EMA/91894/2018

European Medicines Agency decision

P/0054/2018

of 2 March 2018

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for pevonedistat (EMEA-002117-PIP01-17) 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 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 application submitted by Takeda Pharma A/S on 17 March 2017 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 26 January 2018, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

A paediatric investigation plan for pevonedistat, concentrate for solution for injection/infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for pevonedistat, concentrate for solution for injection/infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for pevonedistat, concentrate for solution for injection/infusion, intravenous use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to Takeda Pharma A/S, Dybendal Alle 10, 2630 – Taastrup, Denmark.

EMA/PDCO/760549/2017
London, 26 January 2018

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-002117-PIP01-17

Scope of the application

Active substance(s):

Pevonedistat

Condition(s):

Treatment of acute myeloid leukaemia (AML)

Treatment of myelodysplastic syndromes (MDS)

Pharmaceutical form(s):

Concentrate for solution for injection/infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Takeda Pharma A/S

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Takeda Pharma A/S submitted for agreement to the European Medicines Agency on 17 March 2017 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 25 April 2017.

Supplementary information was provided by the applicant on 3 November 2017. The applicant proposed modifications to the paediatric investigation plan.

Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 17(1) of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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 (AML)

The waiver applies to:

- the paediatric population from birth to less than 1 month of age;
- concentrate for solution for injection/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 (MDS)

The waiver applies to:

- the paediatric population from birth to less than 1 months of age;
- concentrate for solution for injection/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 (AML)

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 injection/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 AML or relapsed or refractory 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 AML or relapsed or refractory 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 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 (MDS)

2.2.1. Indication(s) targeted by the PIP

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

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 injection/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 2030
Deferral for one or more measures contained in the paediatric investigation plan:	Yes