EMA/256056/2019

European Medicines Agency decision

P/0191/2019

of 17 May 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral for N-(trans-3-(5-((R)-1-hydroxyethyl)-1,3,4-oxadiazol-2-yl) cyclobutyl)-3-phenylisoxazole-5-carboxamide (PTI-428) (EMEA-002398-PIP01-18) 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.

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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 application submitted by SFL Regulatory Services GmbH on 22 May 2018 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 29 March 2019, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 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 agreement of a paediatric investigation plan and on the granting of a deferral.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a 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

A paediatric investigation plan for N-(trans-3-(5-((R)-1-hydroxyethyl)-1,3,4-oxadiazol-2-yl) cyclobutyl)-3-phenylisoxazole-5-carboxamide (PTI-428), capsule, hard, age-appropriate oral solid dosage form, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for N-(trans-3-(5-((R)-1-hydroxyethyl)-1,3,4-oxadiazol-2-yl) cyclobutyl)-3-phenylisoxazole-5-carboxamide (PTI-428), capsule, hard, age-appropriate oral solid dosage form, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

This decision is addressed to SFL Regulatory Services GmbH, Europaplatz 2/1/2, 1150 - Vienna, Austria.

EMA/PDCO/113726/2019
Amsterdam, 29 March 2019

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral

EMEA-002398-PIP01-18

Scope of the application

Active substance(s):

N-(trans-3-(5-((R)-1-hydroxyethyl)-1,3,4-oxadiazol-2-yl) cyclobutyl)-3-phenylisoxazole-5-carboxamide (PTI-428)

Condition(s):

Treatment of cystic fibrosis

Pharmaceutical form(s):

Capsule, hard

Age-appropriate oral solid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

SFL Regulatory Services GmbH

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, SFL Regulatory Services GmbH submitted for agreement to the European Medicines Agency on 22 May 2018 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 26 June 2018.

Supplementary information was provided by the applicant on 26 November 2018. The applicant proposed modifications to the paediatric investigation plan and withdrew its request for a waiver.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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 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 in individuals with cystic fibrosis who are homozygous for the F508del mutation and are receiving treatment with a CFTR modulator

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)

Capsule, hard

Age-appropriate oral solid dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of an age-appropriate oral solid dosage form for children aged 6 to less than 12 years old. Development of lower strength of the existing dose form appropriate to the paediatric population. **Study 2** Development of an age-appropriate oral solid dosage form for use in children from birth to less than 6 years of age.
Non-clinical studies	3	**Study 3** Dose range-finding toxicity study in juvenile rats **Study 4** 8-week definitive toxicity study in juvenile rats **Study 5** Combination toxicity study in adult rats

Clinical studies	6	**Study 6** Randomized, double-blind, placebo-controlled, study to evaluate the efficacy and safety of PTI-428 in adolescents (and adults) with CF who are on background treatment with a CFTR modulator **Study 7** Two-part study to evaluate the safety, pharmacokinetics (PK) and the efficacy of PTI-428 in children with CF age 6 to less than 12 years who are on background treatment with a CFTR modulator. **Study 8** Two-part, single-arm, multicentre study to evaluate the safety, PK, pharmacodynamics (PD), and efficacy of PTI-428 in children 2 to less than 6 years of age with CF who are on background treatment with a CFTR modulator. **Study 9** Two-part, single-arm, multicentre study to evaluate the safety, PK, PD and efficacy of PTI-428 in children less than 2 years of age with CF who are on background treatment with a CFTR modulator. **Study 10** Rollover open-label, 96-week long-term safety and efficacy study in subjects with CF, 6 to less than 18 years of age (and adults) who have completed study 6 or 7. **Study 11** Rollover open-label, 96-week long-term safety and efficacy study in children with CF less than 6 years of age who have completed study 8 or 9.
Extrapolation, modelling and simulation studies	2	**Study 12** Modelling and simulation study for dose selection in children from birth to less than 12 years of age and adolescents. **Study 13** Extrapolation study by modelling and simulation of efficacy and pharmacodynamic endpoints using data obtained in adolescents and adults to support extrapolation of efficacy to patients less than 12 years of age.
Other studies	0	Not applicable.
Other measures	0	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 September 2027
Deferral for one or more measures contained in the paediatric investigation plan:	Yes