

EMA/709120/2022

European Medicines Agency decision P/0383/2022

of 9 September 2022

on the acceptance of a modification of an agreed paediatric investigation plan for baloxavir marboxil (Xofluza), (EMEA-002440-PIP01-18-M03) 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 726/2004¹,

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 Agency²,

Having regard to the European Medicines Agency's decision P/0300/2019 issued on 2 September 2019, the decision P/0029/2021 issued on 29 January 2021 and the decision P/0486/2021 issued on 3 December 2021,

Having regard to the application submitted by Roche Registration GmbH on 13 April 2022 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 22 July 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 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/254250/2022
Amsterdam, 22 July 2022

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMA-002440-PIP01-18-M03

Scope of the application

Active substance(s):

Baloxavir marboxil

Invented name:

Xofluza

Condition(s):

Treatment of influenza infection

Prevention of influenza infection

Authorised indication(s):

See Annex II

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

Information about the authorised medicinal product:

See Annex II

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 13 April 2022 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 and the decision P/0486/2021 issued on 3 December 2021.

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

The procedure started on 23 May 2022.

Scope of the modification

Some timelines 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 and to the deferral 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 is removed with the current 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 is removed with the current 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 is removed with the current procedure EMEA-002440-PIP01-18-M01. Study 9 is removed with the current 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 is removed with the current procedure EMEA-002440-PIP01-18-M01.
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 for oral suspension

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

Condition(s) and authorised indication(s):

1. Treatment of influenza infection

Authorised indication(s):

- Xofluza is indicated for the treatment of uncomplicated influenza in patients aged 12 years and above.

2. Prevention of influenza infection

Authorised indication(s):

- Xofluza is indicated for for post-exposure prophylaxis of influenza in individuals aged 12 years and above.

Authorised pharmaceutical form(s):

Film-coated tablets

Authorised route(s) of administration:

Oral use