EMA/901099/2022

European Medicines Agency decision

P/0503/2022

of 1 December 2022

on the acceptance of a modification of an agreed 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 (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 / ritonavir (Paxlovid), (EMEA-003081-PIP01-21-M02) 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

P/0503/2022

of 1 December 2022

on the acceptance of a modification of an agreed 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 (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 / ritonavir (Paxlovid), (EMEA-003081-PIP01-21-M02) 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0566/2021 issued on 21 December 2021,

Having regard to the application submitted by Pfizer Europe MA EEIG on 8 August 2022 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 11 November 2022, 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.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed 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 (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 / ritonavir (Paxlovid), film-coated tablet, age-appropriate oral dosage form, oral use, 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 Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 – Bruxelles, Belgium.

EMA/PDCO/697896/2022
Amsterdam, 11 November 2022

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

EMEA-003081-PIP01-21-M02

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

(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 / ritonavir

Invented name and authorisation status:

See Annex II

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 22 of Regulation (EC) No 1901/2006 as amended, Pfizer Europe MA EEIG submitted to the European Medicines Agency on 8 August 2022 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0566/2021 issued on 21 December 2021.

The application for modification proposed changes to the agreed paediatric investigation pan.

The procedure started on 12 September 2022.

Scope of the modification

Some measures 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 in the scope set out in the Annex I of this opinion.

   The Paediatric Committee member of Norway 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 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	Description
Quality-related studies	**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) /ritonavir 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	Not applicable
Clinical studies	**Study 2 (C4671026)** Open-label study to evaluate pharmacokinetics (PK), safety and efficacy of PF-07321332 (in combination with ritonavir) and PF-07321332/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	**Study 3** Population PK modelling to simulate multi-dose administration of PF-07321332 and ritonavir and PF-07321332/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 and PF-07321332/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 and PF-07321332/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	Not applicable
Other measures	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	Description
Quality-related studies	**Study 1** Same as for condition treatment of coronavirus disease 2019 (COVID-19)
Non-clinical studies	Not applicable
Clinical studies	**Study 2** Same as for condition treatment of coronavirus disease 2019 (COVID-19)
Extrapolation, modelling and simulation studies	**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 and PF-07321332 /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	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:	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

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

1. Treatment of coronavirus disease 2019 (COVID-19)

Authorised indication(s):

- Paxlovid is indicated for the treatment of coronavirus disease 2019 (COVID-19) in adults who do not require supplemental oxygen and who are at increased risk for progressing to severe COVID-19:
  - Invented name(s): Paxlovid
  - Authorised pharmaceutical form(s): film-coated tablets
  - Authorised route(s) of administration: oral use
  - Authorised via centralised procedure