EMA/472909/2010

European Medicines Agency decision

P/127/2010

of 28 July 2010

on the acceptance of a modification of an agreed paediatric investigation plan for N-(2,4-Di-tert-butyl-5-hydroxyphenyl)-1,4-dihydro-4-oxoquinoline-3-carboxamide, (EMEA-000335-PIP01-08-M03) 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 7418 8409
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

European Medicines Agency decision

P/127/2010

of 28 July 2010

on the acceptance of a modification of an agreed paediatric investigation plan for N-(2,4-Di-tert-butyl-5-hydroxyphenyl)-1,4-dihydro-4-oxoquinoline-3-carboxamide, (EMEA-000335-PIP01-08-M03) 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, and the decision P/17/2010 issued on 8 February 2010,

Having regard to the application submitted by Vertex Pharmaceuticals Incorporated on 1 April 2010 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 11 June 2010, 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 N-(2,4-Di-tert-butyl-5-hydroxyphenyl)-1,4-dihydro-4-oxoquinoline-3-carboxamide, tablet, age appropriate formulation, oral use, including changes to a 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 Incorporated, 130 Waverly Street, Cambridge, 02139, Massachusetts (MA), United States.

Done at London, 28 July 2010

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

EMA/PDCO/341873/2010

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

EMEA-000335-PIP01-08-M03

Scope of the application

Active substance(s):

N-(2,4-Di-tert-butyl-5-hydroxyphenyl)-1,4-dihydro-4-oxoquinoline-3-carboxamide

Condition(s):

Cystic fibrosis

Pharmaceutical form(s):

Tablet
Age appropriate formulation

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Vertex Pharmaceuticals Incorporated

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 1 April 2010 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, and the decision P/17/2010 issued on 8 February 2010.
The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral.

The procedure started on 15 April 2010.

Scope of the modification

Some of the agreed measures and timelines of the original Opinion have been modified.

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

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 annex(es) and appendix.

London, 11 June 2010

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman

(Signature on file)

Annex I

The measures and timelines of the agreed paediatric investigation plan

1. Condition(s)

Cystic fibrosis

2. Waiver

Not applicable

3. Paediatric Investigation Plan

3.1. Condition to be investigated

Cystic fibrosis

3.1.1. Indication targeted by the PIP

Treatment of cystic fibrosis

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

From birth to less than 18 years of age.

3.1.3. Pharmaceutical form(s)

- Tablet for oral use.
- Age appropriate formulation for children below 6 years of age for oral use.

3.1.4. Studies

Area	**Number of studies**	**Description**
Quality		Tablet Age appropriate formulation for children below 6 years of age
Non-clinical		Juvenile animal study
Clinical		1) A randomized, double-blind, placebo-controlled, parallel group study to evaluate the efficacy and safety of VX-770 (=N-(2,4-Di-tert-butyl-5-hydroxyphenyl)-1,4-dihydro-4-oxoquinoline-3-carboxamide) 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 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 (adults) and children with CF with at least 1 Allele of a Class III (Non-G551D), Class IV, or Class V *CFTR* Mutation, age 6 to less than 18 years.

		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 randomised, double-blind, placebo-controlled, multicentre study in children with CF with a G551D-*CFTR* Mutation, age 6 to less than 18 years to evaluate the effect of long-term treatment withVX-770 on CF progression. 7) A randomized, double-blind, placebo-controlled, crossover study to evaluate the effect of 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* 8) A PK/PD study in children with CF from birth to less than 6 years.

4. 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 December 2015
Deferral for one or more studies contained in the paediatric investigation plan:	Yes