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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/P46/027

Note

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

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1. Introduction

On 22nd June 2018, the MAH submitted an overview of a previously completed Phase IV study, involving paediatric patients, for Opatanol hydrochloride 0.2% eye drops, in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

A short critical expert overview has been provided.

2. Scientific discussion

2.1. Information on the development program

Study SMA-10-13 was a Phase IV, interventional, non-randomized, open-label, single-group study with a 7-day treatment period designed to evaluate patient perceptions of olopatadine hydrochloride 0.2% eye drops, solution dosed once daily in patients ≥ 12 years of age who were previously treated with twice-daily, topical, ocular, anti-allergy medications (specifically bepotastine, epinastine, or ketotifen).

Study SMA-10-13 was a stand-alone study.

2.2. Information on the pharmaceutical formulation used in the study

Olopatadine hydrochloride is a potent selective anti-allergic/anti-histaminic agent that exerts its effects through multiple distinct mechanisms of actions. It antagonizes histamine (the primary mediator of allergic response in humans) and prevents histamine-induced inflammatory cytokine production.

The first product containing olopatadine hydrochloride for ocular use (olopatadine hydrochloride 0.1% eye drops, solution) was registered in the United States in December 1996. Olopatadine hydrochloride 0.1% (i.e., 1 mg/mL) eye drops, solution received marketing authorization as OPATANOL in the European Union (EU) on 17-May-2002. In addition, olopatadine hydrochloride for nasal use was approved in the United States on 18-Apr-2008. It has not been registered in the EU or any other country for nasal use.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final overview/summary report for:

- Study SMA-10-13 was a Phase IV, interventional, non-randomized, open-label, single-group study with a 7-day treatment period designed to evaluate patient perceptions of olopatadine hydrochloride 0.2% eye drops, solution dosed once daily in patients ≥ 12 years of age who were previously treated with twice-daily, topical, ocular, anti-allergy medications (specifically bepotastine, epinastine, or ketotifen).

The study started in June 2010 and was completed in August 2010. The study was conducted at 12 study sites in the United States and enrolled 215 subjects. Records indicate that 7 subjects <18 years of age were enrolled in this study.

It is important to highlight that limited clinical data are available in relation to this study.

In this context, the MAH has submitted a summary overview of this previously-completed study as part of a commitment to provide information on paediatric clinical trial use of olopatadine in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

2.3.2. Clinical study

Clinical study number and title

Study SMA-10-13 was a Phase IV, interventional, non-randomized, open-label, single-group study with a 7-day treatment period designed to evaluate patient perceptions of olopatadine hydrochloride 0.2% eye drops, solution dosed once daily in patients ≥ 12 years of age who were previously treated with twice-daily, topical, ocular, anti-allergy medications (specifically bepotastine, epinastine, or ketotifen).

Description

The purpose of the study was to evaluate patient perceptions of olopatadine hydrochloride 0.2% eye drops, solution dosed once daily over a seven day period in patients ≥ 12 years of age who were previously treated with twice-daily, topical, ocular, anti-allergy medications.

Methods

Objective(s)

The primary objectives of the study were to provide an evaluation of patient's perceptions and quality of life associated with the use of topical Olopatadine 0.2% eye drops for the treatment of allergic conjunctivitis over a seven day treatment period.

Study design

Phase IV, interventional, non-randomized, open-label, single-group study with a 7-day treatment period of olopatadine hydrochloride 0.2% eye drops solution dosed once daily.

Study population /Sample size

Population: patients ≥ 12 years of age who were previously treated with twice-daily, topical, ocular, anti-allergy medications (specifically bepotastine, epinastine, or ketotifen).

Eligible patients had a history of allergic conjunctivitis and had previously been treated with protocol-specified anti-allergy medications for at least 7 days within 6 months prior to Visit 1.

215 subjects from 12 investigational sites in the United States participated in this single-arm, open-label trial, including 7 subjects < 18 years of age. A total of 214 participants completed the study.

Treatments

Olopatadine hydrochloride 0.2% eye drops solution: one drop self-administered in each eye once daily for 7 days.

Outcomes/endpoints

The primary endpoint in this study was the overall patient satisfaction with once daily 7 day treatment with topical ophthalmic solution of olopatadine 0.2%, as assessed by the patient via a questionnaire.

Statistical Methods

Not applicable.

Results

Please note that only limited clinical data is available for this study.

Recruitment / Number analysed

Baseline data

Baseline Measures

	Olopatadine 0.2%
Overall Participants Analyzed [Units: Participants]	215
Age [Units: Participants]	
<=18 years	7
Between 18 and 65 years	127
>=65 years	81
Age [Units: Years] Mean (Standard Deviation)	55.03 (18.58)
Gender [Units: Participants]	
Female	141
Male	74

Efficacy results

The primary efficacy endpoint in this study was overall patient satisfaction that was assessed by the patient on a questionnaire. On Day 0, the patient was instructed to select a single response to the statement, "Overall, how satisfied are you with your current eye allergy medication?" On Day 7, the

patient was instructed to select a single response to the statement, "Overall, how satisfied are you with olopatadine 0.2%?"

A 5-point scale was used: very satisfied, satisfied, undecided, dissatisfied, very dissatisfied.

Results were reported as the percentage of patients who responded, "very satisfied" or "satisfied."

After 7 days of treatment with olopatadine hydrochloride 0.2%, a significantly greater percentage of enrolled patients reported being satisfied with olopatadine hydrochloride 0.2% (i.e., stated that they were very satisfied or somewhat satisfied) compared with the percentage of all enrolled patients who recalled being satisfied with their previously used medications (89.3% versus 69.8%, respectively; $p < 0.001$). Differences in satisfaction that favoured olopatadine hydrochloride 0.2% were further observed within each of the previous medication subgroups. Among patients who previously used bepotastine, 85.9% reported being satisfied with olopatadine hydrochloride 0.2% while 61.0% recalled being satisfied with bepotastine ($p< 0.001$). Among previous epinastine users, 89.0% reported being satisfied with olopatadine hydrochloride 0.2% while 72.6% recalled being satisfied with epinastine ($p = 0.003$). Among previous ketotifen users, 93.7% reported being satisfied with olopatadine hydrochloride 0.2% while 78.1% recalled being satisfied with ketotifen ($p < 0.001$).

Safety results

Two serious adverse events (stomach pain and colorectal cancer) were reported in this study.

In each case, the adverse event was severe in intensity and assessed as not related to study treatment, and did not result in study discontinuation.

Five non-serious adverse events were reported during the study, and none occurred in more than one subject. One adverse event (worsening of allergic conjunctivitis) was assessed as related to treatment and resulted in discontinuation from the study. Conjunctivitis is listed as an ADR in the current EU SmPC for Opatanol 1 mg/mL eye drops, solution.

The remaining 4 adverse events (headache, liver mass, bronchitis, and cellulitis on the nose) were assessed as not related to treatment.

No new safety concerns were noted at the time of study conduct and posting of results.

2.3.3. Discussion on clinical aspects

Olopatadine hydrochloride is registered in the EU for ophthalmological administration in children from the age of 3 years onwards for the treatment of seasonal allergic conjunctivitis.

This legacy study from 2010 provides limited additional clinical information in respect of topical use of olopatadine hydrochloride eye drops when used over one week in a very small number of paediatric patients with allergic conjunctivitis aged between 12-18 years (n=7).

Based on the limited available data from this study, no changes are proposed to the paediatric information of the current olopatadine hydrochloride CCDS or the Summary of Product Characteristics of the approved ophthalmic olopatadine hydrochloride formulation in the EU.

This conclusion is endorsed. No new safety concerns were identified with olopatadine hydrochloride 0.2% eye drops, solution when administered once daily for 7 days in a population of patients $\geq$ 12 years of age with allergic conjunctivitis who had previously been treated with twice-daily, topical, ocular, anti-allergy medications (specifically bepotastine, epinastine, or ketotifen).

Based on a review of the available clinical data, the benefit-risk assessment for olopatadine hydrochloride 0.2% eye drops, solution remains positive for the currently approved indications outlined in the CCDS and justifies the continued use of the product in the approved paediatric patient populations.

3. Rapporteur's overall conclusion and recommendation

In summary, an overview of the clinical data available for this study, which was completed in 2010, provides limited information on the paediatric use of olopatadine eye drop solution.

In the EU, Opatanol 1 mg/mL eye drops, solution (containing 1mg olopatadine as hydrochloride per 1ml) is currently authorised for the treatment of ocular signs and symptoms of seasonal allergic conjunctivitis in adults and paediatric patients from 3 years onwards.

In this study, a total of 7 paediatric patients aged between 12-18 years were enrolled and received once daily topical olopatadine 0.2 % eye drops for seven days only.

The primary endpoint was an evaluation of patient satisfaction with olopatadine eye drops administered once daily over 7 days.

It is acknowledged that only limited clinical data is provided.

No new safety or efficacy concerns relating to topical use of the active substance olopatadine hydrochloride arise from the limited data presented.

Based on the data provided, it is considered that no changes to the paediatric information of the current olopatadine hydrochloride CCDS or the Summary of Product Characteristics of the approved ophthalmic olopatadine hydrochloride formulation in the EU are required as a result of the limited data available from this study.

This study does not impact on the current B/R balance of olopatadine hydrochloride in the EU, which remains positive.

☒ **Fulfilled:**

No regulatory action required.

4. Additional clarification requested

Not applicable.