EMA/767367/2021

European Medicines Agency decision

P/0566/2021

of 21 December 2021

on the agreement of a paediatric investigation plan and on the granting of a deferral for (1R,2S,5S)-N-((1S)-1-Cyano-2-((3S)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido)butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide (EMEA-003081-PIP01-21) 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.

European Medicines Agency decision

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on the agreement of a paediatric investigation plan and on the granting of a deferral for (1R,2S,5S)-N-((1S)-1-Cyano-2-((3S)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido)butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide (EMEA-003081-PIP01-21) 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 application submitted by Pfizer Europe MA EEIG on 29 July 2021 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 17 December 2021, 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 (1R,2S,5S)-N-((1S)-1-Cyano-2-((3S)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido)butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide, film-coated tablet, age-appropriate oral 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 (1R,2S,5S)-N-((1S)-1-Cyano-2-((3S)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido)butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide, film-coated tablet, age-appropriate oral 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 Pfizer Europe MA EEIG, 17 Boulevard de la Plaine, 1050 – Bruxelles, Belgium.

EMA/PDCO/708271/2021
Amsterdam, 17 December 2021

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

EMEA-003081-PIP01-21

Scope of the application

Active substance(s):

(1R,2S,5S)-N-((1S)-1-Cyano-2-((3S)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido)butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide

Condition(s):

Treatment of coronavirus disease 2019 (COVID-19)

Prevention of coronavirus disease 2019 (COVID-19)

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate oral dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Pfizer Europe MA EEIG

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Pfizer Europe MA EEIG submitted for agreement to the European Medicines Agency on 29 July 2021 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 14 September 2021.

Supplementary information was provided by the applicant on 26 November 2021. The applicant proposed modifications to the paediatric investigation plan and withdrew its request for a waiver and amended the scope of the Paediatric Investigation Plan to include another condition.

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 coronavirus disease 2019 (COVID-19)

2.1.1. Indication(s) targeted by the PIP

Treatment of coronavirus disease 2019 (COVID-19) from birth to less than 18 years of age

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 dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an age-appropriate oral formulation of (1R,2S,5S)-N-((1S)-1-Cyano-2-((3S)-2-oxopyrrolidin-3-yl)ethyl)-3-((2S)-3,3-dimethyl-2-(2,2,2-trifluoroacetamido)butanoyl)-6,6-dimethyl-3-azabicyclo[3.1.0]hexane-2-carboxamide (PF-07321332) (to be used in combination with ritonavir- an age-appropriate formulation suitable for the age subset from birth to less than 6 years of age) for children from birth to less than 6 years of age and/or unable to swallow the current available film-coated tablets.
Non-clinical studies	0	Not applicable
Clinical studies	1	**Study 2 (C4671026)** Open-label study to evaluate pharmacokinetics (PK), safety and efficacy of PF-07321332 (in combination with ritonavir) in children from birth to less than 18 years of age with coronavirus disease 2019 for treatment of COVID-19 at risk of progression to severe COVID-19.

Extrapolation, modelling and simulation studies	3	**Study 3** Population PK modelling to simulate multi-dose administration of PF-07321332 and ritonavir across age groups in children from birth to less than 18 years with coronavirus disease 2019 and to select the doses to be used in the paediatric clinical study 2. **Study 4** Population PK modelling to simulate multi-dose administration of PF-07321332 and ritonavir across age groups in children from birth to less than 18 years with coronavirus disease 2019 for the treatment of coronavirus disease 2019 and in healthy children for the prevention of coronavirus disease 2019 to select final paediatric dose recommendations by matching exposures to adults. **Study 5** Extrapolation study of efficacy and safety of PF-07321332 and ritonavir from adults to children from birth to less than 18 years of age with coronavirus disease 2019 at risk of progression to severe COVID-19.
Other studies	0	Not applicable
Other measures	0	Not applicable

2.2. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By December 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

2.3. Condition:

Prevention of coronavirus disease 2019 (COVID-19)

2.3.1. Indication(s) targeted by the PIP

Prevention of coronavirus disease 2019 (COVID-19) from birth to less than 18 years of age.

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

From birth to less than 18 years of age

2.3.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate oral dosage form

2.3.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Same as for condition treatment of coronavirus disease 2019 (COVID-19)
Non-clinical studies	0	Not applicable
Clinical studies	1	**Study 2** Same as for condition treatment of coronavirus disease 2019 (COVID-19)
Extrapolation, modelling and simulation studies	3	**Study 3** Same as for condition treatment of coronavirus disease 2019 (COVID-19) **Study 4** Same as for condition treatment of coronavirus disease 2019 (COVID-19) **Study 6** Extrapolation study of efficacy and safety of PF-07321332 and ritonavir from healthy adults to healthy children from birth to less than 18 years of age for the prevention of coronavirus disease 2019
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:	No
Date of completion of the paediatric investigation plan:	By August 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes