EMA/413795/2024

European Medicines Agency decision

P/0329/2024

of 13 September 2024

on the acceptance of a modification of an agreed paediatric investigation plan for tasimelteon (Hetlioz), (EMEA-001531-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/0141/2014 issued on 28 May 2014, the decision P/0123/2015 issued on 5 June 2015, the decision P/0053/2016 issued on 18 March 2016 and the decision P/0215/2018 issued on 17 July 2018,

Having regard to the application submitted by Vanda Pharmaceuticals Netherlands B.V. on 25 April 2024 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 26 July 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 tasimelteon (Hetlioz), capsule, hard, age-appropriate liquid 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 Vanda Pharmaceuticals Netherlands B.V., 10 Basisweg, 1043 AP – Amsterdam, The Netherlands.

EMA/PDCO/223504/2024 Corr[1]
Amsterdam, 26 July 2024

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

EMEA-001531-PIP01-13-M06

Scope of the application

Active substance(s):

Tasimelteon

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of disorders of the sleep-wake schedule

Pharmaceutical form(s):

Capsule, hard

Age-appropriate liquid form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Vanda Pharmaceuticals Netherlands B.V.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Vanda Pharmaceuticals Netherlands B.V. submitted to the European Medicines Agency on 25 April 2024 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/0141/2014 issued on 28 May 2014, the decision P/0123/2015 issued on 5 June 2015, the decision P/0053/2016 issued on 18 March 2016 and the decision P/0215/2018 issued on 17 July 2018.

[1] 5 September 2024

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

The procedure started on 27 May 2024.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified. The condition of the PIP has been updated.

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 disorders of the sleep-wake schedule

The waiver applies to:

- the paediatric population from birth to less than 3 years;
- capsule, hard and age-appropriate liquid form for 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).

2. Paediatric investigation plan

2.1. Condition

Treatment of disorders of the sleep-wake schedule

2.1.1. Indication(s) targeted by the PIP

Treatment of non-24-hour sleep-wake disorder in the totally blind

Treatment of nighttime sleep disturbances in Smith-Magenis Syndrome

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

From 3 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Capsule, hard

Age-appropriate oral liquid form

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of an age-appropriate formulation
Non-clinical studies	**Study 2** Juvenile toxicity study
Clinical studies	**Study 3** Open-label, single dose, non-controlled trial to evaluate the pharmacokinetics of tasimelteon in children from 3 years to less than 18 years of age with Non-24 hours sleep-wake disorder; have Autism Spectrum Disorder (ASD) and Smith Magenis Syndrome (SMS), or another neurodevelopmental disorder with a sleep complaint (VP-VEC-162-4201).

	Study 4 Double-blind, placebo-controlled, randomised withdrawal trial to evaluate maintenance effect of 2 fixed doses of tasimelteon compared to placebo in children from 3 to less than 18 years of age who have no conscious light perception and have non-24-hour sleep-wake disorder (VP-VEC-162-4203). **Study 5** Study deleted in EMEA-001531-PIP01-13-M06 **Study 8** Study added in EMEA-001531-PIP01-13-M06 Double-blind, randomized, two-period crossover study evaluating the effects of tasimelteon compared to placebo on sleep disturbances of paediatric patients from 3 years to less than 18 years of age (and adults) with Smith-Magenis Syndrome (SMS) (VP-VEC-162-2401).
Extrapolation, modelling and simulation studies	**Study 6** Modelling and simulation study to find the appropriate dose of tasimelteon in non-24 paediatric children from 3 to less than 18 years of age with comparable systemic exposure to the adult dosing. **Study 7** Extrapolation of tasimelteon Non-24 efficacy data observed in adult subjects compared to paediatric subjects.
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 December 2030
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 Non-24-Hour Sleep-Wake Disorder (Non-24) in totally blind adults

Authorised indication(s):

- Hetlioz is indicated for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) in totally blind adults
  - Invented name(s): Hetlioz
  - Authorised pharmaceutical form(s): Hard capsule
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure