EMA/347368/2023

European Medicines Agency decision

P/0359/2023

of 8 September 2023

on the acceptance of a modification of an agreed paediatric investigation plan for baloxavir marboxil (Xofluza), (EMEA-002440-PIP01-18-M05) 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 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/0029/2021 issued on 29 January 2021, the decision P/0486/2021 issued on 3 December 2021, the decision P/0383/2022 issued on 9 September 2022, and the decision P/0093/2023 issued on 10 March 2023,

Having regard to the application submitted by Roche Registration GmbH on 24 April 2023 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 July 2023, 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 baloxavir marboxil (Xofluza), film-coated tablet, granules for oral suspension, 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 Roche Registration GmbH, Emil-Barell-Strasse 1, 79639 - Grenzach-Wyhlen, Germany.

EMA/PDCO/214902/2023
Amsterdam, 21 July 2023

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

EMEA-002440-PIP01-18-M05

Scope of the application

Active substance(s):

Baloxavir marboxil

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of influenza infection

Prevention of influenza infection

Pharmaceutical form(s):

Film-coated tablet

Granules for oral suspension

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Roche Registration GmbH

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Roche Registration GmbH submitted to the European Medicines Agency on 24 April 2023 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0300/2019 issued on 2 September 2019, the decision P/0029/2021 issued on 29 January 2021, the decision P/0486/2021 issued on 3 December 2021, the decision P/0383/2022 issued on 9 September 2022, and the decision P/0093/2023 issued on 10 March 2023.

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

The procedure started on 22 May 2023.

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 influenza infection

2.1.1. Indication(s) targeted by the PIP

Treatment of influenza infection

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

Granules for oral suspension

2.1.4. Measures

Area	Description
Quality-related studies	Not applicable
Non-clinical studies	Not applicable
Clinical studies	**Study 1 (CP40559)** Multicentre, single-arm, open label study to assess safety, pharmacokinetics, and efficacy of baloxavir marboxil in infants from birth to less than 1 year of age with influenza-like symptoms. **Study 2 (CP40563)** Multicentre, randomised, double-blind, active-controlled study to assess the safety, pharmacokinetics, and efficacy of baloxavir marboxil compared to oseltamivir in children from 1 year to less than 12 years of age with influenza-like symptoms. **Study 3 *(*CP40617*)*** Randomised, double-blind, placebo-controlled, multicenter study to assess efficacy, safety, and pharmacokinetics of baloxavir marboxil in combination with a standard of care neuraminidase inhibitor (SOC NAI), compared with a matching placebo in combination with a SOC NAI in adolescents who require hospitalization for severe influenza, or who contract severe influenza during hospitalization (and adults).

	Study 4 *Removed with procedure EMEA-002440-PIP01-18-M01.*
Extrapolation, modelling and simulation studies	**Study 5 (M&S Study 1)** Population PK model in otherwise healthy and high-risk adult and paediatric subjects, evaluating relevant demographic covariates that may influence systemic drug exposure. **Study 6** *Removed with procedure EMEA-002440-PIP01-18-M01.* **Study 7 (M&S Study 3)** Modelling and simulation study in Otherwise Healthy and High risk patients evaluating exposure-response using viral kinetic modelling and primary efficacy endpoints. **Study 8** *Removed with procedure EMEA-002440-PIP01-18-M01.* **Study 9** *Removed with procedure EMEA-002440-PIP01-18-M01.* **Study 10 (Extrapolation study 1)** Partial extrapolation of PK, PD (virology, virus titres) and efficacy (primary endpoint, time to symptom alleviation) in otherwise healthy paediatric patients from birth to less than 12 years of age. **Study 11 (Extrapolation study 2)** Complete extrapolation of PD and efficacy (primary endpoint, time to symptom alleviation) in High-Risk paediatric patients from birth to less than 12 years of age. **Study 12** *Removed with procedure EMEA-002440-PIP01-18-M01.* **Study 14** (Extrapolation study 3) *Added in procedure EMEA-002440-PIP01-18-M04.* Extrapolation of efficacy based on PK drug exposure matching from adults and adolescents to children aged from birth to less than 12 years to support the development of a weight-based bracket dosing.
Other studies	Not applicable
Other measures	Not applicable

2.2. Condition:

Prevention of influenza infection

2.2.1. Indication(s) targeted by the PIP

Post-exposure prophylaxis

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)

Film-coated tablet

Granules in sachets

2.2.4. Measures

Area	Description
Quality-related studies	Not applicable
Non-clinical studies	Not applicable
Clinical studies	**Study 13** Randomised, double-blind, multicenter, parallel-group, placebo-controlled comparative study to evaluate the efficacy and safety of a single oral dose of baloxavir marboxil in the prevention of influenza virus infection in paediatric subjects from birth to less than 18 years of age who are household members of influenza-infected index patients.
Extrapolation, modelling and simulation studies	Not applicable
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 December 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. Treatment of influenza infection

Authorised indication(s):

- Treatment of uncomplicated influenza in patients aged 12 years and above.
  - Invented name(s): Xofluza
  - Authorised pharmaceutical form(s): Film-coated tablet
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure

2. Prevention of influenza infection

Authorised indication(s):

- Post-exposure prophylaxis of influenza in individuals aged 12 years and above.
  - Invented name(s): Xofluza
  - Authorised pharmaceutical form(s): Film-coated tablet
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure