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 (MHRA-100522-PIP01-22-M01) and to the deferral

MHRA-101167-PIP01-23-M01

Scope of the Application

Active Substance(s)

CABOZANTINIB

Condition(s)

Treatment of malignant solid tumours

Pharmaceutical Form(s)

Capsule, hard, Tablet

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Ipsen Pharma

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Ipsen Pharma submitted to the licensing authority on 01/09/2023 15:17 BST an application for a Modification

The procedure started on 04/12/2023 09:28 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 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-101167-PIP01-23-M01

Of 24/09/2024 13:07 BST

On the adopted decision for CABOZANTINIB (MHRA-101167-PIP01-23-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 , ORAL USE .

This decision is addressed to Ipsen Pharma, 65 quai George Gorse, Boulogne-Billancourt, FRANCE, 92100

ANNEX I

1. Waiver

1.1 Condition:

Treatment of malignant solid tumours The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 2 years of age Pharmaceutical form(s): Capsule, hard Tablet Route(s) of administration: ORAL USE Reason for granting waiver: on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

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. The indication 'Treatment of advanced or metastatic medullary thyroid cancer' was deleted during procedure MHRA-101167-PIP01-23-M01.

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):

Capsule, hard Tablet

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Study 1 Deleted during procedure MHRA-101167-PIP01-23-M01.
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	3	Study 4 (XL184-011) Open-label trial to evaluate toxicity, tolerability, pharmacokinetics and pharmacodynamics of cabozantinib in children aged 2 years and above to less than 18 years of age with refractory or relapsed malignant solid tumours. Study 5 (XL184-005) Deleted during procedure MHRA-101167-PIP01-23-M01. Study 6 (XL184-208) Open label, randomised controlled trial to evaluate pharmacokinetics (PK), safety and efficacy of cabozantinib as maintenance treatment add on to best supportive care (BSC) compared to BSC in patients from 5 years to less than 18 years of age (and adults) with unresectable residual osteosarcoma (OS) at diagnosis or first relapse after standard treatment. Study 7 (XL189) Open-label trial to evaluate the safety and activity of cabozantinib in children aged 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:	30/06/2023
Deferral of one or more studies contained in the paediatric investigation plan:	Yes