EMA/325926/2011

European Medicines Agency decision

P/105/2011

of 4 May 2011

on the acceptance of a modification of an agreed paediatric investigation plan for everolimus (Certican and associated names) (EMEA-000019-PIP06-09-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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.

7 Westferry Circus • Canary Wharf • London E14 4HB • United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8409
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

European Medicines Agency decision

P/105/2011

of 4 May 2011

on the acceptance of a modification of an agreed paediatric investigation plan for everolimus (Certican and associated names) (EMEA-000019-PIP06-09-M01) 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/207/2010 issued on 29 October 2010,

Having regard to the application submitted by Novartis Europharm Limited on 10 January 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 18 March 2011, in accordance with Article 22 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation 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 to the deferral 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 deferral and 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 (Certican and associated names), tablet, dispersible tablet, age appropriate liquid formulation, oral use, including changes to the deferral and 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, 4 May 2011

For the European Medicines Agency
Andreas Pott
Acting Executive Director

(Signature on file)

EMA/PDCO/200839/2011

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

EMEA-000019-PIP06-09-M01

Scope of the application

Active substance(s):

Everolimus

Invented name:

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

Age appropriate liquid formulation

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

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8409
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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 10 January 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 application for modification proposed changes to the agreed paediatric investigation plan and to the deferral and to the waiver.

The procedure started on 19 January 2011.

Scope of the modification

The condition prevention of rejection of transplanted liver has been introduced in the paediatric investigation plan.

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 and to the waiver 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, 18 March 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, age appropriate liquid formulation 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 12 months;
- for tablet, dispersible tablet, age appropriate liquid formulation 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).

1.3. Condition: Prevention of rejection of transplanted liver

The waiver applies to:

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

2. Paediatric Investigation Plan

2.1. Condition to be investigated

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, age appropriate liquid formulation

2.1.4. Studies

Area	Number of studies	Description
Quality	1	Study 1 Development of age appropriate oral liquid formulation (same as for condition Prevention of rejection of transplanted heart).
Non-clinical	0	Not applicable.
Clinical	1	Study 2 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 to be investigated

Prevention of rejection of transplanted heart

2.2.1. Indication(s) targeted by the PIP

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

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

From 1 year to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Tablet, dispersible tablet, age appropriate liquid formulation

2.2.4. Studies

Area	Number of studies	Description
Quality	1	Study 1 Development of age appropriate oral liquid formulation (same as for condition Prevention of rejection of transplanted kidney).
Non-clinical	0	Not applicable.
Clinical	1	Study 3 Open label, randomised, multicentre study to evaluate efficacy, tolerability and safety of everolimus in paediatric heart transplant recipients from 1 to less than 18 years old.

2.3. Condition to be investigated

Prevention of rejection of transplanted liver

2.3.1. 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.

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

From 1 month to less than 18 years of age.

2.3.3. Pharmaceutical form(s)

Tablet, dispersible tablet, age appropriate liquid formulation

2.3.4. Studies

Area	Number of studies	Description
Quality	0	Not applicable.
Non-clinical	0	Not applicable.
Clinical	1	Study 4 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

Area	Number of studies	Description
		sequentially in paediatric split liver recipients, from 1 months to 18 years old.

3. Follow-up, completion and deferral of PIP

Measures to address long term follow-up of potential safety issues and efficacy 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

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

RFM: Sweden for MRP

Decentralised / Mutual recognition / National procedure(s) (Outside EEA)

Invented name	Country	Authorised indication
Certican	Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Italy, Latvia, Lithuania,	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.

	Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden	
Everolimus Novartis	Germany, Sweden	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