MHRA
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Canary Wharf
London
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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-100676-PIP01-22-M01

Scope of the Application

Active Substance(s)

EMTRICITABINE; TENOFOVIR ALAFENAMIDE FUMARATE

Condition(s)

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

Pharmaceutical Form(s)

Film-coated tablet; Age-appropriate oral formulation

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Gilead Sciences Ltd.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Gilead Sciences Ltd. submitted to the licensing authority on 14/09/2022 11:24 BST an application for a Modification

The procedure started on 21/02/2023 09:57 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-100676-PIP01-22-M01

Of 31/05/2023 14:59 BST

On the adopted decision for EMTRICITABINE; TENOFOVIR ALAFENAMIDE FUMARATE (MHRA-100676-PIP01-22-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 EMTRICITABINE; TENOFOVIR ALAFENAMIDE FUMARATE, Film-coated tablet; Age-appropriate oral formulation , ORAL USE .

This decision is addressed to Gilead Sciences Ltd., 280 High Holborn, London, UNITED KINGDOM, WC1V7EE

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 4 weeks of age Pharmaceutical form(s): Film-coated tablet Age-appropriate oral formulation Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subset(s).

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) infected paediatric patients in combination with other antiretroviral (ARV) agents

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

The paediatric population from 4 weeks to less than 18 years of age

2.4 Pharmaceutical Form(s):

Film-coated tablet Age-appropriate oral formulation

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	Study 1 Development of film-coated tablets for use in children weighing 14 to less than 25 kg. Study 2 Development of an age-appropriate oral formulation for use in children from 4 weeks and weighing $\geq$ 3kg to less than 14 kg of weight, and in children from 14 to less than 25 kg of weight unable to swallow tablets.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	3	Study 3 (GS-US-311-1269) Open-label, uncontrolled trial to evaluate pharmacokinetics (PK), safety, tolerability and efficacy of emtricitabine /tenofovir alafenamide (F/TAF) fixed-dose combination (FDC) in children from 2 years to less than 18 years of age with HIV-1 infection, who are virologically suppressed on an antiretroviral (ARV) regimen or treatment-naïve. Study 4 deleted in EMEA-001577-PIP02-14-M03. Study 5 deleted in EMEA-001577-PIP02-14-M04. Study 8 (GU-US-292-0106) (This study is the same as study 2 of the elvitegravir / cobicistat / emtricitabine / tenofovir alafenamide PIP EMEA-001460-PIP01-13-M01 and subsequent modifications

		thereof). Open-label, multicentre, two-part, single-arm trial to evaluate the pharmacokinetics (PK), safety, tolerability, and antiviral activity of the elvitegravir/ cobicistat / emtricitabine/tenofovir alafenamide single tablet regimen (E/C/F/TAF STR) in HIV-1 infected antiretroviral treatment-naïve, adolescents (from 12 to less than 18 years of age) and virologically suppressed children (from 6 to less than 12 years of age). Study 9 (GU-US-216-0128) (Added in MHRA-100676-PIP01-22-M01. This is the same as study 4 of the cobicistat PIP MHRA-100677-PIP01-22-M01 and subsequent modifications thereof.) Open-label trial to evaluate pharmacokinetics (PK), safety, and efficacy of cobicistat-boosted protease inhibitors and once daily emtricitabine /tenofovir alafenamide each administered as part of a combined ARV regimen in HIV-1 infected children from 4 weeks to less than 18 years of age.
Extrapolation, Modeling & Simulation Studies	2	Study 6 Population PK model of the use of the F/TAF FDC in combination with boosted or unboosted third antiretroviral agents in children from 4 weeks to less than 18 years of age. Study 7 Extrapolation study to support the use of the F/TAF FDC in combination with boosted or unboosted third antiretroviral agents in children from 4 weeks to less than 18 years.
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:	31/01/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes