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-100450-PIP01-22-M01

Scope of the Application

Active Substance(s)

ALPELISIB

Condition(s)

PIK3CA Related Overgrowth Spectrum (PROS)

Pharmaceutical Form(s)

Film-coated tablet, Granules

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

NOVARTIS PHARMACEUTICALS UK LTD

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, NOVARTIS PHARMACEUTICALS UK LTD submitted to the licensing authority on 28/02/2022 23:30 GMT an application for a Modification

The procedure started on 12/04/2022 15:43 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 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-100450-PIP01-22-M01

Of 22/04/2022 12:25 BST

On the adopted decision for ALPELISIB (MHRA-100450-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 ALPELISIB, Film-coated tablet, Granules , Oral use .

This decision is addressed to NOVARTIS PHARMACEUTICALS UK LTD, 2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane,, London, United Kingdom, W12 7FQ

ANNEX I

1. Waiver

1.1 Condition:

Treatment of (Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Subunit Alpha) PIK3CA related overgrowth spectrum. 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):

Treatment of PIK3CA Related Overgrowth Spectrum (PROS)

2.2 Indication(s) targeted by the PIP:

Treatment of PIK3CA Related Overgrowth Spectrum (PROS)

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

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	1	Study 1 Development of granules for the paediatric population from 2 to less than 6 years of age and for those not able to use the film-coated tablets.
Non-Clinical Studies	0	Not applicable
Clinical Studies	1	Study 2 Efficacy, safety and pharmacokinetics double-blind randomised, placebo-controlled study of alpelisib in (adults and) paediatric patients from 2 to less than 18 years of age with PROS.
Extrapolation, Modeling & Simulation Studies	1	Study 3 Modelling and simulation study for establishing the appropriate dose of alpelisib of granule formulation in paediatric patients from 2 to less than 6 years of age.
Other Studies	1	Study 4 Site-based retrospective, non-interventional chart review study of paediatric (and adult) male and female patients with PIK3CA related overgrowth spectrum (PROS) to assess changes in clinical and functional outcomes as well as safety in patients with PROS treated with alpelisib.
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:	31/12/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes