**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-100440-PIP01-22-M02) and to the deferral

MHRA-100440-PIP01-22-M03

# Scope of the Application

## Active Substance(s)

EMTRICITABINE; BICTEGRAVIR; TENOFOVIR ALAFENAMIDE

## 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 27/09/2024 18:07 BST an application for a Modification

The procedure started on 05/11/2024 08:35 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-100440-PIP01-22-M03

Of 13/02/2025 17:48 GMT

On the adopted decision for EMTRICITABINE; BICTEGRAVIR; TENOFOVIR ALAFENAMIDE (MHRA-100440-PIP01-22-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 EMTRICITABINE; BICTEGRAVIR; TENOFOVIR ALAFENAMIDE, 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) infection in paediatric patients without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

## 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 of lower strength appropriate for use in children at least 2 years of age and weighing from 14 to less than 25 kg. Study 2 Development of an age-appropriate oral formulation for use in children at least 4 weeks of age and weighing from 3 to less than 14 kg, and in children weighing less than 25 kg unable to swallow tablets. |
| **Non-Clinical Studies** | 1 | Study 3 (TX-141-2045) Prenatal and postnatal reproductive toxicity study of bictegravir (BIC 2; GS-9883) in rats. Study 4 deleted in procedure EMEA-001766-PIP01-15-M01. |
| **Clinical Studies** | 2 | Study 5 (GS-US-380-1474) Single arm, two-part study to evaluate the pharmacokinetics (part A), safety, tolerability and efficacy (part B) of the bictegravir/emtricitabine/ tenofovir alafenamide (B/F/TAF) fixed-dose combination (FDC) in HIV-1 infected, virologically suppressed adolescents and children down to 2 years of age and weighing at least 14 kg and in infants down to 4 weeks of age and weighing at least 3 kg who have been on an antiretroviral (ARV) regimen at |

| | | |
|---|---|---|
| | | least 1 months prior to screening or are treatment naïve. Study 6 Study deleted in procedure EMEA-001766-PIP01-15-M02. Study 7 (GS-US-380-4547) Open-label, randomised study in healthy adult volunteers to determine the bioavailability of the age-appropriate oral formulation developed in Study 2 relative to the adult film-coated tablet. |
| **Extrapolation, Modeling & Simulation Studies** | 1 | Study 8 Modelling and Simulation study to support dose finding and the extrapolation of use of the B/F/TAF FDC in children from 4 weeks to less than 18 years of age who are infected with HIV-1. Study 9 Study deleted in procedure EMEA-001766-PIP01-15-M02. |
| **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:** | 31/03/2026 |
| **Deferral of one or more studies contained in the paediatric investigation plan:** | Yes |