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

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan, grant a deferral and grant a waiver.

MHRA-100019-PIP01-21

Scope of the Application

Active Substance(s)

2-(3-(4-(1H-INDAZOL-5-YLAMINO)QUINAZOLIN-2-YL)PHENOXY)-N-ISOPROPYLACETAMIDE-METHANE SULFONIC ACID SALT

Condition(s)

Treatment of chronic Graft versus Host Disease (cGVHD)

Pharmaceutical Form(s)

Film-coated tablet

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

Kadmon International, Ltd.

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Kadmon International, Ltd. submitted to the licensing authority on 18/01/2021 14:51 GMT an application for a Paediatric Investigation Plan

The procedure started on 03/02/2021 09:58 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 agree a paediatric investigation plan, grant a deferral and grant a waiver.

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-100019-PIP01-21

Of 09/04/2021 15:56 BST

On the adopted decision for 2-(3-(4-(1H-INDAZOL-5-YLAMINO)QUINAZOLIN-2-YL)PHENOXY)-N-ISOPROPYLACETAMIDE-METHANE SULFONIC ACID SALT (MHRA-100019-PIP01-21) 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 a paediatric investigation plan.

This decision applies to a Paediatric Investigation Plan for 2-(3-(4-(1H-INDAZOL-5-YLAMINO)QUINAZOLIN-2-YL)PHENOXY)-N-ISOPROPYLACETAMIDE-METHANE SULFONIC ACID SALT, Film-coated tablet , Oral use .

This decision is addressed to Kadmon International, Ltd., Suite A, 6 Honduras Street, London, United Kingdom, EC1Y 0TH

ANNEX I

1. Waiver

1.1 Condition:

Treatment of chronic Graft versus Host Disease (cGVHD) The waiver applies to Paediatric Subsets: •Preterm newborn infants •Term newborn infants (from birth to less than 28 days) •Children (from 28 days old to less than 3 months old. Pharmaceutical form(s): Film-coated tablet 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 (cGVHD)

2.2 Indication(s) targeted by the PIP:

Belumosudil is indicated for the treatment of children with cGVHD after failure of at least one prior line of systemic therapy.

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

•Children (from 3 months to less than 12 years) •Adolescents (from 12 to less than 18 years)

2.4 Pharmaceutical Form(s):

Film-coated tablet

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	Study 1 Development of an age-appropriate dosage form. Study 2 Generation of data on dose delivery devices, stability and compatibility with different routes of administration
Non-Clinical Studies	2	Study 3 Dose range-finding juvenile toxicity study in Sprague-dawley rats. Study 4 Definitive juvenile toxicity study in Sprague-dawley rats.
Clinical Studies	2	Study 5 Open label, randomised, multi-centre study to evaluate the efficacy, safety and pharmacokinetics of belumosudil in adolescent subjects with Chronic Graft Versus Host Disease (cGVHD) Study 6 Dose finding, safety and effectiveness study of belumosudil in paediatric subjects with cGVHD
Extrapolation, Modeling & Simulation Studies	3	Study 7 Allometrically scaled population PK model to propose doses for paediatric patients aged over 3 months to less than 12 years. Study 8 Physiology-based pharmacokinetic (PBPK) model to support paediatric dose prediction for children in the > 3 month to less than 2-year age range. Study 9 Extrapolation study to provide efficacy assumptions in the paediatric population (from 3 months to less

		than 18 years old) using available adult and paediatric data.
Other Studies	0	Not applicable
Other Measures	1	Finalised study synopsis and design of a comparative Phase 3 clinical study

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	31/08/2026
Deferral of one or more studies contained in the paediatric investigation plan:	Yes