EMA/169119/2014

European Medicines Agency decision

P/0105/2014

of 5 May 2014

on the acceptance of a modification of an agreed paediatric investigation plan for everolimus (Afinitor, Certican and associated names) (EMEA-000019-PIP06-09-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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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/207/2010 issued on 29 October 2010, the decision P/105/2011 issued on 4 May 2011, the decision P/0006/2012 issued on 24 January 2012, the decision P/0059/2013 issued on 26 March 2013, and the decision P/0251/2013 issued on 29 October 2013,

Having regard to the application submitted by Novartis Europharm Limited on 19 December 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 21 March 2014, in accordance with Article 22 of Regulation (EC) No 1901/2006, and Article 21 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 to the deferral.

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

Changes to the agreed paediatric investigation plan for everolimus (Afinitor, Certican and associated names), tablet, dispersible tablet, oral use, including changes to the deferral, 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 Limited, Wimblehurst Road, RH12 5AB - Horsham, West Sussex, United Kingdom.

Done at London, 5 May 2014

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

EMA/PDCO/22762/2014

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

EMEA-000019-PIP06-09-M05

Scope of the application

Active substance(s):

Everolimus

Invented name:

Afinitor

Certican and associated names

Condition(s):

Prevention of rejection of transplanted kidney

Prevention of rejection of transplanted heart

Prevention of rejection of transplanted liver

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 19 December 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/207/2010 issued on 29 October 2010, the decision P/105/2011 issued on 4 May 2011, the decision P/0006/2012 issued on 24 January 2012, the decision P/0059/2013 issued on 26 March 2013, and the decision P/0251/2013 issued on 29 October 2013.

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

The procedure started on 21 January 2014.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified and 1 study 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 and to the deferral 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, 21 March 2014

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: prevention of rejection of transplanted kidney

The waiver applies to:

- children from birth to less than 12 months;
- for tablet, 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).

1.2. Condition: prevention of rejection of transplanted heart

The waiver applies to:

- children from birth to less than 18 years;
- for tablet, dispersible tablet, for oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

1.3. Condition: prevention of rejection of transplanted liver

The waiver applies to:

- neonates (from birth to less than 28 days);
- for tablet, dispersible tablet, for oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan (PIP)

2.1. Condition: prevention of rejection of transplanted kidney

2.1.1. Indication(s) targeted by the PIP

Prevention of acute rejection in de novo paediatric recipients of a renal transplant from 1 to less than 18 years old.

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

From 1 year to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Tablet, dispersible tablet.

2.1.4. Measures

Area	Number of studies	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	1	**Study 1** Open label, randomised, multicentre study to evaluate efficacy, tolerability and safety of everolimus in paediatric kidney transplant recipients from 1 to less than 18 years old.
Extrapolation, modelling & simulation studies	1	**Study 3** Extrapolation study to evaluate the use of everolimus in organ transplantation in children from 1 to less than 18 years of age.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition: prevention of rejection of transplanted liver

2.2.1. Indication(s) targeted by the PIP

Prevention of acute rejection in paediatric recipients of a liver transplant from 1 month to less than 18 years old.

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

From 1 month to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Tablet, dispersible tablet.

2.2.4. Measures

Area	Number of studies	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.

Clinical studies	1	**Study 2** Open label, single arm, multicentre, prospective, observational study to evaluate safety/tolerability, pharmacokinetics and treatment effect of everolimus in combination with reduced CNI in paediatric liver allograft transplant recipients from 1 month to 18 years old.
Extrapolation, modelling & simulation studies	1	**Study 3** Analysis of existing in house and literature data on efficacy and safety of everolimus.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By March 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 neuroendocrine tumours of pancreatic origin

Authorised indications:

- Treatment of unresectable or metastatic, well- or moderately-differentiated neuroendocrine tumours of pancreatic origin in adults with progressive disease.

2. Treatment of renal cell carcinoma

Authorised indications:

- Treatment of patients with advanced renal cell carcinoma, whose disease has progressed on or after treatment with VEGF-targeted therapy.

3. Prevention of organ rejection in allogeneic renal or cardiac transplant

Authorised indications:

- Prophylaxis of organ rejection in adult patients at low to moderate immunological risk receiving an allogeneic renal or cardiac transplant in combination with ciclosporin for microemulsion and corticosteroids.
- Prophylaxis of organ rejection in adult patients at low to moderate immunological risk receiving an allogeneic renal or cardiac transplant in combination with ciclosporin for microemulsion and corticosteroids.

Authorised pharmaceutical form(s):

Tablet, dispersible tablet.

Authorised route(s) of administration:

Oral use.