EMA/344395/2023

European Medicines Agency decision

P/0309/2023

of 7 August 2023

on the acceptance of a modification of an agreed paediatric investigation plan for cabozantinib (Cometriq, Cabometyx), (EMEA-001143-PIP01-11-M06) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

European Medicines Agency decision

P/0309/2023

of 7 August 2023

on the acceptance of a modification of an agreed paediatric investigation plan for cabozantinib (Cometriq, Cabometyx), (EMEA-001143-PIP01-11-M06) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0128/2012 issued on 4 July 2012, decision P/0134/2016 issued on 20 May 2016, decision P/0331/2019 issued on 11 September 2019, decision P/0282/2021 issued on 19 July 2021 and the decision P/0357/2022 issued on 11 August 2022,

Having regard to the application submitted by Ipsen Pharma on 20 March 2023 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 23 June 2023, in accordance with Article 22 of Regulation (EC) No 1901/2006 and Article 13 of said Regulation,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan and to the deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

(3) It is therefore appropriate to adopt a decision granting a waiver.

[1] OJ L 378, 27.12.2006, p.1, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for cabozantinib (Cometriq, Cabometyx), capsule, hard, film-coated tablet, oral use, including changes to the deferral, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

A waiver for cabozantinib (Cometriq, Cabometyx), capsule, hard, film-coated tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

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

EMA/PDCO/141844/2023
Amsterdam, 23 June 2023

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-001143-PIP01-11-M06

Scope of the application

Active substance(s):

Cabozantinib

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of malignant solid tumours

Pharmaceutical form(s):

Capsule, hard

Film-coated tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Ipsen Pharma

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Ipsen Pharma submitted to the European Medicines Agency on 20 March 2023 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0128/2012 issued on 4 July 2012, decision P/0134/2016 issued on 20 May 2016, decision P/0331/2019 issued on 11 September 2019, decision P/0282/2021 issued on 19 July 2021 and the decision P/0357/2022 issued on 11 August 2022.

The application for modification proposed changes to the agreed paediatric investigation plan and to the deferral and requested a waiver.

The procedure started on 24 April 2023.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. A waiver for a paediatric subset has been granted. A pharmaceutical form was deleted.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan and to the deferral in the scope set out in the Annex I of this opinion;
   - to grant a waiver for one or more subsets of the paediatric population concluded in accordance with Article 11(1)(c) of Regulation (EC) No 1901/2006 as amended, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   The Paediatric Committee member of Norway agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed paediatric investigation plan (PIP)

1. Waiver

1.1. Condition:

Treatment of malignant solid tumours

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- capsule, hard, film-coated table, oral use;

  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).

2. Paediatric Investigation Plan

2.1. Condition

Treatment of malignant solid tumours

2.1.1. 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.

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From 2 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Capsule, hard

Film coated tablet

2.1.4. Studies

Area	**Description**
Quality	**Study 1** (deleted during EMEA-001143-PIP01-11-M06)
Non-clinical	**Study 2 (XL184-NC-032)** Juvenile toxicity and toxicokinetic study. **Study 3** Comprehensive paediatric non-clinical efficacy testing program.
Clinical	**Study 4 (XL184-011)**

	Open-label trial to evaluate toxicity, tolerability, pharmacokinetics and pharmacodynamics of cabozantinib in children from 2 years to less than 18 years of age with refractory or relapsed malignant solid tumours. **Study 5 (XL184-005)** (deleted during EMEA-001143-PIP01-11-M06) **Study 7 (XL189)** Open-label trial to evaluate the safety and activity of cabozantinib in children from 2 years to less than 18 years of age (and young adults) with a relapsed or refractory solid malignant tumour. **Study 6 (XL184-208)** (modified during EMEA-001143-PIP01-11-M06) 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.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By June 2028
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s):

1. Treatment of renal cell carcinoma

Authorised indication(s):

- Treatment of advanced renal cell carcinoma - as first-line treatment of adult patients with intermediate or poor risk - in adults following prior vascular endothelial growth factor (VEGF)-targeted therapy.
- In combination with nivolumab, for first-line treatment of advanced renal cell carcinoma in adults.

2. Treatment of hepatocellular carcinoma

Authorised indication(s):

- Treatment of hepatocellular carcinoma in adults who have previously been treated with sorafenib.

3. Treatment of medullary thyroid carcinoma

Authorised indication(s):

- Treatment of adult patients with progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma.

4. Treatment of Differentiated thyroid carcinoma

Authorised indication(s):

- Treatment of adult patients with locally advanced or metastatic differentiated thyroid carcinoma (DTC), refractory or not eligible to radioactive iodine (RAI) who have progressed during or after prior systemic therapy.

Authorised pharmaceutical form(s):

Capsule, hard

Tablet

Authorised route(s) of administration:

Oral use