European Medicines Agency

Doc. Ref. EMEA/622947/2008
P/111/2008

EUROPEAN MEDICINES AGENCY DECISION

of 1 December 2008

on the application for agreement of a Paediatric Investigation Plan for telbivudine (Sebivo), EMEA-000065-PIP01-07, in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

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 1 December 2008

on the application for agreement of a Paediatric Investigation Plan for telbivudine (Sebivo), EMEA-000065-PIP01-07, 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 Novartis Europharm Limited on 17 October 2007 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 17 October 2008, 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 a positive opinion.

(2) It is therefore appropriate to adopt a Decision following the Paediatric Committee's opinion on the Paediatric Investigation Plan.

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

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

[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 telbivudine (Sebivo), oral solution, film-coated tablet, 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 waiver for telbivudine (Sebivo), oral solution, film-coated tablet, 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 deferral for telbivudine (Sebivo), oral solution, film-coated tablet, 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 Novartis Europharm Limited, Wimblehurst Road, Horsham, RH12 5AB, United Kingdom.

Done at London, 1 December 2008

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

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

London, 17 October 2008
Doc. Ref. EMEA/PDCO493754/2008
EMEA-000065-PIP01-07

POSITIVE OPINION OF THE PAEDIATRIC COMMITTEE ON A REQUEST FOR AGREEMENT OF A PAEDIATRIC INVESTIGATION PLAN FOR

Scope of the application

Active substance:
Telbivudine

Invented name:
Sebivo

Condition(s):
Chronic hepatitis B

Pharmaceutical form(s):
Oral solution
Film-coated tablet

Route(s) of administration:
Oral use

Name/corporate name of the PIP applicant:
Novartis Europharm 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, Novartis Europharm Limited submitted for agreement to the EMEA on 17 October 2007 a paediatric investigation plan for the above mentioned medicinal product.

The procedure started on 22 November 2007.

Supplementary information was provided by the applicant on 14 August 2008.

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 Regulation (EC) No 1901/2006 as amended,
- to grant a deferral in accordance with Article 21 of Regulation (EC) No 1901/2006 as amended,
- to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of Regulation (EC) No 1901/2006 as amended and concluded in accordance with Article 11(1)(c) of Regulation (EC) No 1901/2006 as amended, 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 member(s) do agree(s) 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, 17 October 2008

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)

Chronic hepatitis B

B. WAIVER

Condition

- **Children with HBe-Antigen (HBeAg)-positive compensated chronic hepatitis B (CHB)**

The waiver applies to:

Preterm newborn infants, Term Infants and toddlers from 0 to less than 24 months, for telbivudine film-coated tablet and oral solution for oral 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.

- **Children with HBeAg-negative compensated chronic hepatitis B**

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 24 months), for telbivudine film-coated tablet and oral solution for oral use, on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfill a therapeutic need of the paediatric population

- **Children with decompensated chronic hepatitis B**

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 24 months), for telbivudine film-coated tablet and oral solution for oral 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.

- **Children with chronic hepatitis B in the immunotolerant phase**

The waiver applies to:

Children aged 0 to less than 18 years, soft capsules, oral use for telbivudine film-coated tablet and oral solution for oral 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**

Chronic hepatitis B

- **Proposed PIP indication**

Treatment of children with HBeAg-positive compensated chronic hepatitis B, HBeAg-negative compensated chronic hepatitis B and decompensated chronic hepatitis B

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

From 2 to less than 18 years of age

- **Formulation(s)**

Film-coated tablet for oral use
Oral solution with dosing cup and syringe for oral use

- **Studies**

Area	Number of studies	Description
Quality	1	Development of an oral solution (20 mg/ml) with dosing cup and syringe for oral use
Non-clinical	2	A 20 days oral (gavage) neonatal and juvenile development dose range-finding study in rats A 10 weeks oral (gavage) study in juvenile rats to evaluate telbivudine effect on the postnatal development.
Clinical	5	1) Open-Label, single-dose study in children and adolescents with Chronic Hepatitis B Virus Infection from 2 to less than 18 years of age to evaluate pharmacokinetics, safety and tolerability of telbivudine 2) Randomised, double-blind, placebo-controlled, multi-centre study to evaluate pharmacokinetics, efficacy and safety of telbivudine in children and adolescents aged from 2 to less than 18 years with compensated HBeAg-positive chronic hepatitis B virus infection 3) Randomised open label multi-centre study to evaluate efficacy and safety, of telbivudine in children and adolescents with compensated HBeAg-negative chronic hepatitis B virus infection in patients aged from 2 to less than 18 years 4) Randomised open label multicenter study to evaluate efficacy and safety, of telbivudine in children and adolescents with decompensated chronic hepatitis B virus infection in patients aged from 2 to less than 18 years 5) A cross-sectional, multi-center retrospective data collection study in Western and Asian countries in children and adolescents with chronic hepatits B virus infection in patients aged from 2-to less than18 years

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 September 2018**
Deferral for initiation of some or all studies contained in the paediatric investigation plan:	**Yes**
Deferral for completion of some or all studies contained in the paediatric investigation plan:	**Yes**

ANNEX II

INFORMATION ABOUT THE AUTHORISED MEDICINAL PRODUCT

EU Number	Invented name	Strength	Pharmaceutical Form	Route of Administration	Packaging	Content	Package size
EU/1/07/388/001	Sebivo	600 mg	Film-coated tablet	Oral use	blister (PVC/alu)		28 tablets
EU/1/07/388/002	Sebivo	600 mg	Film-coated tablet	Oral use	blister (PVC/alu)		98 tablets