EMA/440018/2019

European Medicines Agency decision

P/0300/2019

of 2 September 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral for baloxavir marboxil (EMEA-002440-PIP01-18) 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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Roche Registration GmbH on 26 October 2018 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 26 July 2019, 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

A paediatric investigation plan for baloxavir marboxil, film-coated tablet, granules for oral suspension, oral 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 baloxavir marboxil, film-coated tablet, granules for oral suspension, oral 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 Roche Registration GmbH, Emil-Barell-Strasse 1, 79639 - Grenzach-Wyhlen, Germany.

EMA/PDCO/237497/2019 Corr
Amsterdam, 26 July 2019

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

EMEA-002440-PIP01-18

Scope of the application

Active substance(s):

Baloxavir marboxil

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 16(1) of Regulation (EC) No 1901/2006 as amended, Roche Registration GmbH submitted for agreement to the European Medicines Agency on 26 October 2018 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 4 December 2018.

Supplementary information was provided by the applicant on 16 April 2019. 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 Norwegian Paediatric Committee member 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 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 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	**Number of measures**	**Description**
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	4	**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 (Hospitalised Paediatrics) Multicenter, single-arm, open-label study to assess the single and multiple dose pharmacokinetics and safety of baloxavir marboxil in combination with a standard of care neuraminidase inhibitor (SOC NAI) in paediatric patients from birth to less than 18 years of age who are hospitalised for severe influenza and present within 96 hours of symptom onset.
Extrapolation, modelling and simulation studies	8	**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** (M&S Study 2) Population PK model in adult, adolescent and paediatric hospitalised population. Linear population PK model accounting for relevant demographic covariates that may influence systemic drug exposure. **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** (M&S Study 4) Modelling and simulation study in Hospitalised Adult and Adolescent patients evaluating exposure-response using viral kinetic modelling and primary efficacy endpoints PK-Viral kinetic modelling. **Study 9** (M&S Study 5) Physiologically based PK (PBPK) model for baloxavir. **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** (Extrapolation study 3) Extrapolation of PK, PD (virology, virus titres) and efficacy (primary endpoint, time to symptom alleviation) in hospitalised paediatric patients from birth to less than 12 years of age.
Other studies	0	Not applicable.
Other measures	0	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	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	1	**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	0	Not applicable.
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 July 2029
Deferral for one or more measures contained in the paediatric investigation plan:	Yes