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-100233-PIP01-21-M01

Scope of the Application

Active Substance(s)

CABOZANTINIB

Condition(s)

Treatment of malignant solid tumours

Pharmaceutical Form(s)

Capsule, hard; Tablet; Age-appropriate formulation

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

Ipsen Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Ipsen Limited submitted to the licensing authority on 04/10/2021 11:34 BST an application for a Modification

The procedure started on 29/07/2022 14:52 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-100233-PIP01-21-M01

Of 12/08/2022 14:34 BST

On the adopted decision for CABOZANTINIB (MHRA-100233-PIP01-21-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 CABOZANTINIB, Capsule, hard; Tablet; Age-appropriate formulation , Oral use .

This decision is addressed to Ipsen Limited, 190 Bath Road, Slough, Buckinghamshire, United Kingdom, SL1 3XE , Slough, United Kingdom, SL1 3XE

ANNEX I

1. Waiver

1.1 Condition:

Not applicable.

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of malignant solid tumours

2.2 Indication(s) targeted by the PIP:

Treatment of refractory malignant solid tumours that are associated with MET, VEGFR, and/or RET pathway activation as a result of mutation, overexpression or amplification. Treatment of advanced or metastatic medullary thyroid cancer.

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

All subsets of the paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Capsule, hard; Tablet; Age-appropriate formulation

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Development of an age-appropriate formulation.
Non-Clinical Studies	2	Study 2 (XL184-NC-032) Juvenile toxicity and toxicokinetic study. Study 3 Comprehensive paediatric non-clinical efficacy testing program.
Clinical Studies	4	Study 4 (XL184-011) Open-label trial to evaluate toxicity, tolerability, pharmacokinetics and pharmacodynamics of cabozantinib in children age 2 years and above to less than 18 years of age with refractory or relapsed malignant solid tumours. Study 5 (XL184-005) Trial to evaluate relative bioavailability (in adults). Study 6 (XL184-208) Randomised, double-blind, controlled, parallel-group safety and efficacy clinical trial of cabozantinib in patients aged from birth to less than 18 years with a malignant solid tumour(s) determined based on results of studies 3 and 4. Study 7 (XL189) Open-label trial to evaluate the safety and activity of cabozantinib in children age 2 years and above to less than 18 years of age (and young adults) with a relapsed or refractory solid malignant tumour.
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:	31/01/2024
Deferral of one or more studies contained in the paediatric investigation plan:	Yes