



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/370542/2015

European Medicines Agency decision

P/0152/2015

of 10 July 2015

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for selumetinib (EMEA-001585-PIP01-13) 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 726/2004¹,

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 Agency²,

Having regard to the application submitted by AstraZeneca AB on 8 November 2013 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 22 May 2015, 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 granting 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 granting 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 selumetinib, capsule, hard, age-appropriate oral dosage form, 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 selumetinib, capsule, hard, age-appropriate oral dosage form, 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 selumetinib, capsule, hard, age-appropriate oral dosage form, 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 4

This decision is addressed to AstraZeneca AB, SE-151 85 – Sodertalje, Sweden.

Done at London, 10 July 2015

For the European Medicines Agency
Jordi Llinares Garcia
Head of Division (ad interim)
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/144165/2015 **Corr**

London, 22 May 2015

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

EMA-001585-PIP01-13

Scope of the application

Active substance(s):

Selumetinib

Condition(s):

Treatment of neurofibromatosis type 1

Treatment of melanoma

Treatment of thyroid cancer

Pharmaceutical form(s):

Capsule, hard

Age-appropriate oral dosage form

Route(s) of administration:

Oral use

Name / corporate name of the PIP applicant:

AstraZeneca AB

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, AstraZeneca AB submitted for agreement to the European Medicines Agency on 8 November 2013 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 16 September 2014.

Supplementary information was provided by the applicant on 10 February 2015. The applicant proposed modifications to the paediatric investigation plan.

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 grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

The Norwegian Paediatric Committee members agree 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 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 neurofibromatosis type 1

The waiver applies to:

- the paediatric population from birth to less than 1 years of age;
- for capsule, hard, and age-appropriate dosage form, for 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).

1.2. Condition:

Treatment of thyroid cancer

The waiver applies to:

- the paediatric population from birth to less than 12 years of age;
- for capsule, hard, and age-appropriate dosage form, for 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 neurofibromatosis type 1

2.1.1. Indication(s) targeted by the PIP

Treatment of inoperable neurofibromatosis type 1 (NF1) related plexiform neurofibromas in children and adolescents

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

From 1 year to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Capsule, hard

Age-appropriate oral dosage form

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	Study 1: Age-appropriate form for oral use Study 2: Generation of data supporting a use of the hard capsule
Non-clinical studies	1	Study 3: Carcinogenicity studies
Clinical studies	3	Study 4: Single-arm, open-label, multiple-dose study to evaluate the safety, toxicity, pharmacokinetics and activity of selumetinib in paediatric patients from 3 to less than 18 years with neurofibromatosis 1 (NF1) and inoperable plexiform neurofibroma. Study 5: Open-label, non-controlled, multiple-dose, multi-centre study to evaluate pharmacokinetics, pharmacodynamics, safety, acceptability and activity of selumetinib in children with from 2 to less than 18 years (and young adults) with neurofibromatosis 1 (NF1) and inoperable, symptomatic plexiform neurofibromas or with asymptomatic plexiform neurofibromas Study 6: Placebo-controlled, double-blind, randomised-withdrawal study to evaluate pharmacokinetics, safety, tolerability and activity of selumetinib in children from 1 to less than 7 years of age with inoperable symptomatic plexiform neurofibromas associated with neurofibromatosis 1
Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition:

Treatment of melanoma

2.2.1. Indication(s) targeted by the PIP

Selumetinib in combination with dacarbazine for treatment for adolescents with metastatic uveal melanoma previously untreated with systemic therapy

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

From 12 year to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Capsule, hard

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	0	Not applicable.
Extrapolation, modelling and simulation studies	1	Study 7: Uveal melanoma extrapolation from adults to children from 12 to less than 18 years old based on study 4 and 5
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.3. Condition:

Treatment of thyroid cancer

2.3.1. Indication(s) targeted by the PIP

Selumetinib in combination with radioactive iodine therapy for treatment of adolescents newly-diagnosed with differentiated thyroid cancer who are at high risk of primary treatment failure

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

From 12 year to less than 18 years of age.

2.3.3. Pharmaceutical form(s)

Capsule, hard

2.3.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	0	Not applicable.
Clinical studies	0	Not applicable.
Extrapolation, modelling and simulation studies	1	Study 8: Differentiated thyroid cancer extrapolation from adults to children from 12 to less than 18 years old based on study 4 and 5
Other studies	0	Not applicable.
Other measures	0	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By September 2022
Deferral for one or more measures contained in the paediatric investigation plan:	Yes