EMA/776286/2013

European Medicines Agency decision

P/0003/2014

of 22 January 2014

on the acceptance of a modification of an agreed paediatric investigation plan for everolimus (Votubia) (EMEA-000019-PIP02-07-M05) 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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on the acceptance of a modification of an agreed paediatric investigation plan for everolimus (Votubia) (EMEA-000019-PIP02-07-M05) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/124/2008 issued on 5 December 2008, the decision P/105/2010 issued on 25 June 2010, the decision P/127/2011 issued on 8 June 2011 and the decision P/0058/2013 issued on 26 March 2013,

Having regard to the application submitted by Novartis Europharm Ltd on 22 October 2013 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 6 December 2013, in accordance with Article 22 of Regulation (EC) No 1901/2006,

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.

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

[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

This decision is addressed to Novartis Europharm Ltd, Wimblehurst Road, RH12 5AB - Horsham, West Sussex, United Kingdom.

Done at London, 22 January 2014

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/663832/2013

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

EMEA-000019-PIP02-07-M05

Scope of the application

Active substance(s):

Everolimus

Invented name:

Votubia

Condition(s):

Treatment of subependymal giant cell astrocytoma

Treatment of angiomyolipoma

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 Ltd

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 Ltd submitted to the European Medicines Agency on 22 October 2013 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/124/2008 issued on 5 December 2008, the decision P/105/2010 issued on 25 June 2010, the decision P/127/2011 issued on 8 June 2011, and the decision P/0058/2013 issued on 26 March 2013.

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

The procedure started on 19 November 2013.

Scope of the modification

The timeline of a measure of the Paediatric Investigation Plan was modified.

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.

   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 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 European Medicines Agency, together with its annexes and appendix.

London, 6 December 2013

On behalf of the Paediatric Committee
Dr Dirk Mentzer, Chairman
(Signature on file)

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 angiomyolipoma

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- for tablet for oral use and dispersible tablet for oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2. Paediatric Investigation Plan

2.1. Condition: treatment of subependymal giant cell astrocytoma

2.1.1. Indication(s) targeted by the PIP

Treatment of patients with subependymal giant cell astrocytomas (SEGA) associated with tuberous sclerosis complex (TSC).

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

From birth to less than 18 years.

2.1.3. Pharmaceutical form(s)

Tablet for oral use, including strength of 2.5 mg, 5 mg and 10 mg.

Dispersible tablet for oral use, including strengths of 1 mg, 2 mg, 3 mg and 5 m.

2.1.4. Measures

Area	Number of measures	Description
Quality		Not applicable.
Non-clinical		Not applicable.
Clinical	3	**Measure 1:** Relative bioavailability study between intact 1 mg tablet and 1 mg tablet dispersed in water in adults **Measure 2:** Bioequivalence study between intact 1 mg tablet and 5 mg dispersible tablet in adults.

Area	Number of measures	Description
		Measure 3: Randomized, double-blind, placebo-controlled, parallel-group, dose-titration, comparative, multi-centre study to evaluate pharmacokinetics, safety, tolerability and activity of everolimus in children from birth to less than 18 years of age.

3. Follow-up, completion and deferral of PIP

Concerns on potential long-term safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By December 2015
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 subependymal giant cell astrocytoma associated with tuberous sclerosis complex

   Authorised indication(s):

   - 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.

2. Renal angiomyolipoma associated with tuberous sclerosis complex

   Authorised indication(s):

   - 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.

Authorised pharmaceutical form(s):

Tablet, dispersible tablet

Authorised route(s) of administration:

Oral use