EMA/512496/2023

European Medicines Agency decision

P/0469/2023

of 1 December 2023

on the acceptance of a modification of an agreed paediatric investigation plan for tapentadol (hydrochloride) (Palexia, Tapentadol Libra-Pharm, Yantil, and Ationdo), (EMEA-000325-PIP01-08-M11) 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/48/2009 issued on 24 March 2009, the decision P/0280/2013 issued on 8 November 2013, the decision P/0095/2014 issued on 7 April 2014, the decision P/0042/2016 issued on 26 February 2016, the decision P/0319/2016 issued on 2 December 2016, the decision P/0148/2017 issued on 7 June 2017, the decision P/0318/2017 issued on 31 October 2017, the decision P/0111/2018 issued on 11 April 2018, and the decision P/0258/2020 issued on 15 July 2020,

Having regard to the application submitted by Grünenthal GmbH on 30 June 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 13 October 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 tapentadol (hydrochloride) (Palexia, Tapentadol Libra-Pharm, Yantil and Ationdo), prolonged-release tablet, prolonged-release granules, 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 Grünenthal GmbH, Zieglerstrasse 6, 52078 – Aachen, Germany.

EMA/PDCO/322617/2023
Amsterdam, 13 October 2023

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

EMEA-000325-PIP01-08-M11

Scope of the application

Active substance(s):

Tapentadol (hydrochloride)

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of chronic pain

Pharmaceutical form(s):

Prolonged-release tablet

Prolonged-release granules

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Grünenthal GmbH

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Grünenthal GmbH submitted to the European Medicines Agency on 30 June 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/48/2009 issued on 24 March 2009, the decision P/0280/2013 issued on 8 November 2013, the decision P/0095/2014 issued on 7 April 2014, the decision P/0042/2016 issued on 26 February 2016, the decision P/0319/2016 issued on 2 December 2016, the decision P/0148/2017 issued on 7 June 2017, the decision P/0318/2017 issued on 31 October 2017, the decision P/0111/2018 issued on 11 April 2018, and the decision P/0258/2020 issued on 15 July 2020.

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

The procedure started on 14 August 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 chronic pain

2.1.1. Indication(s) targeted by the PIP

Treatment of chronic pain

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)

Prolonged-release tablet

Prolonged-release granules

2.1.4. Measures

Area	Description
Quality - related studies	**Study 1** Development of prolonged release granules for oral use
Non-clinical studies	**Study 2** Juvenile rat toxicity study
Clinical studies	**Study 3** Randomised, open-label, cross-over relative bioavailability trial to compare a tapentadol multiparticulate (or alternative) formulation and the prolonged release tablets in healthy subjects. **Study 4** A randomised, open-label, active-controlled, multi-centre study to evaluate the safety and the efficacy of tapentadol PR in patients from 6 to less than 18 years old suffering from pain requiring prolonged-release (PR) opioid. **Study 5** Open-label, single-arm, multiple-dose, multi-site trial to characterize the pharmacokinetic profile of tapentadol PR granules in children aged 2 and 5 years old suffering from pain requiring PR opioid treatment.

Extrapolation, modelling and simulation studies	**Study 6** Modelling and simulation study **Study 7** (added in procedure EMEA-000325-PIP01-08-M08) Extrapolation study
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 February 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:

Condition(s) and authorised indication(s)

1. Treatment of chronic pain

Authorised indication(s):

- Management of severe chronic pain in adults, which can be adequately managed only with opioid analgesics.
    - Invented name(s): Palexia, Tapentadol Libra-Pharm, Yantil and Ationdo
    - Authorised pharmaceutical form(s): Prolonged-release tablets
    - Authorised route(s) of administration: Oral
    - Authorised via decentralised procedure.

2. Treatment of acute pain

Authorised indication(s):

- Relief of moderate to severe acute pain in adults, which can be adequately managed only with opioid analgesics.
    - Invented name(s): Palexia, Tapentadol Libra-Pharm, Yantil and Ationdo
    - Authorised pharmaceutical form(s): Film-coated tablets
    - Authorised route(s) of administration: Oral use
    - Authorised via decentralised procedure.
- Relief of moderate to severe acute pain in children from 2 years of age and in adults, which can be adequately managed only with opioid analgesics.
    - Invented name(s): Palexia, Tapentadol Libra-Pharm and Yantil
    - Authorised pharmaceutical form(s): Oral solution
    - Authorised route(s) of administration: Oral use
    - Authorised via decentralised procedure.