EMA/25160/2012

European Medicines Agency decision

P/0006/2012

of 24 January 2012

on the acceptance of a modification of an agreed paediatric investigation plan for everolimus (Afinitor), (Certican and associated names), (EMEA-000019-PIP06-09-M02) 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,

Having regard to the application submitted by Novartis Europharm Limited on 30 September 2011 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 9 December 2011, in accordance with Article 22 of Regulation (EC) No 1901/2006, and of its own motion in accordance with Article 12 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 waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the 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 (Afinitor), (Certican and associated names), tablet, dispersible tablet, oral use, including changes to the waiver, 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, 24 January 2012

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

EMA/PDCO/813622/2011

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

EMEA-000019-PIP06-09-M02

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 30 September 2011 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 application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 12 October 2011.

Scope of the modification

Some measures of the Paediatric Investigation Plan have been modified. The waiver for one condition has been granted.

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 set out in the Annex I of this opinion.
   - to grant a waiver for one or more subsets of the paediatric population on its own motion in accordance with Article 12 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 Norwegian Paediatric Committee member agrees 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 annex(es) and appendix.

London, 09 December 2011

On behalf of the Paediatric Committee
Dr Daniel Brasseur, 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:

- newborn infants (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

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. Studies

Area	Number of studies	Description
Quality	0	N.A.
Non-clinical	0	Not applicable.
Clinical	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.

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. Studies

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	1	Study 2 Open label, single arm, multicentre, prospective, observational study to evaluate safety/tolerability and efficacy of everolimus in combination with reduced CNI in de novo paediatric full-size liver allograft recipients, and sequentially in paediatric split liver recipients, from 1 months to 18 years old.

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 2016
Deferral for one or more studies 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:

   Afinitor is indicated for the treatment of patients with advanced renal cell carcinoma, whose disease has progressed on or after treatment with VEGF-targeted therapy.

2. Treatment of renal cell carcinoma

   Authorised indications:

   Afinitor is indicated for the treatment of unresectable or metastatic, well- or moderately-differentiated neuroendocrine tumours of pancreatic origin in adults with progressive disease.

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

   Authorised indications:

   Certican is indicated for the prophylaxis of organ rejection in adult patients at low to moderate immunological risk receiving an allogeneic renal or cardiac transplant. Certican should be used in combination with ciclosporin for microemulsion and corticosteroids.

   Everolimus Novartis is indicated for the prophylaxis of organ rejection in adult patients at low to moderate immunological risk receiving an allogeneic renal or cardiac transplant. Everolimus Novartis should be used in combination with ciclosporin for microemulsion and corticosteroids

EU Number	**(Invented) name**	**Strength**	**Pharmaceutical Form**	**Route of Administration**	**Packaging**	**Content (concentration)**	**Package size**
EU/1/09/538/001	Afinitor	5 mg	Tablet	Oral use	blister (alu/PA/alu/PVC)		30 tablets
EU/1/09/538/002	Afinitor	5 mg	Tablet	Oral use	blister (alu/PA/alu/PVC)		60 tablets
EU/1/09/538/003	Afinitor	5 mg	Tablet	Oral use	blister (alu/PA/alu/PVC)		90 tablets
EU/1/09/538/004	Afinitor	10 mg	Tablet	Oral use	blister (alu/PA/alu/PVC)		30 tablets
EU/1/09/538/005	Afinitor	10 mg	Tablet	Oral use	blister (alu/PA/alu/PVC)		60 tablets
EU/1/09/538/006	Afinitor	10 mg	Tablet	Oral use	blister (alu/PA/alu/PVC)		90 tablets
EU/1/09/538/007	Afinitor	5 mg	Tablet	Oral use	blister (alu/PA/alu/PVC)		10 tablets
EU/1/09/538/008	Afinitor	10 mg	Tablet	Oral use	blister (alu/PA/alu/PVC)		10 tablets

Invented name **Name**	**Strength**	**Pharmaceutical form**	**Route of administration**
Certican associated names	0.1, 0.25, 0.5, 0.75 and 1.0 mg	Tablet and dispersible tablet	Oral use