EMA/755963/2012

European Medicines Agency decision

P/0300/2012

of 20 December 2012

on the acceptance of a modification of an agreed paediatric investigation plan for ivacaftor (Kalydeco), (EMEA-000335-PIP01-08-M07) 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.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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on the acceptance of a modification of an agreed paediatric investigation plan for ivacaftor (Kalydeco), (EMEA-000335-PIP01-08-M07) 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/30/2009 issued on 23 February 2009, the decision P/250/2009 issued on 18 December 2009, the decision P/17/2010 issued on 8 February 2010, the decision P/127/2010 issued on 28 July 2010, the decision P/191/2011 issued on 3 August 2011 and the decision P/0039/2012 issued on 24 February 2012 and the decision P/0155/2012 issued on 24 July 2012,

Having regard to the application submitted by Vertex Pharmaceuticals Incorporated on 20 August 2012 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 9 November 2012, 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 ivacaftor (Kalydeco), film-coated tablet, age appropriate formulation, 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 Vertex Pharmaceuticals Incorporated, 130 Waverly Street, MA 02139 - Cambridge, Massachusetts, United States.

Done at London, 20 December 2012

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

EMA/PDCO/554467/2012

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

EMEA-000335-PIP01-08-M07

Scope of the application

Active substance(s):

Ivacaftor

Invented name:

Kalydeco

Condition(s):

Treatment of cystic fibrosis

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Age appropriate formulation

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Vertex Pharmaceuticals Incorporated

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, Vertex Pharmaceuticals Incorporated submitted to the European Medicines Agency on 20 August2012 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/30/2009 issued on 23 February 2009, the decision P/250/2009 issued on 18 December 2009, the decision P/17/2010 issued on 8 February 2010, the decision P/127/2010 issued on 28 July 2010, the decision P/191/2011 issued on 3 August 2011 and the decision P/0039/2012 issued on 24 February 2012 and the decision P/0155/2012 issued on 24 July 2012.

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

The procedure started on 12 September 2012.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been 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 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, 9 November 2012

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

Not applicable.

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of cystic fibrosis.

2.1.1. Indication(s) targeted by the PIP

Treatment of cystic fibrosis.

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

From birth to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

- Film-coated tablet for oral use.
- Age appropriate formulation for children below 6 years of age for oral use.

2.1.4. Studies

Area	Number of studies	Description
Quality		Film-coated tablet. Age appropriate formulation for children below 6 years of age with acceptability, palatability, and compatibility testing.
Non-clinical		An Oral (Gavage) Toxicity and Toxicokinetics Study in Juvenile Rats, with Recovery.
Clinical	9	1. A randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of ivacaftor (VX-770) in adolescents 12 to less than 18 years old (and adults) with Cystic Fibrosis (CF) and G551D Mutation. 2. A randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of ivacaftor (VX-770) in children with CF and G551D mutation age 6 to less than 12 years. 3. A randomised, double-blind, placebo-controlled, multicentre study in patients with CF with at least 1 Allele of a R117H-CFTR mutation, age 6 years and older. 4. A randomised, double-blind, placebo-controlled, multicentre study in (adults) and children with CF with the ΔF508/ΔF508-CFTR mutation, age 12 to less than 18 years.

		5. Rollover long-term safety and efficacy study in (adults) and children with CF age 6 years and older with at least one allele of G551D-CFTR mutation. 6. A randomized, double-blind, placebo-controlled, crossover study to evaluate the effect of ivacaftor (VX-770) on lung clearance index in subjects with cystic fibrosis with the G551D mutation and a FEV1 above 90% predicted, 6 years and older. 7. A 2-part open-label study to evaluate the safety, PK, and PD of ivacaftor (VX-770) in subjects with cystic fibrosis and a CFTR gating mutation, aged 2 to less than 6 years. 8. An open-label study to evaluate the safety, PK, and PD of ivacaftor (VX-770) in newborns, infants and toddlers less than 24 months of age with cystic fibrosis and a CFTR gating mutation. 9. A two part, randomised, double blind, placebo controlled, crossover study with an open label period to evaluate the efficacy and safety of ivacaftor in patients with Cystic Fibrosis aged 6 years or older, who have a non-G551D CFTR gating mutation.

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 December 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):

Treatment of cystic fibrosis

Authorised indications:

Kalydeco is indicated for the treatment of cystic fibrosis (CF) in patients age 6 years and older who have a G551D mutation in the CFTR gene.

Authorised pharmaceutical formulation(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use