MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral.

MHRA-100195-PIP01-21-M03

Scope of the Application

Active Substance(s)

BALOXAVIR MARBOXIL

Condition(s)

Treatment of Influenza, Prevention of Influenza

Pharmaceutical Form(s)

Film-coated tablet, Granules for oral suspension

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Roche Products Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Roche Products Limited submitted to the licensing authority on 07/02/2023 15:40 GMT an application for a Modification

The procedure started on 15/06/2023 07:59 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral.

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-100195-PIP01-21-M03

Of 26/06/2023 13:21 BST

On the adopted decision for BALOXAVIR MARBOXIL (MHRA-100195-PIP01-21-M03) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan).

This decision applies to a Modification for BALOXAVIR MARBOXIL, Film-coated tablet, Granules for oral suspension , ORAL USE .

This decision is addressed to Roche Products Limited, 6 Falcon Way, Shire Park,, Welwyn Garden City, UNITED KINGDOM, AL7 1TW

ANNEX I

1. Waiver

1.1 Condition:

Not applicable for the Treatment of influenza. 1.2 Condition Not applicable for the Prevention of influenza.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of influenza. Prevention of influenza

2.2 Indication(s) targeted by the PIP:

Treatment of influenza. Post-exposure prophylaxis of influenza.

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from birth to less than 18 years of age. The paediatric population from birth to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Film-coated tablet Granules for oral suspension

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	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, multicentre 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 hospitalisation for severe influenza, or who contract severe influenza during hospitalisation (and adults). Study 4 This study was removed during procedure EMEA-002440-PIP01-18-M01. Study 13 Randomised, double-blind, multicentre, 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, Modeling & Simulation Studies	4	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 This study was removed during 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 This study was removed during procedure EMEA-002440-PIP01-18-M01. Study 9 This study was removed during 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 This study was removed during procedure EMEA-002440-PIP01-18-M01. Study 14 (Extrapolation study 3) (This study was added during procedure MHRA-100195-PIP01-21-M03.) Extrapolation of efficacy based on PK-exposure matching from adults and adolescents to children from birth to less than 12 years of age to support the development of a weight-based bracket dosing.

Other Studies	0	Not applicable.
Other Measures	0	Not applicable.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	31/12/2024
Deferral of one or more studies contained in the paediatric investigation plan:	Yes