EMA/167583/2024

European Medicines Agency decision

P/0134/2024

of 25 April 2024

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

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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 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/0152/2015 issued on 10 July 2015, the decision P/0137/2016 issued on 20 May 2016, the decision P/0072/2018 issued on 16 March 2018, the decision P/0279/2019 issued on 16 August 2019 and the decision P/0341/2021 issued on 12 August 2021.

Having regard to the application submitted by AstraZeneca AB on 15 December 2023 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 22 March 2024, 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 and to the deferral.

(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.

[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 selumetinib (Koselugo), capsule, hard, age-appropriate oral dosage form, 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

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

EMA/PDCO/13888/2024
Amsterdam, 22 March 2024

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

EMEA-001585-PIP01-13-M06

Scope of the application

Active substance(s):

Selumetinib

Invented name and authorisation status:

See Annex II

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 15 December 2023 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, the decision P/0137/2016 issued on 20 May 2016, the decision P/0072/2018 issued on 16 March 2018, the decision P/0279/2019 issued on 16 August 2019 and the decision P/0341/2021 issued on 12 August 2021.

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

The procedure started on 22 January 2024.

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 and to the deferral in the scope set out in the Annex I of this opinion.

   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 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 18 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 birth 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 neurofibromatosis type 1 (NF1) related inoperable 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	Description
Quality-related studies	**Study 1** Development of an age-appropriate form for oral use (Q001) **Study 2** Generation of data supporting the use of the hard capsule
Non-clinical studies	**Study 3** Carcinogenicity studies
Clinical studies	**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. (ISS62440035, part A) **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. (ISS62440035, part B) **Study 6** Single-arm, open-label 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	Not applicable
Other studies	Not applicable
Other measures	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 November 2024
Deferral for one or more measures 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 neurofibromatosis type I

Authorised indication(s):

- Koselugo as monotherapy is indicated for the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in paediatric patients with neurofibromatosis type 1 (NF1) aged 3years and above
  - Invented name(s): Koselugo
  - Authorised pharmaceutical form(s): hard capsules
  - Authorised route(s) of administration: oral use
  - Authorised via centralised