EMA/666624/2017

European Medicines Agency decision

P/0316/2017

of 31 October 2017

on the acceptance of a modification of an agreed paediatric investigation plan for everolimus (Votubia), (EMEA-000019-PIP08-12-M03) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

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 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 European Medicines Agency's decision P/0012/2013 issued on 23 January 2013, the decision P/0236/2015 issued on 30 October 2015 and the decision P/0124/2016 issued on 15 April 2016,

Having regard to the application submitted by Novartis Europharm Limited on 23 June 2017 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and proposing a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 15 September 2017, in accordance with Article 22 of Regulation (EC) No 1901/2006, and Article 13 of said Regulation,

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

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision on the granting of 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

Changes to the agreed paediatric investigation plan for everolimus (Votubia), tablet, dispersible tablet, oral use, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

A waiver for everolimus (Votubia), tablet, dispersible tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

This decision is addressed to Novartis Europharm Limited, Frimley Business Park, GU16 7SR – Camberley, United Kingdom.

EMA/PDCO/436079/2017
London, 15 September 2017

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-000019-PIP08-12-M03

Scope of the application

Active substance(s):

Everolimus

Invented name:

Votubia

Condition(s):

Treatment of Tuberous Sclerosis Complex

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Tablet

Dispersible 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

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Limited submitted to the European Medicines Agency on 23 June 2017 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0012/2013 issued on 23 January 2013, the decision P/0236/2015 issued on 30 October 2015 and the decision P/0124/2016 issued on 15 April 2016.

The application for modification proposed changes to the agreed paediatric investigation plan and proposed a waiver.

The procedure started on 18 July 2017.

Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified. A waiver for a new paediatric subset has been added.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion;
   - to grant a waiver for one or more subsets of the paediatric population 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 Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed Paediatric Investigation Plan

1. Waiver

1.1. Condition

Treatment of Tuberous Sclerosis Complex

The waiver applies to:

- the paediatric population from birth to less than 6 months of age;
- tablet, dispersible tablet, for oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan

2.1. Condition

Treatment of Tuberous Sclerosis Complex

2.1.1. Indication(s) targeted by the PIP

Treatment of refractory partial-onset seizures associated with Tuberous Sclerosis Complex (TSC)

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 6 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Tablet

Dispersible tablet

2.1.4. Studies

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of dispersible tablet for oral use, including strengths of 2 mg, 3 mg and 5 mg.
Non-clinical studies	0	Not applicable.
Clinical studies	1	**Study 2** Core phase of randomised, double blind placebo controlled, two trough ranges, multicentre, trial to evaluate efficacy, safety, pharmacokinetics, of everolimus as adjunctive therapy in children from 1 year to less than 18 years of age (and adults) in patients with tuberous sclerosis complex (TSC) who have refractory partial-onset seizures. [CRAD001M2304 (Core Phase)].

		Study 3 *Deleted in modification procedure EMEA-000019-PIP08-M03.*
Extrapolation, modelling and simulation studies	1	**Study 4** *Added in modification procedure EMEA-000019-PIP08-M03.* Modelling and simulation study to predict PK and short- and long-term efficacy of everolimus in children from 6 months to less than 2 years of age.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By March 2018
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of tuberous sclerosis complex (TSC)

Authorised indication(s):

- Refractory seizures associated with tuberous sclerosis complex (TSC)

  Votubia is indicated as adjunctive treatment of patients aged 2 years and older whose refractory partial-onset seizures, with or without secondary generalisation, are associated with tuberous sclerosis complex (TSC).

- Renal angiomyolipoma associated with tuberous sclerosis complex (TSC)

  Votubia is indicated for the treatment of adult patients with renal angiomyolipoma associated with tuberous sclerosis complex (TSC) who are at risk of complications (based on factors such as tumour size or presence of aneurysm, or presence of multiple or bilateral tumours) but who do not require immediate surgery.

  The evidence is based on analysis of change in sum of angiomyolipoma volume.

- Subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC)

  Votubia is indicated for the treatment of patients with subependymal giant cell astrocytoma (SEGA) associated with tuberous sclerosis complex (TSC) who require therapeutic intervention but are not amenable to surgery.

  The evidence is based on analysis of change in SEGA volume. Further clinical benefit, such as improvement in disease related symptoms, has not been demonstrated.

Authorised pharmaceutical formulation(s):

Tablet

Dispersible tablet

Authorised route(s) of administration:

Oral use