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-100300-PIP01-21-M02) and to the deferral

MHRA-100300-PIP01-21-M03

Scope of the Application

Active Substance(s)

DARUNAVIR; COBICISTAT

Condition(s)

Treatment of human immunodeficiency virus (HIV-1) infection

Pharmaceutical Form(s)

Film-coated tablet, Dispersible tablet

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Jannsen Cilag-Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Jannsen Cilag-Limited submitted to the licensing authority on 07/08/2023 15:34 BST an application for a Modification

The procedure started on 29/11/2023 15:40 GMT

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-100300-PIP01-21-M03

Of 06/12/2023 18:48 GMT

On the adopted decision for DARUNAVIR; COBICISTAT (MHRA-100300-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 DARUNAVIR; COBICISTAT, Film-coated tablet, Dispersible tablet , ORAL USE .

This decision is addressed to Jannsen Cilag-Limited, 50-100 Holmers Farm Way, High Wycombe, UNITED KINGDOM, HP12 4EG

ANNEX I

1. Waiver

1.1 Condition:

Treatment of human immunodeficiency virus (HIV-1) infection. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 3 years of age. Pharmaceutical form(s): Film-coated tablet Dispersible tablet Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan:

2.1 Condition(s):

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

2.2 Indication(s) targeted by the PIP:

Treatment of human immunodeficiency virus (HIV-1) infection in paediatric patients from 3 to less than 18 years.

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

The paediatric population from 3 years to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Film-coated tablet Dispersible tablet

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	3	Study 1 Acceptability assessment of adult film-coated tablets in children from 12 to less than 18 years of age. Study 2 Development of a scored film-coated tablet for patients from 6 to less than 12 years and/or weighing at least 25 kg. Study 3 Deleted during procedure EMEA-001280-PIP01-12-M03. Study 8 Development of a dispersible tablet for children from 3 years of age and older and weighing 15 to < 25 kg with acceptability assessments. Added during procedure EMEA-001280-PIP01-12-M02.
Non-Clinical Studies	0	Not Applicable.
Clinical Studies	3	Study 4 (TMC114-228) Phase II, open-label multiple dose trial. Part I: Pharmacokinetic study to determine the recommended paediatric dose and to evaluate short-term safety, tolerability and efficacy of darunavir. Part II: To evaluate long-term safety, tolerability and efficacy of the selected paediatric dose of darunavir. Study 5 (TMC114-C230) Phase II, open-label trial to investigate pharmacokinetics, long-term safety, tolerability and antiviral activity of the selected adult dose of darunavir in treatment-naïve HIV-1 infected

		adolescents from 12 years to less than 18 years of age. Study 6 (GS-US-216-0128) Open-label trial to evaluate pharmacokinetics, safety, and efficacy of once daily cobicistat-boosted darunavir administered as part of a combined antiretroviral regimen in HIV-1 infected treatment experienced children from 3 years to less than 18 years of age.
Extrapolation, Modeling & Simulation Studies	1	Study 7 (TMC114-C0000013) Extrapolation of pharmacokinetic, safety and efficacy data on darunavir and cobicistat from studies including at least TMC114-228, TMC114-C230 and GS-US-216-0128 (measures 4, 5 and 6) to children from 3 years to less than 18 years of age for darunavir/cobicistat fixed dose combination for treatment of HIV-1 infection.
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:	31/03/2025
Deferral of one or more studies contained in the paediatric investigation plan:	Yes