EMA/428959/2012

European Medicines Agency decision

P/0128/2012

of 4 July 2012

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the refusal of a waiver for cabozantinib (EMEA-001143-PIP01-11) 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 application submitted by Exelixis, Inc. on 9 May 2011 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 16 May 2012, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation 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 agreement of a paediatric investigation plan and on the granting of a deferral and on the refusal of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

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

(4) It is therefore appropriate to adopt a decision refusing a waiver.

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

Has adopted this decision:

Article 1

A paediatric investigation plan for cabozantinib, capsule, hard, tablet, age-appropriate formulation, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for cabozantinib, capsule, hard, tablet, age-appropriate formulation, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for cabozantinib, capsule, hard, tablet, age-appropriate formulation, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby refused.

Article 4

This decision is addressed to Exelixis, Inc., 210 East Grand Avenue, 94080-0511 South San Francisco, CA, USA.

Done at London, 4 July 2012

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/232855/2012 Corr

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and on the refusal of a waiver

EMEA-001143-PIP01-11

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:

Exelixis, Inc.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Exelixis, Inc. submitted for agreement to the European Medicines Agency on 9 May 2011 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 15 June 2011.

Supplementary information was provided by the applicant on 27 February 2012. The applicant proposed modifications to the paediatric investigation plan and to the waiver.

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Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 18 of said Regulation,
   - to grant a deferral in accordance with Article 21 of said Regulation,
   - to refuse the granting of a waiver in accordance with Article 13 of said Regulation, for some of the subsets of the paediatric population and the above mentioned condition as it does not meet the grounds detailed in Article 11(1) of said Regulation.

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

2. The measures and timelines of the agreed 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 annex(es) and appendix.

London, 16 May 2012

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman
(Signature on file)

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

1. Waiver

The request for the waiver applied to:

- The paediatric population from birth to less than 2 years of age;
- For age-appropriate formulation, tablet and capsule, hard, for oral use.

The waiver request does not provide evidence to support the following grounds set out in Article 11(1) of Regulation (EC) No 1901/2006 that:

(a) The specific medicinal product is likely to be ineffective or unsafe in the paediatric population;

Because:

- The PDCO disagreed with the applicant's argumentation that the specific MP is likely to be ineffective or unsafe.

The waiver request is therefore refused by the PDCO.

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: Juvenile toxicity and toxicokinetic study. Study 3: Comprehensive paediatric non-clinical efficacy testing program.
Clinical	3	Study 4: Open-label trial to evaluate toxicity, tolerability, pharmacokinetics and pharmacodynamics of cabozantinib in children with refractory or relapsed malignant solid tumours. Study 5: Trial to evaluate relative bioavailability (in adults). Study 6: 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 December 2016
Deferral for one or more studies contained in the paediatric investigation plan:	Yes