EMA/103747/2023

European Medicines Agency decision

P/0119/2023

of 13 April 2023

on the agreement of a paediatric investigation plan and on the granting of a deferral for tixagevimab / cilgavimab (Evusheld), (EMEA-003079-PIP01-22) 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 agreement of a paediatric investigation plan and on the granting of a deferral for tixagevimab / cilgavimab (Evusheld), (EMEA-003079-PIP01-22) 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 application submitted by AstraZeneca AB on 22 April 2022 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 24 February 2023, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

A paediatric investigation plan for tixagevimab / cilgavimab, solution for injection, intramuscular use, intravenous 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 tixagevimab / cilgavimab, solution for injection, intramuscular use, intravenous 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 AstraZeneca AB, Forskargatan 18, SE-151 85 - Södertälje, Sweden.

EMA/PDCO/914997/2022
Amsterdam, 24 February 2023

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

EMEA-003079-PIP01-22

Scope of the application

Active substance(s):

Tixagevimab / cilgavimab

Invented name and authorisation status:

See Annex II

Condition(s):

Prevention of coronavirus disease 2019 (COVID-19)

Treatment of coronavirus disease 2019 (COVID-19)

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Intramuscular use

Intravenous use

Name/corporate name of the PIP applicant:

AstraZeneca AB

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, AstraZeneca AB submitted for agreement to the European Medicines Agency on 22 April 2022 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 23 May 2022.

Supplementary information was provided by the applicant on 30 November 2022. The applicant proposed modifications to the paediatric investigation plan.

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 Paediatric Committee member of Norway 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 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:

Prevention of coronavirus disease 2019 (COVID-19)

2.1.1. 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

2.1.2. 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	Description
Quality-related studies	Not applicable
Non-clinical studies	Not applicable
Clinical studies	**Study 1 (D8850C00006)** Open label, uncontrolled, single dose study to evaluate pharmacokinetics (PK), pharmacodynamics (PD) and safety of tixagevimab/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)
Modelling and simulation studies	**Study 2** Two-compartment population PK (PopPK) model for dosing prediction and confirmation in paediatric patients from 29 weeks of gestational age (GA) to less than 18 years of age.
Other studies	**Study 3** PK bridging and extrapolation of clinical efficacy and safety to support

	the use of a single-dose of tixagevimab/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.
Extrapolation plan	Studies 1,2, and 3 of this PIP, as well as the adult studies D8850C00001, D8850C00002, D8850C00003, D8851C00001 and ACTIV-3, are part of the extrapolation plan of efficacy data from adults to the paediatric populaiton from birth to less than 18 years of age in the conditions: Pre- exposure prophylaxis of COVID-19.

2.2. Condition:

Treatment of Coronavirus disease 2019 (COVID-19)

2.2.1. Indication(s) targeted by the PIP

Treatment of COVID-19 in paediatric patients with COVID-19 who are at risk of progressing to severe disease

Treatment of COVID-19 in paediatric patients with severe COVID-19

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	Description
Quality-related studies	Not applicable
Non-clinical studies	Not applicable
Clinical studies	**Study 1 (D8850C00006)** Open label, uncontrolled, single dose study to evaluate pharmacokinetics (PK), pharmacodynamics (PD) and safety of tixagevimab/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).*
Modelling and simulation studies	**Study 2** Two-compartment population PK (PopPK) model for 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)*
Other studies	**Study 3** PK bridging and extrapolation of clinical efficacy and safety to support the use of a single-dose of tixagevimab/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)*

Extrapolation plan	Studies 1,2, and 3 of this PIP, as well as the adult studies D8850C00001, D8850C00002, D8850C00003, D8851C00001 and ACTIV-3, are part of the extrapolation plan of efficacy data from adults to the paediatric populaiton from birth to less than 18 years of age in the conditions: Treatment of COVID-19.

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

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Prevention of COVID-19

Authorised indication(s):

- indicated for the pre-exposure prophylaxis of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg
  - Invented name(s): Evusheld
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Intramuscular use
  - Authorised via centralised procedure

2. Treatment of COVID-19

- indicated for the treatment of adults and adolescents (aged 12 years and older weighing at least 40 kg) with COVID-19, who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19
  - Invented name(s): Evusheld
  - Authorised pharmaceutical form(s): Solution for injection
  - Authorised route(s) of administration: Intramuscular use
  - Authorised via centralised procedure