EMA/592149/2013

European Medicines Agency decision

P/0268/2013

of 19 December 2013

on the acceptance of a modification of an agreed paediatric investigation plan for lumacaftor (EMEA-001173-PIP01-11-M01) 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

European Medicines Agency decision

P/0268/2013

of 19 December 2013

on the acceptance of a modification of an agreed paediatric investigation plan for lumacaftor (EMEA-001173-PIP01-11-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/0121/2012 issued on 3 July 2012,

Having regard to the application submitted by Vertex Pharmaceuticals (Europe) Ltd. on 21 June 2013 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the revised opinion of the Paediatric Committee of the European Medicines Agency, issued on 7 November 2013, 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 lumacaftor, film-coated tablet, age appropriate oral formulation, 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) Ltd., 86-88 Jubilee Avenue, Milton Park, OX14 4RW - Abingdon, United Kingdom.

Done at London, 19 December 2013

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

EMA/PDCO/399706/2013 rev.1

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

EMEA-001173-PIP01-11-M01

Scope of the application

Active substance(s):

Lumacaftor

Condition(s):

Treatment of cystic fibrosis

Pharmaceutical form(s):

Film-coated tablet

Age appropriate oral formulation

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Vertex Pharmaceuticals (Europe) Ltd.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Vertex Pharmaceuticals Europe Ltd. submitted to the European Medicines Agency on 21 June 2013 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0121/2012 issued on 3 July 2012.

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

The procedure started on 17 July 2013.

An opinion was adopted by the Paediatric Committee on 13 September 2013.

Following comments raised during the decision-making process, the Paediatric Committee revised its opinion of 13 September 2013.

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

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

Revised 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 revised 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 revised opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annex and appendix.

London, 7 November 2013

On behalf of the Paediatric Committee
Dr Dirk Mentzer, 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 in combination with ivacaftor

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

Age appropriate oral formulation

2.1.4. Measures

Area	Number of measures	Description
Quality	2	1. Development of age-appropriate film-coated tablet for children aged 6 to less than 12 years old. 2. Development of an age appropriate oral formulation for children below 6 years of age with testing of acceptability, palatability, and compatibility of the formulation with common food and drinks.
Non-clinical	7	3. 6-month oral (gavage) toxicity and toxicokinetics study with lumacaftor and VRT-0995096 in rats with a 1-month recovery (VX-809-TX-012). 4. 3-month oral (gavage) toxicity and toxicokinetics study with lumacaftor, ivacaftor, and VRT-0995096 in rats with a 1-month recovery (VX-809-TX-013). 5. 12 month oral (gavage) toxicity and toxicokinetics study with lumacaftor in Beagle dogs with a 1-month recovery (VX-809-TX-014). 6. Developmental and Perinatal/Postnatal Reproduction Toxicity Study in Rats, Including a Postnatal Behavioral/Functional Evaluation (VX-809-TX-017). 7. Fertility and early embryonic development study in rats with lumacaftor and VRT-0995096 (VX-809-TX-016). 8. Oral (gavage) dose range finding study in juvenile rats (VX-809-TX). 9. Oral (gavage) toxicity and toxicokinetics study in juvenile rats with 4-week recovery (VX-809-TX).

Area	Number of measures	Description
Clinical	8	10. Open-label, multi-dose study to evaluate the pharmacokinetics (PK) and safety of lumacaftor in combination with ivacaftor and their respective major circulating metabolites in subjects with Cystic Fibrosis (CF) who are homozygous for the F508del-CFTR mutation aged 6 to less than 12 years. (StudyVX13-809-011). 11. Randomised, double-blind, placebo-controlled study to evaluate efficacy and safety and PK in subjects with CF homozygous for the F508del-CFTR mutation aged 6 to less than 12 years. (Study11). 12. Randomised, double-blind, placebo-controlled study to evaluate efficacy and safety in subjects with CF who are homozygous for the F508del-CFTR mutation aged 12 to less than 18 years (and adults). (Study VX12-809-103). 13. Randomised, double-blind, placebo-controlled study to evaluate efficacy and safety in subjects with CF who are homozygous for the F508del-CFTR mutation aged 12 to less than 18 years (and adults). (Study VX12-809-104). 14. Rollover open-label long-term safety and efficacy study in subjects with CF who are homozygous for the F508del-CFTR mutation aged 6 to less than 18 years (and adults) (StudyVX12-809-105). 15. Pharmacokinetic and safety study in subjects with CF who are homozygous for the F508del-CFTR mutation aged 2 to less than 6 years (Study 15). 16. Pharmacokinetic and safety study in subjects with CF who are homozygous for the F508del-CFTR mutation from birth to less than 2 years of age (Study 16). 17. Relative bioavailability study to characterize the PK of the paediatric age appropriate formulation relative to the tablet formulation in healthy adults.

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 July 2017
Deferral for one or more studies contained in the paediatric investigation plan:	Yes