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

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan

MHRA-100716-PIP01-22-M01

Scope of the Application

Active Substance(s)

RUXOLITINIB PHOSPHATE

Condition(s)

Treatment of chronic Graft versus Host Disease

Pharmaceutical Form(s)

TABLET; AGE-APPROPRIATE ORAL DOSAGE FORM

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 11/10/2022 12:28 BST an application for a Modification

The procedure started on 10/01/2023 08:46 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

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.

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

gov.uk/mhra

Final Decision Letter

MHRA-100716-PIP01-22-M01

Of 20/01/2023 07:29 GMT

On the adopted decision for RUXOLITINIB PHOSPHATE (MHRA-100716-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 RUXOLITINIB PHOSPHATE, TABLET; AGE-APPROPRIATE ORAL DOSAGE FORM , 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 chronic Graft versus Host Disease The waiver applies / applied to: Paediatric Subset(s): Newborn infants (from birth to less than 28 days) Pharmaceutical form(s): TABLET AGE-APPROPRIATE ORAL DOSAGE FORM Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of chronic Graft versus Host Disease

2.2 Indication(s) targeted by the PIP:

Treatment of chronic Graft versus Host disease (cGvHD) after allogeneic haematopoietic stem cell transplantation (HSCT).

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

The paediatric population from 28 days to less than 18 years of age

2.4 Pharmaceutical Form(s):

TABLET AGE-APPROPRIATE ORAL DOSAGE FORM

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	(This is the same as study 1 of the ruxolitinib PIP MHRA-100496-PIP01-22-M01 and subsequent modifications thereof) Study 1 Development of an age-appropriate oral dosage form.
Non-Clinical Studies	1	(This is the same as study 2 of the ruxolitinib PIP MHRA-100496-PIP01-22-M01 and subsequent modifications thereof) Study 2 Definitive juvenile toxicity study in rats.
Clinical Studies	2	Study 3 (INC424 D2301) Open-label, randomised, active-controlled trial to evaluate pharmacokinetics, safety and efficacy of ruxolitinib compared to best available therapy (BAT) in adults and adolescents from 12 to less than 18 years of age with corticosteroid-refractory (SR) cGvHD following allogeneic HSCT. Study 4 (INC424G12201) Open-label uncontrolled trial to evaluate pharmacokinetics, safety and activity of ruxolitinib in children from 28 days to less than 18 years of age with moderate or severe treatment-naïve or SR-cGvHD following allogeneic HSCT.

Extrapolation, Modeling & Simulation Studies	3	Study 5 Population PK (PopPK) modelling and simulation study to support the use of ruxolitinib for the treatment of cGvHD in children from 28 days to less than 18 years of age with treatment-naïve or SR-cGvHD following allogeneic HSCT. Study 6 Physiologically based PK (PBPK) modelling and simulation study to support the use of ruxolitinib for the treatment of cGvHD in children from 28 days to less than 18 years of age with treatment naïve or SR-cGvHD following allogeneic HSCT. Study 7 Extrapolation study to support the use of ruxolitinib for the treatment of cGvHD in children from 28 days to less than 18 years of age with treatment-naïve or SR-cGvHD following allogeneic HSCT.
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:	31/08/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes