EMA/105462/2024

European Medicines Agency decision

P/0110/2024

of 12 April 2024

on the acceptance of a modification of an agreed paediatric investigation plan for catequentinib, (EMEA-002486-PIP04-21-M01) 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/0138/2022 issued on 13 April 2022,

Having regard to the application submitted by Advenchen Laboratories, LLC on 7 November 2023 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 23 February 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.

(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, 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 catequentinib, capsule, hard, age-appropriate oral dosage formulation, 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 Advenchen Laboratories, LLC, 887 Patriot Drive Suite A, 93021 - Moorpüark, CA, USA.

EMA/PDCO/537854/2023
Amsterdam, 23 February 2024

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

EMEA-002486-PIP04-21-M01

Scope of the application

Active substance(s):

Catequentinib

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of soft tissue sarcomas

Treatment of Ewing sarcoma

Pharmaceutical form(s):

Capsule, hard

Age-appropriate oral dosage formulation

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Advenchen Laboratories, LLC

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Advenchen Laboratories, LLC submitted to the European Medicines Agency on 7 November 2023 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0138/2022 issued on 13 April 2022.

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

The procedure started on 3 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 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 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 soft tissue sarcomas

2.1.1. Indication(s) targeted by the PIP

Treatment of soft tissue sarcomas

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

Age-appropriate oral dosage formulation

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of an age-appropriate formulation (powder and solvent for oral suspension) suitable for paediatric patients from birth to less than 12 years of age.
Non-clinical studies	**Study 2** Dose range-finding juvenile rat toxicity study (PND 10). **Study 3** Dose range-finding juvenile rat toxicity study (PND 21). **Study 4** Definitive juvenile rat toxicity study.
Clinical studies	**Study 5** AL3818-US-004-P (part 2.1, part 3.1) Open-label, single arm, dose-finding trial to evaluate the pharmacokinetics, safety and tolerability of catequentinib (AL3818) in children from 2 years to less than 18 years of age with soft tissue sarcoma (refractory, in second or higher relapse or no standard treatment available) including rhabdomyosarcoma, synovial sarcoma and alveolar soft part sarcoma (part 2.1) and open-label, single arm dose-finding trial to evaluate the pharmacokinetics, safety and tolerability of AL3818 in combination with vincristine and irinotecan in

	children from 2 years to less than 18 years of age with Ewing sarcoma (refractory, in second or higher relapse) (part 3.1). **Study 6** AL3818-US-004-P (part 2.2, part 3.2) Open-label, single arm, dose-expansion phase trial to evaluate the pharmacokinetics, safety and anti-tumour activity of catequentinib (AL3818) in children from 2 years to less than 18 years of age with soft tissue sarcoma (refractory, in second or higher relapse or no standard treatment available) including rhabdomyosarcoma, synovial sarcoma and alveolar soft part sarcoma (part 2.2) and open-label, single arm trial dose-expansion phase trial to evaluate the pharmacokinetics, safety and anti-tumour activity of AL3818 in combination with vincristine and irinotecan in children from 2 years to less than 18 years of age with Ewing sarcoma (refractory, in second or higher relapse) (part 3.2). **Study 7** AL3818-US-004-P (part 2.3, part 3.3) Randomised, open-label controlled trial, to assess the efficacy, safety and pharmacokinetics of catequentinib (AL3818) compared to standard therapy in children from 2 years to less than 18 years of age with a soft tissue sarcoma selected based on the results of part 2.2 of study AL3818-US-004-P (study 6) and randomised controlled trial to assess the efficacy, safety and pharmacokinetics of catequentinib (AL3818) in combination with background therapy determined based on the results of part 3.2 of study AL3818-US-004-P compared to background therapy in children from 2 years to less than 18 years of age with Ewing sarcoma (refractory, in second or higher relapse) **Study 9** AL3818-US-004-P (part 6) Randomised, open-label, add-on trial with a dose-finding phase followed by an expansion phase aimed at assessing the efficacy and safety of catequentinib (AL3818) in addition to best known standard of care compared to best-known standard of care (without AL3818) in children from birth to less than 18 years of age with newly diagnosed soft tissue sarcoma
Extrapolation, modelling and simulation studies	Not applicable.
Other studies	Not applicable.
Other measures	Not applicable.

2.2. Condition:

Treatment of Ewing sarcoma

2.2.1. Indication(s) targeted by the PIP

Treatment of Ewing sarcoma

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

From birth to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Capsule, hard

Age-appropriate oral dosage formulation

2.2.4. Measures

Area	Description
Quality-related studies	Study 1 same as study 1 of condition treatment of soft tissue sarcoma.
Non-clinical studies	Study 2 same as study 2 of condition treatment of soft tissue sarcoma. Study 3 same as study 3 of condition treatment of soft tissue sarcoma. Study 4 same as study 4 of condition treatment of soft tissue sarcoma.
Clinical studies	Study 5 same as study 5 of condition treatment of soft tissue sarcoma. Study 6 same as study 6 of condition treatment of soft tissue sarcoma. Study 7 same as study 7 of condition treatment of soft tissue sarcoma. **Study 8** AL3818-US-004-P (part 5) Randomised, open-label, add-on trial with a dose-finding phase followed by an expansion phase aimed at assessing the efficacy, safety and pharmacokinetics of catequentinib (AL3818) in addition to best known standard of care compared to best known standard of care (without AL3818) in children from birth to less than 18 years of age with newly diagnosed metastatic Ewing sarcoma
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 March 2033
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:

The product is not authorised anywhere in the European Community.