EMA/305214/2017

European Medicines Agency decision

P/0147/2017

of 7 June 2017

on the acceptance of a modification of an agreed paediatric investigation plan for ivacaftor (Kalydeco), (EMEA-000335-PIP01-08-M11) 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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

European Medicines Agency decision

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on the acceptance of a modification of an agreed paediatric investigation plan for ivacaftor (Kalydeco), (EMEA-000335-PIP01-08-M11) 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, the decision P/0039/2012 issued on 24 February 2012, the decision P/0155/2012 issued on 24 July 2012, the decision P/0300/2012 issued on 20 December 2012, the decision P/0263/2013 issued on 30 October 2013, the decision P/0060/2014 issued on 7 March 2014 and the decision P/0112/2015 issued on 5 June 2015,

Having regard to the application submitted by Vertex Pharmaceuticals (Europe) Limited on 30 January 2017 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 21 April 2017, 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 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 ivacaftor (Kalydeco), film-coated tablet, granules in sachet, 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 Vertex Pharmaceuticals (Europe) Limited, 2 Kingdom Street, W2 6BD – London, United Kingdom.

EMA/PDCO/75377/2017
London, 21 April 2017

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

EMEA-000335-PIP01-08-M11

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

Granules in sachet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Vertex Pharmaceuticals (Europe) Limited

Information about the authorised medicinal product:

See Annex II

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5510
Send a question via our website www.ema.europa.eu/contact

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Vertex Pharmaceuticals (Europe) Limited submitted to the European Medicines Agency on 30 January 2017 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, the decision P/0039/2012 issued on 24 February 2012, the decision P/0155/2012 issued on 24 July 2012, the decision P/0300/2012 issued on 20 December 2012, the decision P/0263/2013 issued on 30 October 2013, the decision P/0060/2014 issued on 7 March 2014 and the decision P/0112/2015 issued on 5 June 2015.

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

The procedure started on 21 February 2017.

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 and to the deferral in the scope set out in the Annex I of this opinion.

   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 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.

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 (PIP)

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: Granules in sachet

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	1. Development of an age appropriate oral solid formulation for children below 6 years of age with acceptability, palatability, and compatibility testing.
Non-clinical studies	1	2. An Oral (Gavage) Toxicity and Toxicokinetics Study in Juvenile Rats, with Recovery.
Clinical studies	9	3. 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. 4. 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. 5. 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. 6. 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.

		7. 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. 8. 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. 9. 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. 10. A 2-part open-label study to evaluate the safety, PK, and PD of ivacaftor in subjects with cystic fibrosis who are less than 24 months of age and have a CFTR gating mutation. 11. 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.
Extrapolation, modelling and simulation studies		Not applicable.
Other studies		Not applicable.
Other measures		Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By December 2020
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:

Film-coated tablets:

Treatment of patients with cystic fibrosis (CF) aged 6 years and older and weighing 25 kg or more who have one of the following gating (class III) mutations in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N or S549R; also indicated for the treatment of patients with cystic fibrosis (CF) aged 18 years and older who have an R117H mutation in the CFTR gene.

Granules in sachet:

Treatment of children with cystic fibrosis (CF) aged 2 years and older and weighing less than 25 kg who have one of the following gating (class III) mutations in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N or S549R.

Authorised pharmaceutical formulation(s):

Film-coated tablet

Granules in sachet

Authorised route(s) of administration:

Oral use