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 (MHRA-100111-PIP01-21) and to the deferral

MHRA-100111-PIP01-21-M01

Scope of the Application

Active Substance(s)

ISLATRAVIR; DORAVIRINE

Condition(s)

Treatment of human immunodeficiency virus-1 (HIV-1) infection

Pharmaceutical Form(s)

Film-coated tablet; Age appropriate solid dosage form (Granules for oral suspension)

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Merck Sharp & Dohme (UK) Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Merck Sharp & Dohme (UK) Limited submitted to the licensing authority on 27/06/2024 15:26 BST an application for a Modification

The procedure started on 03/09/2024 08:29 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-100111-PIP01-21-M01

Of 24/09/2024 14:29 BST

On the adopted decision for ISLATRAVIR; DORAVIRINE (MHRA-100111-PIP01-21-M01) 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 ISLATRAVIR; DORAVIRINE, Film-coated tablet; Age appropriate solid dosage form (Granules for oral suspension) , ORAL USE .

This decision is addressed to Merck Sharp & Dohme (UK) Limited, 120 Moorgate, London, UNITED KINGDOM, EC2M 6UR

ANNEX I

1. Waiver

1.1 Condition:

Treatment of human immunodeficiency virus-1 (HIV-1) infection. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 28 days of age Pharmaceutical form(s): Tablet Age appropriate solid dosage form (Granules for oral suspension) Route(s) of administration: Oral use Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of human immunodeficiency virus-1 (HIV-1) infection.

2.2 Indication(s) targeted by the PIP:

Treatment of human immunodeficiency virus-1 (HIV-1) infection.

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

The paediatric population from 28 days old to less than 18 years of age

2.4 Pharmaceutical Form(s):

Tablet Age appropriate solid dosage form (Granules for oral suspension)

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an age appropriate oral solid dosage form.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	2	Study 2 (P028) Open label uncontrolled study to evaluate islatravir (MK-8591) PK and the safety and efficacy of doravirine/ islatravir (DOR/ISL) in paediatric participants with HIV-1 infection who are less than 18 years of age and weigh $\geq$35 kg. Study 3 Open label uncontrolled pharmacokinetic (PK), safety and activity study of the fixed dose combination of DOR/ ISL (age appropriate formulation) for paediatric subjects who are at least 28 days of age and weigh less than 35 kg. Study 6 Study added during MHRA-100111-PIP01-21-M01 Open label uncontrolled study to evaluate the pharmacokinetics of islatravir and the safety and antiviral activity of doravirine/islatravir in paediatric patients with HIV-1 infection, who are virologically suppressed (defined as HIV-1 RNA less than 50 copies/ mL) for at least 3 months prior to the screening visit on a stable anti-retroviral (ARV) regimen, without history of virologic failure, and without evidence of resistance to the

		individual components of the fixed-dose combination (FDC).
Extrapolation, Modeling & Simulation Studies	2	Study 4 Modelling and simulation study to support islatravir dose finding in paediatric participants less than 18 years of age and weighing at least 35kg. Study 5 Modelling and simulation study to support islatravir dose finding in paediatric participants who are at least 28 days of age and weigh less than 35 kg.
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:	Yes
Date of completion of the paediatric investigation plan:	31/12/2029
Deferral of one or more studies contained in the paediatric investigation plan:	Yes