European Medicines Agency

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EUROPEAN MEDICINES AGENCY DECISION

of 21 October 2009

on the agreement of a Paediatric Investigation Plan and on the granting of a deferral and on the granting of a waiver for mannitol (EMEA-000436-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.

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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 Pharmaxis Pharmaceuticals Limited on 19 December 2008 under Article 16(1) of Regulation (EC) No 1901/2006 as amended also requesting a waiver under Article 13 of said Regulation and a deferral under Article 20 of said Regulation,

Having regard to the Opinion of the Paediatric Committee of the European Medicines Agency, issued on 18 September 2009, in accordance with Article 18 of Regulation (EC) No 1901/2006 as amended, and Article 13 of said Regulation and Article 21 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 deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a Decision agreeing a Paediatric Investigation Plan.

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

(4) 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 mannitol, inhalation powder, hard capsule, inhalation 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 deferral for mannitol, inhalation powder, hard capsule, inhalation 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

A waiver for mannitol, inhalation powder, hard capsule, inhalation 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 4

This decision is addressed to Pharmaxis Pharmaceuticals Limited, 110 Butterfield, Great Marlings, Luton, LU2 8DL, United Kingdom.

Done at London, 21 October 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/548621/2009
EMEA-000436-PIP01-08

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

Scope of the application

Active substance:
Mannitol

Condition:
Cystic fibrosis with pulmonary disease

Pharmaceutical form:
Inhalation powder, hard capsule

Route of administration:
Inhalation use

Name/corporate name of the PIP applicant:
Pharmaxis Pharmaceuticals Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Pharmaxis Pharmaceuticals Limited submitted for agreement to the EMEA on 19 December 2008 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 5 February 2009.

Supplementary information was provided by the applicant on 10 July 2009.

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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 deferral in accordance with Article 21 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 annexes and appendix.

London, 18 September 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

A. CONDITION(S)

Cystic Fibrosis with pulmonary disease

B. WAIVER

- **Condition**

  Cystic Fibrosis with pulmonary disease

- **Subset(s) of the paediatric population, pharmaceutical form(s) and route(s) of administration covered**

  The waiver applies to:

  Preterm and term newborn infants (from birth to less than 28 days), Infants and toddlers (from 28 days to less than 24 months), Children from 2 to less than 6 years for inhalation powder, hard capsule, inhalation use on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies are not feasible.

C. PAEDIATRIC INVESTIGATION PLAN

- **Condition to be investigated**

  Cystic Fibrosis with pulmonary disease

- **Proposed PIP indication**

  Treatment of patients with cystic fibrosis to improve lung function and reduce pulmonary exacerbations.

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

  Children and adolescents 6 to less than 18 years

- **Formulation(s)**

  Inhalation powder, hard capsule;
  Inhalation use

- **Studies**

Area	Number of studies	Description
Quality	2	1) Microbiological Testing of used inhalers 2) Study to evaluate the effect cleaning the inhaler device might have upon the Aerodynamic Particle Size Distribution (APSD) and Delivered Dose Uniformity (DDU) of mannitol
Clinical	4	3) Determination of the PK of inhaled mannitol after single and multiple dosing in CF patients. 4) Randomised, multicentre, double-blinded, controlled study to

		determine the safety and efficacy of long term administration of inhaled dry powder mannitol in cystic fibrosis. 5) Randomised, multicentre, double-blinded, controlled study to determine the safety and efficacy of long term administration of inhaled dry powder mannitol in cystic fibrosis. 6) Open observational, non-interventional study of inspiratory flow rates and volumes in CF subjects inhaling via a spirometer with the dry powder inhaler device.

Measures to address long term follow-up of potential safety issues and efficacy in relation to paediatric use:	**No**
Date of completion of the paediatric investigation plan:	**By April 2011**
Deferral for some or all studies contained in the paediatric investigation plan:	**Yes**