of the patients were not contact lens wearers (424 patients; 85.0%).

A total of 325 patients (65.1%) included in this study were female, while 174 patients (34.9%) were male. The majority of the patients (429 patients; 86.0%) were White.

Treatments

- Olopatadine hydrochloride 0.77%,
- Vehicle solution/placebo

Outcomes/endpoints

Safety variables and assessments included best-corrected visual acuity (BCVA), slit-lamp examinations (SLEs), intraocular pressure (IOP) measurements, dilated fundus examinations (DFEs), vital signs (pulse and blood pressure), and adverse events (AEs).

Statistical Methods

Of the 500 randomized patients, 1 patient in the olopatadine hydrochloride 0.77% group was excluded from the safety analysis set because the patient was randomized in error and, therefore, did not receive study drug.

The safety analysis set included all patients who received ≥ 1 dose of study drug. Patients were analyzed according to the actual treatment received. Descriptive statistics including mean, standard deviation, median, minimum, and maximum were provided for ocular safety and vital signs parameters by treatment group. In addition, counts and percentages were presented by treatment group for patients exceeding pre-specified thresholds on the ocular safety and vital signs parameters as well as for patients with occurrence of adverse experiences. No formal statistical hypothesis testing was planned or conducted. The safety analysis also included an evaluation of both AEs and safety related parameters according to age.

Results

Recruitment/ Number analysed

Overall, 518 patients were screened, of whom 500 patients completed screening, while 18 patients failed screening. All patients who completed screening were randomized (500 patients; 100%) at Baseline (Visit 1, Day 0); of these, 331 patients were randomized to receive olopatadine hydrochloride 0.77%, while 169 patients were randomized to receive vehicle.

Baseline data

Efficacy results

Not applicable for this safety study.

Safety results

Adverse Events

An overview of deaths, serious AEs (SAEs), and AEs leading to study discontinuation was presented for the safety analysis set. There were no deaths or SAEs reported during the study.

A total of 2 patients (1.2%) in the vehicle group discontinued the study due to non-serious AEs, none of which were considered to be related the study drug, while no patients in the olopatadine hydrochloride 0.77% group were discontinued from the study due to AEs.

A review of significant AEs (i.e. AEs that lead to an intervention, including withdrawal of study medication, dose reduction, or significant concomitant therapy) reported during the study identified no safety issues for olopatadine hydrochloride 0.77%.

Best-corrected visual acuity

No clinically relevant differences between the treatment groups in terms of visual acuity for the overall safety population or for the individual age groups were observed over the course of the study.

Ocular signs

An assessment of ocular sign parameters was performed at Baseline and at each subsequent office visit (Weeks 1, 3, and 6) using a slit-lamp. A change in an ocular sign parameter was defined as an increase of ≥ 1 units from Baseline for either eye compared to the same eye at Baseline.No clinically relevant differences between the treatment groups in terms of ocular signs for the overall safety population or for the individual age groups was observed over the course of the study.

Intraocular pressure

An assessment of IOP was performed for both eyes for all patients at Baseline and at the last office visit (Week 6).

No clinically relevant differences between the treatment groups in terms of IOP for the overall safety population or for the individual age groups were observed over the course of the study.

Dilated fundus examination

Dilated fundus examination was performed for all patients at Baseline and at the last office visit (Week 6) No clinically relevant differences between treatment groups in terms of DFE for the overall safety population or for the individual age groups were observed over the course of the study

Vital signs

Cardiovascular parameters were measured for all patients at Baseline and at the last office visit (Week 6).

A review of these data revealed that mean changes in cardiovascular parameters from Baseline were minimal, with no discernible trend towards increases or decreases for the overall safety population or individual age groups over the course of the study. No clinically relevant differences was observed over the course of the study.

2.3.3. Discussion on clinical aspects

Overall, there were no unexpected safety findings in the 499 patients with asymptomatic eyes, following treatment with olopatadine hydrochloride 0.77% ophthalmic solution or vehicle, when administered once daily in both eyes for up to 6 weeks.

Based upon a review of AEs which included an assessment of incidence, seriousness (serious/non-serious), treatment-relatedness, rate of discontinuation due to AEs, and individual AE characteristics (e.g. severity, onset, duration), olopatadine hydrochloride 0.77% ophthalmic solution was well-tolerated and no clinically relevant differences were identified between the olopatadine hydrochloride 0.77% group and the vehicle group.

No discernible trends from baseline or clinically relevant differences between the olopatadine hydrochloride 0.77% group and the vehicle group were observed, based upon a review of safety parameters which included BCVA, ocular sign parameters, IOP, dilated fundus parameters, and vital signs.

3. Rapporteur's CHMP overall conclusion and recommendation

In conclusion, the benefit-risk assessment for olopatadine hydrochloride 0.77% ophthalmic solution remains positive for the currently approved indications and justifies the continued use of the product in the approved paediatric patient populations No changes to the paediatric information of the current olopatadine hydrochloride Company Core Data Sheet or the Summary of Product Characteristics are proposed as a result of this study.

☒ Fulfilled:

No regulatory action required.

4. Additional clarification requested

None