**MHRA**
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

**gov.uk/mhra**

# Decision Cover Letter

## Decision of the licensing authority to:

accept of change(s) to the agreed paediatric investigation plan (MHRA-100062-PIP01-21)

MHRA-100062-PIP01-21-M01

# Scope of the Application

## Active Substance(s)

VANZACAFTOR CALCIUM DIHYDRATE; TEZACAFTOR; DEUTIVACAFTOR

## Condition(s)

Treatment of cystic fibrosis

## Pharmaceutical Form(s)

Film-coated tablet; Age-appropriate oral solid dosage form

## Route(s) of Administration

ORAL USE

## Name / Corporate name of the PIP applicant

Vertex Pharmaceuticals Incorporated

## Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Vertex Pharmaceuticals Incorporated submitted to the licensing authority on 16/03/2026 14:19 GMT an application for a Modification

The procedure started on 30/03/2026 09:40 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

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-100062-PIP01-21-M01

Of 03/07/2026 07:45 BST

On the adopted decision for VANZACAFTOR CALCIUM DIHYDRATE; TEZACAFTOR; DEUTIVACAFTOR (MHRA-100062-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 VANZACAFTOR CALCIUM DIHYDRATE; TEZACAFTOR; DEUTIVACAFTOR, Film-coated tablet; Age-appropriate oral solid dosage form , ORAL USE .

This decision is addressed to Vertex Pharmaceuticals Incorporated, 2 Kingdom Street, Paddington, UNITED KINGDOM, W2 6BD

## ANNEX I

### 1. Waiver

### 1.1 Condition:

| |
|---|
| Treatment of cystic fibrosis The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Film-coated tablet Age-appropriate oral solid dosage form 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 cystic fibrosis |

## 2.2 Indication(s) targeted by the PIP:

| |
|---|
| Treatment of cystic fibrosis |

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

| |
|---|
| The paediatric population from 1 year to less than 18 years of age |

## 2.4 Pharmaceutical Form(s):

| |
|---|
| Film-coated tablet Age-appropriate oral solid dosage form |

## 2.5 Studies:

| Study Type | Number of Studies | Study Description |
|---|---|---|
| **Quality Measures** | 2 | Study 1 (Study Q-1) Development of an age-appropriate oral formulation for children from 1 year to less than 6 years of age. Study 2 (Study Q-2) Development of a fixed dose combination (FDC) film coated tablet with lower strength for all 3 active components (VX-121, TEZ, and D-IVA), and with a maximum dimension of 14 mm, for children aged from 6 years to less than 12 years of age. |
| **Non-Clinical Studies** | 1 | Study 3 (Study N-1) Definitive toxicity and toxicokinetic study in juvenile rats to support clinical evaluation of VX-121/TEZ/D-IVA in children from 1 year to less than 6 years of age with cystic fibrosis (CF). |
| **Clinical Studies** | 4 | Study 4 (Study C-1) Randomised, double-blind, controlled study to assess the efficacy and safety of the fixed-dose combination (FDC) of VX-121/TEZ/D-IVA in adolescents from 12 years to less than 18 years of age (and adults) with cystic fibrosis (CF) who are heterozygous for F508del and a CTFR mutation of minimal function (F/MF genotype). Study 5 (Study C-2) Randomised, double-blind, controlled study to assess the efficacy and safety of the |

| | | |
|---|---|---|
| | | fixed-dose combination (FDC) of VX-121/TEZ/D-IVA in adolescents from 12 years to less than 18 years of age (and adults) with cystic fibrosis (CF) who are homozygous for F508del (F/F genotype) or have other F508del-anchored genotypes with responsive alleles. Study 6 (Study C-3) Rollover, open-label, long-term safety study of VX-121/TEZ/ D-IVA in children from 12 years to less than 18 years of age (and adults). Study 7(Study C-4) Two-part, single-arm, study to evaluate the safety and pharmacokinetics (PK) of VX-121/ TEZ/D-IVA in children from 1 year to less than 12 years of age with CF who have at least one F508del allele. |
| **Extrapolation, Modeling & Simulation Studies** | 2 | Study 8 (Study M-1) Modelling and simulation study for dose selection in children from 1 year to less than 12 years of age. Study 9 (Study E-1) Modelling and simulation study of efficacy and pharmacodynamics endpoints in children from 1 year to less than 12 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:** | Yes |
| **Date of completion of the paediatric investigation plan:** | 31/12/2030 |
| **Deferral of one or more studies contained in the paediatric investigation plan:** | Yes |