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-100094-PIP01-21-M01

Scope of the Application

Active Substance(s)

DORAVIRINE; LAMIVUDINE; TENOFOVIR DISOPROXIL FUMARATE

Condition(s)

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

Pharmaceutical Form(s)

Tablets; Granules

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

Merck Sharp and Dohme (UK) Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Merck Sharp and Dohme (UK) Limited submitted to the licensing authority on 14/04/2021 11:38 BST an application for a Modification

The procedure started on 22/10/2021 16:36 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-100094-PIP01-21-M01

Of 03/11/2021 12:11 GMT

On the adopted decision for DORAVIRINE; LAMIVUDINE; TENOFOVIR DISOPROXIL FUMARATE (MHRA-100094-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 DORAVIRINE; LAMIVUDINE; TENOFOVIR DISOPROXIL FUMARATE, Tablets; Granules , Oral use .

This decision is addressed to Merck Sharp and 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): All subsets of the paediatric population from birth to less than 6 years of age for the granules, oral use All subsets of the paediatric population from birth to less than 12 years of age and weighing less than 35 kg for the tablet, oral use Pharmaceutical form(s): Tablets; Granules 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:

Antiretroviral combination therapy, for the treatment of HIV-1 infection in adults and in children aged 6 years to less than 18 years of age

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

The paediatric population from 6 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Tablets; Granules

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an age appropriate oral solid dosage form for the fixed dose combination doravirine / lamivudine / tenofovir (disoproxil fumarate)
Non-Clinical Studies	2	Study 2 Dose range-finding juvenile toxicity study Study 3 Definitive juvenile toxicity study.
Clinical Studies	2	Study 4 Open-label two periods trial to evaluate pharmacokinetic, safety, and activity, of doravirine and doravirine fixed dose combination (FDC) with lamivudine and tenofovir disoproxil fumarate in HIV-1 infected adolescents from 12 to less than 18 years of age weighing at least 35 kg. Study 5 Open-label pharmacokinetic with sentinel cohort, safety, and activity study of doravirine in HIV-1 paediatric patients who are at least 4 weeks and less than 12 years of age. Study 6 Study deleted in MHRA-100094-PIP01-21-M01 Study 7 Study deleted in MHRA-100094-PIP01-21-M01 Study 8 Study deleted in MHRA-100094-PIP01-21-M01 Study 9 Study deleted in MHRA-100094-PIP01-21-M01
Extrapolation, Modeling & Simulation Studies	1	Study 10 Modelling and simulation and

		extrapolation study of the use of doravirine in paediatric patients from birth to less than 18 years of age and of the use of FDC of DOR/3TC/TDF in children from 6 years to less than 18 years of age.
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:	31/01/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes