EMA/394138/2021

European Medicines Agency decision

P/0282/2021

of 19 July 2021

on the acceptance of a modification of an agreed paediatric investigation plan for cabozantinib (Cometriq, Cabometyx), (EMEA-001143-PIP01-11-M03) 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.

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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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary 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, the decision P/0134/2016 issued on 20 May 2016 and the decision P/0331/2019 issued on 11 September 2019,

Having regard to the application submitted by Ipsen Pharma on 22 March 2021 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 25 June 2021, in accordance with Article 22 of Regulation (EC) No 1901/2006,

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.

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

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

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for cabozantinib (Cometriq, Cabometyx), age-appropriate oral solid dosage form, capsule, hard, tablet, oral use, 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

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

EMA/PDCO/210880/2021
Amsterdam, 25 June 2021

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

EMEA-001143-PIP01-11-M03

Scope of the application

Active substance(s):

Cabozantinib

Invented name:

Cometriq

Cabometyx

Condition(s):

Treatment of malignant solid tumours

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Age-appropriate oral solid dosage form

Capsule, hard

Tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Ipsen Pharma

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Ipsen Pharma submitted to the European Medicines Agency on 22 March 2021 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, the decision P/0134/2016 issued on 20 May 2016 and the decision P/0331/2019 issued on 11 September 2019.

The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 27 April 2021.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

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 in the scope set out in the Annex I of this opinion.
2. The measures and timelines of the paediatric investigation plan 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

Not applicable

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.
- Treatment of advanced or metastatic medullary thyroid cancer.

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Capsule, hard

Tablet

Age-appropriate formulation

2.1.4. Studies

Area	Number of studies	Description
Quality	1	**Study 1** Development of an age-appropriate formulation.
Non-clinical	2	**Study 2 (XL184-NC-032)** Juvenile toxicity and toxicokinetic study. **Study 3** Comprehensive paediatric non-clinical efficacy testing program.
Clinical	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 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. **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.

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 January 2023
Deferral for one or more studies contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

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.

Authorised pharmaceutical form(s):

Capsule, hard

Tablet

Authorised route(s) of administration:

Oral use