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 (EMEA-001585-PIP01-13-M03) and to the deferral

MHRA-101543-PIP01-24-M01

Scope of the Application

Active Substance(s)

SELUMETINIB HYDROGEN SULFATE

Condition(s)

Treatment of neurofibromatosis type 1, Treatment of thyroid cancer, Treatment of melanoma

Pharmaceutical Form(s)

Capsule, hard, Granules

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

AstraZeneca UK Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, AstraZeneca UK Limited submitted to the licensing authority on 11/07/2024 14:57 BST an application for a Modification

The procedure started on 06/09/2024 10:18 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-101543-PIP01-24-M01

Of 20/11/2024 11:06 GMT

On the adopted decision for SELUMETINIB HYDROGEN SULFATE (MHRA-101543-PIP01-24-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 SELUMETINIB HYDROGEN SULFATE, Capsule, hard, Granules , ORAL USE .

This decision is addressed to AstraZeneca UK Limited, 2 Pancras Square, 8th Floor, London, UNITED KINGDOM, N1C 4AG

ANNEX I

1. Waiver

1.1 Condition:

Condition 1: Treatment of neurofibromatosis type 1 The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Capsule, hard 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). Reason for Refusing Waiver: Not Applicable Condition 2: Treatment of thyroid cancer The waiver applies / applied to: Paediatric Subset(s): All subsets of the paediatric population from birth to less than 18 years of age Pharmaceutical form(s): Capsule, hard 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). Reason for Refusing Waiver: Not Applicable Condition 3: Treatment of melanoma The waiver applies / applied to: Paediatric Subset(s): All subsets of the paediatric population from birth to less than 18 years of age Pharmaceutical form(s): 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 ineffective.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of neurofibromatosis type 1

2.2 Indication(s) targeted by the PIP:

Treatment of neurofibromatosis type 1 (NF1) related inoperable plexiform neurofibromas in children and adolescents

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):

Capsule, hard Granules

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	2	Study 1 Development of an age-appropriate form for oral use (Q001). Study 2 Generation of data supporting the use of the hard capsule.
Non-Clinical Studies	1	Study 3 Carcinogenicity studies.
Clinical Studies	3	Study 4 (ISS62440035, part A) Single-arm, open-label, multiple-dose study to evaluate the safety, toxicity, pharmacokinetics and activity of selumetinib in paediatric patients from 3 to less than 18 years with neurofibromatosis 1 (NF1) and inoperable plexiform neurofibroma. Study 5 (ISS62440035, part B) Open-label, non-controlled, multiple-dose, multi-centre study to evaluate pharmacokinetics, pharmacodynamics, safety, acceptability and activity of selumetinib in children with from

		2 to less than 18 years (and young adults) with neurofibromatosis 1 (NF1) and inoperable, symptomatic plexiform neurofibromas. Study 6 Single-arm, open-label study to evaluate pharmacokinetics, safety, tolerability and activity of selumetinib in children from 1 to less than 7 years of age with inoperable symptomatic plexiform neurofibromas associated with neurofibromatosis 1. Study 7 Deleted in procedure EMEA-01585-PIP01-13-M01.
Extrapolation, Modeling & Simulation Studies	0	Not applicable.
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:	30/11/2024
Deferral of one or more studies contained in the paediatric investigation plan:	Yes