18 August 2009
EMEA/530385/2009
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Opatanol

Olopatadine

Procedure No.: EMEA/H/C/000407/A45/0013

CHMP assessment report for paediatric use studies submitted according to Article 45 of the Regulation (EC) No 1901/2006

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

Disclaimer: The assessment report was drafted before the launch of the European Medicines Agency's new corporate identity in December 2009. This report therefore has a different appearance to documents currently produced by the Agency

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ADMINISTRATIVE INFORMATION

Invented name of the medicinal product(s):	Opatanol
INN (or common name) of the active substance(s):	olopatadine
MAH (s):	Alcon

I. EXECUTIVE SUMMARY

The MAH has provided no clinical study reports but 24 references. Most of the references provided relate to the use of olopatadine 0.1% eye drops in general. Additional papers relate to the unlicensed olopatadine 0.2% eye drops and olopatadine nasal spray and provide limited evidence of use in children and adolescents respectively

- **Recommendation**

The Rapporteur agrees with the MAH that no further action is required.

II. RECOMMENDATION

III. INTRODUCTION

The MAH has submitted a number of published reports for olopatadine, in accordance with Article 45 of the Regulation (EC) No 1901/2006, as amended on medicinal products for paediatric use.

A short critical expert overview has also been provided.

The MAH stated that the submitted paediatric studies do not influence the benefit risk for Opatanol and that there is no consequential regulatory action.

IV. SCIENTIFIC DISCUSSION

IV.1 Information on the pharmaceutical formulation used in the clinical study(ies)

The only licensed olopatadine is Opatanol is 1mg/ml eye drop solution. The papers included studies using 2mg/ml olopadatine and an olopatadine nasal spray, neither of which is available in the EU.

IV.2 Non-clinical aspects

No non clinical studies have been submitted

IV.3 Clinical aspects

1. Introduction

No clinical study reports were submitted.
The MAH has submitted 24 papers most of which dealt with olopatadine in general in the context of treatment of allergic conjunctivitis.

Specific papers deal with: Olopatadine 0.2%:
Lichtenstein S.J., Pasquine T.A.; Edwards M.R.; Wells D.T.; Robertson S.M., Gross R.D.
Safety and tolerability of olopatadine 0.2% in children and adolescents.
Journal of Ocular Pharmacology and Therapeutics(United States) August 1, 2007 , 23/4 (366-371)

And Lichtenstein et al review of safety and efficacy of olopatadine 0.2%

There is also a paper of a study with Olopatadine 0.6%
Effects of Olopatadine Hydrochloride Nasal Spray 0.6% in the Treatment of Seasonal Allergic Rhinitis: A Phase 111,Multicentre, Randomised, Double-Blind, Active- and Placebo-Controlled Study in Adolescents and Adults by Shah, Nayak, Ratner et al

There is also
One paper (Houchin and Rogol) on Idiopathic Growth Hormone Deficiency (?), and two papers on Lodoxamide

2. Discussion on clinical aspects

In the original dossier for olopatadine 0.1%, there were 268 children and adolescents included among the 900 subjects or patients in the studies of at least 4 weeks duration. Children over 4 years were included in the efficacy studies and safety data were available from children more than 3 years.
Olopatadine 0.1% eye drops were licensed for use in children older than 3 years of age.
The usual dose of the ophthalmic formulation is one drop in each eye twice daily (olopatadine 1 mg/ml) and one a day (olopatadine 2 mg/ml).

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The clinical expert cites a paper by Chapin MJ, Geroge MA, Abelson MB. Olopatadine: Broadening choices for the treatment of allergic conjunctivitis. Today's Therapeutic Trends 1999;17(1):67-84
This paper mentions a 6-week safety study to evaluate paediatric tolerance of ophthalmic olopatadine 1 mg/ml eye drops in children 3 years of age and older where eye drops were administered three times a day for 6 weeks. Parameters used to assess the efficacy were ocular redness and itching and patient's condition improved after using product.
Results obtained from this study apparently showed no change in visual acuity, no change in slit lamp or any fundus examination findings. There was neither rebound conjunctival hyperaemia nor change in heart rate or blood pressure. With regard to adverse reactions, the report states that there were no significant differences between adults and children. Analysing adverse events, the most frequently reported adverse events were asthenia, foreign body sensation, headache, ocular discomfort, ocular hyperaemia, ocular pruritus and superficial keratitis. All of them were reported with an incidence lower than 1.5 %.
The expert concludes that this mention of this study demonstrates that olopatadine for ophthalmic use is safe in adults but also in children older than 3 years. However, it appears that this study has not been published although the authors state that the data are on file.

The MAH has provided two references to other studies performed to evaluate the safety and efficacy of olopatadine 2 mg/ml eye drops, which is not licensed in the EU.

These studies included 44 children aged from 10 to 17 years. Results obtained from these studies concluded that olopatadine reduced significantly the signs and symptoms of allergic conjunctivitis, as well as suggesting that olopatadine 2 mg/ml was effective for up to 24 hours after instillation and is a safe product used in children older than 3 years when dosed once a day. No serious adverse event was reported in either study. The most frequent adverse event reported was ocular dryness occurring in a percentage lower than 2%. Other ocular effects reported were ocular discomfort and ocular fatigue. No treatment was necessary to relieve these symptoms.

One further study was carried out in 126 patients between 3 and 17 years of age using olopatadine 2 mg/ml eye drops for 6 weeks. No serious adverse events were reported in this study and no treatment-related changes from visual acuity, IOP, pulse, blood pressure or dilated fundus examinations were found. The only adverse event reported was discomfort (1.1%). Events resolved without treatment. No systemic adverse events related to therapy were reported during the study. At the end of the study, authors concluded that olopatadine 2 mg/ml administered once a day was safe and well tolerated in children and adolescents.

Nasal spray: No olopatadine nasal spray formulation is licensed in the EU.
One study was carried out to evaluate safety and efficacy of olopatadine nasal spray. Patients enrolled in this study included children from 12 to 18 years of age. No serious adverse events were reported during the period of the study. Additionally, non-serious adverse events reported were mild to moderate, usually were resolved without treatment, and did not interrupt patient continuation in the study. The most common adverse event reported was bitter taste, and it seemed to be dose-related. No safety issues were identified and data demonstrated that treatment with olopatadine nasal spray provides relief from allergy symptoms.
Therefore, it can be said that this study did not suggest any new safety issues with the nasal spray.

V. RAPPORTEUR'S OVERALL CONCLUSION AND RECOMMENDATION

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- **Overall conclusion**

Most of the references provided relate to the use of olopatadine 0.1% eye drops. Additional papers relate to the unlicensed olopatadine 0.2% eye drops and olopatadine nasal spray and provide limited evidence of use in children and adolescents respectively

- **Recommendation**

The Rapporteur agrees with the MAH that no further action is required.