European Medicines Agency

Doc. Ref. EMEA/347310/2009
P/112/2009

EUROPEAN MEDICINES AGENCY DECISION

of 15 June 2009

on the agreement of a Paediatric Investigation Plan and on the granting of a waiver for dexamethasone/ciprofloxacin hydrochloride (EMEA-000444-PIP01-08) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

DISCLAIMER: This Decision does not entitle to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006, as amended.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 86 70
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

EUROPEAN MEDICINES AGENCY DECISION

of 15 June 2009

on the agreement of a Paediatric Investigation Plan and on the granting of a waiver for dexamethasone/ciprofloxacin hydrochloride (EMEA-000444-PIP01-08) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

THE EUROPEAN MEDICINES AGENCY,

Having regard to the Treaty establishing the European Community,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use as amended and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Alcon Pharma GmbH on 7 November 2008 under Article 16(1) of Regulation (EC) No 1901/2006 as amended also requesting a waiver under Article 13 of said Regulation,

Having regard to the Opinion of the Paediatric Committee of the European Medicines Agency, issued on 30 April 209, in accordance with Article 18 of Regulation (EC) No 1901/2006 as amended, and Article 13 of said Regulation,

Having regard to Article 25 of Regulation (EC) No 1901/2006 as amended,

WHEREAS:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the agreement of a Paediatric Investigation Plan and on the granting of a waiver,

(2) It is therefore appropriate to adopt a Decision granting a Paediatric Investigation Plan,

(3) It is therefore appropriate to adopt a Decision granting a waiver.

[1] OJ L 378, 27.12.2006, p.1
[2] OJ L 136, 30.4.2004, p. 1

HAS ADOPTED THIS DECISION:

Article 1

A Paediatric Investigation Plan for dexamethasone/ciprofloxacin hydrochloride, ear drops, suspension, auricular use, the details of which are set out in the Opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A waiver for dexamethasone/ciprofloxacin hydrochloride, ear drops, suspension, auricular use, the details of which are set out in the Opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

This decision is addressed to Alcon Pharma GmbH, Blankreutestrasse 1, 79108 Freiburg, Germany.

Done at London, 15 June 2009

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

Doc. Ref. EMEA/PDCO/262290/2009
EMEA-000444-PIP01-08

OPINION OF THE PAEDIATRIC COMMITTEE ON THE AGREEMENT OF A PAEDIATRIC INVESTIGATION PLAN AND A WAIVER

Scope of the application

Active substance(s):
Dexamethasone/ciprofloxacin hydrochloride

Condition(s):
Otitis media, unspecified
Other infective otitis externa

Pharmaceutical form(s):
Ear drops, suspension

Route(s) of administration:
Auricular use

Name/corporate name of the PIP applicant:
Alcon Pharma GmbH

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Alcon Pharma GmbH submitted for agreement to the EMEA on 7 November 2008 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 11 December 2008.

Supplementary information was provided by the applicant on 20 February 2009.

A meeting with the Paediatric Committee took place on 28 April 2009.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 70 40
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

- to agree the paediatric investigation plan in accordance with Article 18 of said Regulation,

- to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

The Icelandic and the Norwegian Paediatric Committee members agree with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the Agency, together with its annex(es) and appendix.

London, 30 April 2009

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman

(Signature on file)

ANNEX I

THE MEASURES AND TIMELINES OF THE AGREED PAEDIATRIC INVESTIGATION PLAN AND THE SUBSET(S) OF THE PAEDIATRIC POPULATION AND CONDITION(S) COVERED BY THE WAIVER

A. CONDITION(S)

Acute otitis media

Acute otitis externa

B. WAIVER

- **Condition**

Acute otitis media

The waiver applies to:

– Preterm newborn infants, Term newborn infants (from birth to less than 28 days), Infants and toddlers (from 28 days to less than 7 months) for the suspension for topical use on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

- **Condition**

Acute otitis externa

The waiver applies to:

– Preterm newborn infants, Term newborn infants (from birth to less than 28 days), Infants and toddlers (from 28 days to less than 13 months) for the suspension for topical use on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

C. PAEDIATRIC INVESTIGATION PLAN

- **Condition to be investigated**

1) Acute otitis media
2) Acute otitis externa

- **Proposed PIP indication**

- **Subset(s) of the paediatric population concerned by the paediatric development**

1) From 7 months to less than 18 years.
2) From 13 months to less than 18 years.

- **Formulation(s)**

suspension for auricular use

- **Studies**

Area	Number of studies	Description
Quality		Not applicable
Non-clinical		Not applicable
Clinical	6	A randomized, observer-blind, multicentre, active-controlled, parallel-group study to evaluate - therapeutic non-inferiority of ciprofloxacin relative to hydrocortisol/neomycin based on clinical response at the test of cure (TOC) visit (Day 18); - therapeutic non-inferiority of dexamethasone/ciprofloxacin relative to ciprofloxacin based on clinical response at the TOC visit; - therapeutic noninferiority of dexamethasone/ciprofloxacin relative to hydrocortisol/neomycin based on clinical response at the TOC visit; and - superiority of dexamethasone/ciprofloxacin relative to ciprofloxacin for time to cessation of ear pain. - therapeutic non-inferiority of ciprofloxacin relative to hydrocortisol/neomycin, in patients of at least 1 year of age A multicentre, active-controlled, randomized, observer-masked, parallel-group study to demonstrate statistical non-inferiority (clinical equivalence) of dexamethasone/ciprofloxacin and hydrocortisol/neomycin in patients of at least 1 year of age A multicentre, active-controlled, randomized, patient-masked, parallel group study to demonstrate therapeutic superiority of dexamethasone/ciprofloxacin relative to ciprofloxacin in the cessation of otorrhoea; and to evaluate the efficacy and safety of topical dexamethasone/ciprofloxacin suspension for the treatment of patients with acute otitis media with otorrhoea and tympanostomy tubes (AOMT) in paediatric patients, from 6 months to 12 years of age A multicentre, active-controlled, randomized, observer-masked, parallel groups to demonstrate the non-inferiority of dexamethasone/ciprofloxacin otic suspension relative to ofloxacin otic solution in clinical and microbiological response at the test of cure (TOC)

		visit; and to evaluate the efficacy and safety of dexamethasone/ciprofloxacin otic suspension for the treatment of patients with acute otitis media and otorrhoea with tympanostomy tubes (AOMT) in paediatric patients, from 6 months to 12 years of age An open-label, randomized, multicentre, single-dose, active-control, parallel study to evaluate the pharmacokinetic profile of a single topical otic dose of dexamethasone/ciprofloxacin otic suspension (dexamethasone/ciprofloxacin) or ciprofloxacin ophthalmic solution in pediatric patients, following tympanostomy tube surgery in male or female children, adolescents, and young adults, 6 months to 21 years of age A randomized, parallel group, multicentre, observer-masked, active-controlled, two-armed study to describe the safety and efficacy of dexamethasone/ciprofloxacin otic suspension relative to amoxicillin ES-600 oral suspension for the treatment of acute otitis media with otorrhoea through tympanostomy tubes (AOMT) in pediatric patients, 6 months to 12 years of age

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	**No**
Date of completion of the paediatric investigation plan:	**N/A**
Deferral for some or all studies contained in the paediatric investigation plan:	**No**