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-100076-PIP01-21-M01

Scope of the Application

Active Substance(s)

TENOFOVIR DISOPROXIL FUMARATE

Condition(s)

Treatment of human immunodeficiency virus (HIV-1) infection, Treatment of chronic viral hepatitis B

Pharmaceutical Form(s)

Film-coated tablet, Granules

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 26/03/2021 21:33 GMT an application for a

The procedure started on 25/11/2021 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-100076-PIP01-21-M01

Of 03/12/2021 18:04 GMT

On the adopted decision for TENOFOVIR DISOPROXIL FUMARATE (MHRA-100076-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 for TENOFOVIR DISOPROXIL FUMARATE, Film-coated tablet, Granules , Oral use .

This decision is addressed to Gilead Sciences Ltd, 280 High Holborn, London, United Kingdom, WC1V 7EE

ANNEX I

1. Waiver

1.1 Condition:

Treatment of human immunodeficiency virus (HIV-1) infection; Treatment of chronic viral hepatitis B The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Film-coated tablet; Granules 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):

1. Treatment of human immunodeficiency virus (HIV-1) infection; 2. Treatment of chronic viral hepatitis B

2.2 Indication(s) targeted by the PIP:

1. In combination with other antiretroviral medicinal products for the treatment of HIV 1 infection in antiretroviral treatment experienced paediatric patients; 2. For treatment of chronic hepatitis B in paediatric patients from 2 years of age with compensated liver disease.

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

For both conditions: All subsets of the paediatric population from 2 years to less than 18 years of age

2.4 Pharmaceutical Form(s):

Film-coated tablet; Granules

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: GS-US-104-0321 Double-Blind, Placebo Controlled Study of the Safety and Efficacy of Tenofovir DF as Part of an Optimized Antiretroviral Regimen in HIV 1 Infected Adolescents. Study 2: GS-US- 104-0352 Randomized, Open Label Study Comparing the Safety and Efficacy of Switching Stavudine or Zidovudine to Tenofovir Disoproxil Fumarate versus Continuing Stavudine or Zidovudine in Virologically Suppressed HIV-Infected Children Taking Highly Active Antiretroviral Therapy. Study 3: Deleted in procedure EMEA-000533-PIP01-08-M07 Study 4: GS-US-174-0115. A Randomized, Double-Blind Evaluation of the Antiviral Efficacy, Safety, and Tolerability of Tenofovir Disoproxil Fumarate Versus Placebo in Adolescents with Chronic Hepatitis B Infection. Study 5: A safety and efficacy or pharmacokinetic study of

		tenofovir DF in children aged 2 to < 12 years with chronic HBV infection. Study 6: Deleted in procedure MHRA-100076-PIP01-21-M01
Extrapolation, Modeling & Simulation Studies	0	Not applicable
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:	30/06/2020
Deferral of one or more studies contained in the paediatric investigation plan:	Yes