European Medicines Agency

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EUROPEAN MEDICINES AGENCY DECISION

of 4 November 2009

on the agreement of a Paediatric Investigation Plan and on the granting of a deferral and on the granting of a waiver for ambrisentan (Volibris) (EMEA-000434-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 Glaxo Group Limited on 4 November 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 ambrisentan, Volibris, film-coated tablets / dry powder in a single dose sachet, oral 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 ambrisentan, Volibris, film-coated tablets / dry powder in a single dose sachet**,** oral 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 ambrisentan, Volibris, film-coated tablets / dry powder in a single dose sachet, oral 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 Glaxo Group Limited, Greenford Road, Greenford, Middlesex, London, UB6 0HE, United Kingdom.

Done at London, 4 November 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/553563/2009
EMEA-000434-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(s):
Ambrisentan

(Invented) name:
Volibris

Condition(s):
Primary and secondary pulmonary hypertension

Pharmaceutical form(s):
Film-coated tablets
Dry powder in a single dose sachet

Route(s) of administration:
Oral use

Name/corporate name of the PIP applicant:
Glaxo Group Limited

Information about the authorised medicinal product: see Annex II

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Glaxo Group Limited submitted for agreement to the EMEA on 4 November 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 11 December 2008.

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)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population

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 AND THE SUBSET(S) OF THE PAEDIATRIC POPULATION AND CONDITION(S) COVERED BY THE WAIVER

A. CONDITION(S)

Primary and secondary pulmonary hypertension

B. WAIVER

- **Condition**

  Primary and secondary pulmonary hypertension

  – The waiver applies to:
    From birth to less than 1 year of age

  – For Film-coated tablets and dry powder in a single use sachet for oral use

  – On the grounds that the specific medicinal product is likely to be unsafe

C. PAEDIATRIC INVESTIGATION PLAN

- **Condition to be investigated**

  Primary and secondary pulmonary hypertension

- **Proposed PIP indication**

  Idiopathic (IPAH) and familial (FPAH) pulmonary hypertension; Associated pulmonary hypertension (APAH)

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

  From 1 year to less than 18 years.

- **Formulation(s)**

  - Film-coated tablets for oral use
  - Dry powder in a single dose sachet for oral use

- **Studies**

Area	Number of studies	Description
Quality	2	- Film coated tablets 2.5 mg for oral use - Dry powder in a single dose sachet for oral use
Non-clinical	1	A 2 week juvenile animal study to determine tolerability and toxicokinetics of ambrisentan
Non-clinical	1	A 8-week juvenile animal study to determine oral toxicology and toxicokinetic of ambrisentan including an 8 weeks recovery period.
Clinical	1	A 24 weeks randomized, open label, multi-centre, comparative trial to evaluate safety, efficacy and population PK of ambrisentan low and high dose for the treatment of children from 8 years of age to less than 18 years of age with Pulmonary Arterial Hypertension.
Clinical	1	bioavailability study to compare the pharmacokinetic profile of the dry powder in a single dose sachet for oral use with the existing film coated tablets of ambrisentan
Clinical	1	A 24 weeks randomized, open label, multi-centre, comparative trial to evaluate safety, efficacy and PK of ambrisentan low and high dose for the treatment of children from 1 year of age to less than 8 years of age with Pulmonary Arterial Hypertension.

Measures to address long term follow-up of potential safety issues in relation to paediatric use:	**Yes**
Date of completion of the paediatric investigation plan:	**By December 2016**
Deferral for some or all studies contained in the paediatric investigation plan:	**Yes**

ANNEX II

INFORMATION ABOUT THE AUTHORISED MEDICINAL PRODUCT

EU Number	**Invented name Name**	**Strength**	**Pharmaceutical form**	**Route of administration**	**Packaging**	**Content (concentration)**	**Package size**
EU/1/08/451/001	Volibris	5 mg	Film-coated tablet	Oral use	blister (PVC/PVdC/alu)		10 tablets
EU/1/08/451/002	Volibris	5 mg	Film-coated tablet	Oral use	blister (PVC/PVdC/alu)		30 tablets
EU/1/08/451/003	Volibris	10 mg	Film-coated tablet	Oral use	blister (PVC/PVdC/alu)		10 tablets
EU/1/08/451/004	Volibris	10 mg	Film-coated tablet	Oral use	blister (PVC/PVdC/alu)		30 tablets