MHRA
10 South Colonnade
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 (MHRA-100075-PIP01-21-M02) and to the deferral

MHRA-100075-PIP01-21-M03

Scope of the Application

Active Substance(s)

leniolisib

Condition(s)

Treatment of activated phosphoinositide 3-kinase delta (#) syndrome (APDS)

Pharmaceutical Form(s)

Film-coated tablet, Capsule, hard, Granules

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Pharming Technologies B.V.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Pharming Technologies B.V. submitted to the licensing authority on 06/02/2025 20:49 GMT an application for a Modification

The procedure started on 05/03/2025 17:39 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-100075-PIP01-21-M03

Of 13/06/2025 17:08 BST

On the adopted decision for leniolisib (MHRA-100075-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 leniolisib, Film-coated tablet, Capsule, hard, Granules , ORAL USE .

This decision is addressed to Pharming Technologies B.V., Darwinweg 24, Leiden, NETHERLANDS, 2333 CR

ANNEX I

1. Waiver

1.1 Condition:

Treatment of activated phosphoinositide 3-kinase delta (#) syndrome (APDS) 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 Capsule, hard Granules 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 activated phosphoinositide 3-kinase delta (#) syndrome (APDS)

2.2 Indication(s) targeted by the PIP:

Treatment of activated phosphoinositide 3-kinase delta (#) syndrome (APDS)

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 Capsule, hard Granules

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 (PIPLform) Development of an oral age- appropriate formulation.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	5	Study 2 (CCDZ173X2201 -part II) Double-blind, randomised, assessor-blind, placebo-controlled trial to evaluate safety and efficacy of leniolisib compared to placebo in children from 12 years to less than 18 years of age (and adults) with documented activated phosphoinositide 3-kinase delta syndrome (APDS). Study 3 (CCDZ173X2201 - part I) Open label, single arm, dose-finding trial to evaluate pharmacokinetics, safety, activity of leniolisib in children from 12 years to less than 18 years of age (and adults) with documented APDS. Study 4 (CCDZ173X2201E1) Open-label, long term safety and tolerability trial of leniolisib in children from 12 years to less than 18 years of age (and adults) who participated in study CCDZ173X2201 part I or II. Study 5 (PIPCL1) Open-label, single arm, two-part trial to evaluate pharmacokinetics, safety and efficacy of leniolisib in children from 4 years to less than 12 years

		of age with documented APDS. Study 6 (PIPCL2) Open-label, single arm, two-part trial to evaluate pharmacokinetics, safety and efficacy of leniolisib in children from 1 year to less than 7 years of age with documented APDS.
Extrapolation, Modeling & Simulation Studies	1	Study 7 (PIPLMS) Modelling and simulation study to support the use of leniolisib in paediatric patients from 1 year to less than 18 years of age with documented APDS.
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:	30/09/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes