EMA/83697/2018

European Medicines Agency decision

P/0072/2018

of 16 March 2018

on the acceptance of a modification of an agreed paediatric investigation plan for selumetinib (EMEA-001585-PIP01-13-M02) 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.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Contact EMA www.ema.europa.eu/contact

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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/0152/2015 issued on 10 July 2015 and the decision P/0137/2016 issued on 20 May 2016,

Having regard to the application submitted by AstraZeneca AB on 3 November 2017 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 26 January 2018, 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 selumetinib, capsule, hard, age-appropriate oral dosage form, 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 AstraZeneca AB, SE-151 85 – Sodertalje, Sweden.

EMA/PDCO/739897/2017
London, 26 January 2018

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

EMEA-001585-PIP01-13-M02

Scope of the application

Active substance(s):

Selumetinib

Condition(s):

Treatment of neurofibromatosis type 1

Treatment of thyroid cancer

Treatment of melanoma

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 22 of Regulation (EC) No 1901/2006 as amended, AstraZeneca AB submitted to the European Medicines Agency on 3 November 2017 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/0152/2015 issued on 10 July 2015 and the decision P/0137/2016 issued on 20 May 2016.

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

The procedure started on 28 November 2017.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
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Send a question via our website www.ema.europa.eu/contact

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.

   The Norwegian Paediatric Committee member 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 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 year of age;
- capsule, hard, age-appropriate oral dosage form, 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;
- capsule, hard, age-appropriate oral dosage form, 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).

1.3. Condition:

Treatment of melanoma

The waiver applies to:

- the paediatric population from 12 years to less than 18 years of age;
- capsule, hard, age-appropriate oral dosage form, oral use;
- on the grounds that the specific medicinal product is likely to be ineffective.

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 the 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 ***Study 7****: deleted in procedure EMEA-01585-PIP01-13-M01.*
Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition:

Treatment of thyroid cancer

2.2.1. 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

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

From 12 years 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 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