EMA/94105/2022

European Medicines Agency decision

P/0048/2022

of 11 February 2022

on the acceptance of a modification of an agreed paediatric investigation plan for cilgavimab (EMEA-002925-PIP01-20-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.

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on the acceptance of a modification of an agreed paediatric investigation plan for cilgavimab (EMEA-002925-PIP01-20-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 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/0235/2021 issued on 8 June 2021,

Having regard to the application submitted by AstraZeneca AB on 18 October 2021 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 21 January 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 cilgavimab, solution for injection/infusion, intramuscular use, intravenous 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 AstraZeneca AB, Forskargatan 18, SE-151 85 – Södertälje, Sweden.

EMA/PDCO/603114/2021
Amsterdam, 21 January 2022

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

EMEA-002925-PIP01-20-M01

Scope of the application

Active substance(s):

Cilgavimab

Condition(s):

Treatment of Coronavirus disease 2019 (COVID-19)

Prevention of Coronavirus disease 2019 (COVID-19)

Pharmaceutical form(s):

Solution for injection/infusion

Route(s) of administration:

Intramuscular use

Intravenous use

Name/corporate name of the PIP applicant:

AstraZeneca AB

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, AstraZeneca AB submitted to the European Medicines Agency on 18 October 2021 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0235/2021 issued on 8 June 2021.

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

The procedure started on 22 November 2021.

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 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 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 paediatric patients with Coronavirus disease 2019 (COVID-19) who are at risk of progressing to severe disease

Treatment of paediatric patients with severe Coronavirus disease 2019 (COVID-19)

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)

Solution for injection/infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	1	**Study 1 (D8850C00006)** Open label, uncontrolled, single dose study to evaluate pharmacokinetics (PK), pharmacodynamics (PD) and safety of tixagevimab and cilgavimab in children from 29 weeks gestational age (GA) to less than 18 years of age for: • pre-exposure prophylaxis of COVID-19 in children at high risk of developing severe disease (Cohort 1) • treatment of mild to moderate COVID-19 in children at high risk for developing severe disease (Cohort 2) • treatment of severe COVID-19 (Cohort 3) *This study is the same as study 1 in condition Prevention of coronavirus disease 2019 (COVID-19).*

Extrapolation, modelling and simulation studies	3	**Study 2** Two-compartment population PK (PopPK) model for tixagevimab and cilgavimab dosing prediction and confirmation in paediatric patients from 29 weeks of gestational age (GA) to less than 18 years of age. *This study is the same as study 2 in condition Prevention of coronavirus disease 2019 (COVID-19)* **Study 3** PK bridging and extrapolation of clinical efficacy and safety to support the use of a single-dose of tixagevimab and cilgavimab for: • Pre- exposure prophylaxis of COVID-19 (IV and IM route) from adults at high risk of developing severe disease to children from 29 weeks gestational age to less than 18 years of age at risk of developing severe disease. • Treatment of mild-moderate COVID-19 (IV and IM route) from adults with mild-moderate COVID-19 at risk of developing severe disease to children from 29 weeks gestational age to less than 18 years of age with mild-moderate COVID-19 at risk of developing severe disease. • Treatment of severe COVID 19 (IV route) from adults with severe COVID-19 to children from 29 weeks gestational age to less than 18 years of age with severe COVID-19. *This study is the same as study 3 in condition Prevention of coronavirus disease 2019 (COVID-19)* **Study 4** *Study deleted within procedure EMEA-002900-PIP01-20-M01.*
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition:

Prevention of Coronavirus disease 2019 (COVID-19)

2.2.1. Indication(s) targeted by the PIP

Pre-exposure prophylaxis of Coronavirus disease 2019 (COVID-19) in children who are at risk of developing severe disease

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

From birth to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Solution for injection/infusion

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	1	**Study 1 (D8850C00006)** Open label, uncontrolled, single dose study to evaluate pharmacokinetics (PK), pharmacodynamics (PD) and safety of tixagevimab and cilgavimab in children from 29 weeks gestational age (GA) to less than 18 years of age for: • pre-exposure prophylaxis of COVID-19 in children at high risk of developing severe disease (Cohort 1) • treatment of mild to moderate COVID-19 in children at high risk for developing severe disease (Cohort 2) • treatment of severe COVID-19 (Cohort 3) *This study is the same as study 1 in condition Treatment of coronavirus disease 2019 (COVID-19)*
Extrapolation, modelling and simulation studies	3	**Study 2** Two-compartment population PK (PopPK) model for tixagevimab and cilgavimab dosing prediction and confirmation in paediatric patients from 29 weeks of gestational age (GA) to less than 18 years of age. *This study is the same as study 2 in condition Treatment of coronavirus disease 2019 (COVID-19)* **Study 3** PK bridging and extrapolation of clinical efficacy and safety to support the use of a single-dose of tixagevimab and cilgavimab for: • Pre- exposure prophylaxis of COVID-19 (IV and IM route) from adults at high risk of developing severe disease to children

		from 29 weeks gestational age to less than 18 years of age at risk of developing severe disease. • Treatment of mild-moderate COVID-19 (IV and IM route) from adults with mild-moderate COVID-19 at risk of developing severe disease to children from 29 weeks gestational age to less than 18 years of age with mild-moderate COVID-19 at risk of developing severe disease. • Treatment of severe COVID 19 (IV route) from adults with severe COVID-19 to children from 29 weeks gestational age to less than 18 years of age with severe COVID-19. *This study is the same as study 3 in condition Treatment of coronavirus disease 2019 (COVID-19)* **Study 4** *Study deleted within procedure EMEA-002900-PIP01-20-M01.*
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 June 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes