EMA/470767/2021

European Medicines Agency decision

P/0357/2021

of 8 September 2021

on the acceptance of a modification of an agreed paediatric investigation plan for pevonedistat (EMEA-002117-PIP01-17-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 pevonedistat (EMEA-002117-PIP01-17-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 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/0054/2018 issued on 2 March 2018 and the decision P/0386/2019 issued on 29 November 2019,

Having regard to the application submitted by Takeda Pharma A/S on 16 April 2021 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 23 July 2021, 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 pevonedistat, concentrate for solution for infusion, intravenous 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 Takeda Pharma A/S, Delta Park 45, 2665 - Vallensbaek Strand, Denmark.

EMA/PDCO/261262/2021
Amsterdam, 23 July 2021

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

EMEA-002117-PIP01-17-M02

Scope of the application

Active substance(s):

Pevonedistat

Condition(s):

Treatment of acute myeloid leukaemia

Treatment of myelodysplastic syndromes

Pharmaceutical form(s):

Concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Takeda Pharma A/S

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Takeda Pharma A/S submitted to the European Medicines Agency on 16 April 2021 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/0054/2018 issued on 2 March 2018 and the decision P/0386/2019 issued on 29 November 2019.

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

The procedure started on 25 May 2021.

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 acute myeloid leukaemia

The waiver applies to:

- the paediatric population from birth to less than 1 month of age;
- concentrate for solution for infusion, intravenous 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 myelodysplastic syndromes

The waiver applies to:

- the paediatric population from birth to less than 1 months of age;
- concentrate for solution for infusion, intravenous 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 acute myeloid leukaemia

2.1.1. Indication(s) targeted by the PIP

Treatment of paediatric patients with newly diagnosed high risk AML or relapsed or refractory (R/R) AML

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

From 1 month to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Concentrate for solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	2	**Study 1:** Tolerability and dose range-finding study in juvenile rats **Study 2:** Definitive juvenile toxicity study in juvenile rats
Clinical studies	4	**Study 3:** Open-label, uncontrolled trial to estimate the maximum tolerated dose (MTD) and/or recommended Phase 2 dose (RP2D) and to evaluate pharmacokinetics, safety and tolerability of pevonedistat when given in combination with irinotecan and temozolomide in paediatric patients from 6 months to less than 18 years of age (and young adults) with refractory or recurrent solid tumours (ADVL1615). **Study 4:** Open-label, uncontrolled trial to estimate the MTD and/or RP2D and to evaluate pharmacokinetics, safety and tolerability of pevonedistat when given in combination with azacitidine, fludarabine and cytarabine in paediatric patients from 1 month to less than 18 years of age (and young adults) with relapsed or refractory acute myeloid leukaemia (AML) or relapsed or refractory myelodysplastic syndromes (MDS) (ADVL1712). **Study 5:** Open-label, randomised, controlled trial to evaluate safety and efficacy of pevonedistat in combination with azacitidine, fludarabine and cytarabine, compared to fludarabine and cytarabine in paediatric patients from 1 month to less than 18 years of age (and young adults) with relapsed or refractory acute myeloid leukaemia (AML) or relapsed or refractory myelodysplastic syndromes (MDS). **Study 6:** Open-label, uncontrolled (Part 1)/historical-control (Part 2) trial to estimate the MTD and/or RP2D and to evaluate pharmacokinetics, safety, tolerability and activity of pevonedistat in combination with a 7+3 induction regimen (7 days of cytarabine and 3 days idarubicin) in paediatric patients from 1 month to less than 18 years of age with newly diagnosed high-risk acute myeloid leukaemia (AML).
Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2.2. Condition:

Treatment of myelodysplastic syndromes

2.2.1. Indication(s) targeted by the PIP

Treatment of relapsed/refractory (R/R) myelodysplastic syndromes

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

From 1 month to less than 18 years of age

2.2.3. Pharmaceutical form(s)

Concentrate for solution for infusion

2.2.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	2	**Study 1:** same as Condition 1 **Study 2:** same as Condition 1
Clinical studies	3	**Study 3:** same as Condition 1 **Study 4:** same as Condition 1 **Study 5:** same as Condition 1
Extrapolation, modelling and simulation studies	0	Not applicable
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:	No
Date of completion of the paediatric investigation plan:	By December 2032
Deferral for one or more measures contained in the paediatric investigation plan:	Yes