EMA/347489/2023

European Medicines Agency decision

P/0335/2023

of 9 August 2023

on the acceptance of a modification of an agreed paediatric investigation plan for repotrectinib (EMEA-002635-PIP02-21-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.

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on the acceptance of a modification of an agreed paediatric investigation plan for repotrectinib (EMEA-002635-PIP02-21-M02) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/0542/2021 issued on 31 December 2021, and the decision P/0150/2023 issued on 26 April 2023,

Having regard to the application submitted by Bristol-Myers Squibb Pharma EEIG on 25 May 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 21 July 2023, 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 repotrectinib, capsule, hard, age-appropriate oral liquid 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 Bristol-Myers Squibb Pharma EEIG, Plaza 254, Blanchardstown Corporate Park 2, D15 T867 - Dublin 15, Ireland.

EMA/PDCO/274865/2023
Amsterdam, 21 July 2023

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

EMEA-002635-PIP02-21-M02

Scope of the application

Active substance(s):

Repotrectinib

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic neoplasms)

Pharmaceutical form(s):

Capsule, hard

Age-appropriate oral liquid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Bristol-Myers Squibb Pharma EEIG

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Bristol-Myers Squibb Pharma EEIG submitted to the European Medicines Agency on 25 May 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/0542/2021 issued on 31 December 2021, and the decision P/0150/2023 issued on 26 April 2023.

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

The procedure started on 10 July 2023.

Scope of the modification

Some 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

Not applicable

2. Paediatric investigation plan

2.1. Condition:

Treatment of all conditions included in the category of malignant neoplasms (except haematopoietic neoplasms)

2.1.1. Indication(s) targeted by the PIP

Treatment of patients with advanced or metastatic malignancies harbouring NTRK1-3 fusions that have been pretreated with a TRK tyrosine kinase inhibitor

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 liquid dosage form

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of an age-appropriate oral liquid dosage form
Non-clinical studies	**Study 2 (00480)** Dose range-finding juvenile toxicity study **Study 3 (00481)** Definitive juvenile toxicity study
Clinical studies	**Study 4 (TPX-0005-01/TRIDENT-1)** *Deleted during EMEA-002635-PIP02-21-M01* **Study 5 (TPX-0005-07)** Open-label, two part single arm trial to evaluate the recommended phase 2 dose (RP2D) (part 1), pharmacokinetics (PK), pharmacodynamics (PD), safety and activity of repotrectinib in children from birth to less than 18 years of age (and adults), enrolled in two cohorts with tyrosine kinase inhibitor (TKI) pre-treated solid tumours characterised by NTRK1-3 gene fusion (cohort 1) and solid tumours characterised by other ALK/ROS1/NTRK1-3 alterations or NTRK

	fusions without centrally confirmed measurable disease not otherwise eligible for cohort 1.
Extrapolation, modelling and simulation studies	**Study 6** Modelling and simulation study to support the dose finding of the product in children from birth to less than 18 years of age with advanced or metastatic malignancies harbouring NTRK1-3 fusions that have been pretreated with a TRK tyrosine kinase inhibitor. **Study 7** Modelling and simulation study to evaluate the use of the product in children from birth to less than 18 years of age with advanced or metastatic malignancies harbouring NTRK1-3 fusions that have been pretreated with a TRK tyrosine kinase inhibitor.
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 2025
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.