EMA/27567/2024

European Medicines Agency decision

P/0021/2024

of 9 February 2024

on the acceptance of a modification of an agreed paediatric investigation plan for bupivacaine (Exparel), (EMEA-000877-PIP03-17-M05) 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/0402/2018 issued on 7 December 2018, the decision P/0036/2020 issued on 29 January 2020, the decision P/0113/2021 issued on 17 March 2021, the decision P/0342/2021 issued on 9 August 2021, and the decision P/0438/2022 issued on 28 October 2022.

Having regard to the application submitted by Pacira Ltd on 24 August 2023 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 15 December 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 bupivacaine (Exparel), dispersion for injection, perineural use, infiltration 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 Pacira Ireland Ltd, Unit 13 Classon House, Dundrum Business Park, Dundrum, 14 D14W9Y – Dublin, Ireland.

EMA/PDCO/432470/2023
Amsterdam, 15 December 2023

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

EMEA-000877-PIP03-17-M05

Scope of the application

Active substance(s):

Bupivacaine

Invented name and authorisation status:

See Annex II

Condition(s):

Postsurgical analgesia

Pharmaceutical form(s):

Dispersion for injection

Route(s) of administration:

Perineural use

Infiltration use

Name/corporate name of the PIP applicant:

Pacira Ltd

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Pacira Ltd submitted to the European Medicines Agency on 24 August 2023 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/0402/2018 issued on 7 December 2018, the decision P/0036/2020 issued on 29 January 2020, the decision P/0113/2021 issued on 17 March 2021, the decision P/0342/2021 issued on 9 August 2021, and the decision P/0438/2022 issued on 28 October 2022.

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

The procedure started on 16 October 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

1.1. Condition:

Postsurgical analgesia

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- suspension for injection, perineural and infiltration use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition:

Postsurgical analgesia

2.1.1. Indication(s) targeted by the PIP

Local or regional analgesia when administered into the surgical site or as a nerve block in children from 1 year to less than 18 years of age

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

From 1 year to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Suspension for injection

Prolonged-release dispersion for injection

2.1.4. Measures

Area	Description
Quality-related studies	Not applicable
Non-clinical studies	Not applicable
Clinical studies	**Study 1 (402-C-319)** A multicentre study to evaluate the pharmacokinetics and safety of liposomal bupivacaine (hereinafter: Exparel) for postsurgical analgesia in paediatric subjects aged 6 years to less than 17 years of age **Study 2 (402-C-WI2)** Multicentre, double-blind, randomised, bupivacaine-controlled study to evaluate the pharmacokinetics and safety of Exparel for postsurgical analgesia in paediatric patients from birth to less than 6 years of age undergoing cardiac surgery (402-C-WI2)

	Study 3 (402-C-NB1) Multicentre, open-label, randomised, ropivacaine-controlled study to evaluate the safety and pharmacokinetics of Exparel when administered as a nerve block for surgical procedures like anterior cruciate ligament (ACL) repair, upper or lower extremity fractures in paediatric subjects aged 6 years to less than 18 years **Study 4 (402-C-NB2)** Multicentre, open-label, randomised, ropivacaine-controlled study to evaluate the safety and pharmacokinetics of Exparel in paediatric subjects aged 1 to less than 6 years when administered as a nerve block for surgical procedures like repair of fractured femoral shaft (femoral block), hand or forearm surgery (axillary block), or inguinal hernia repair (ilio-inguinal block) **Study 5 (402-C-WI3)** (New study added during modification EMEA-000877-PIP03-17-M04) Multicentre, double-blind, randomised, bupivacaine-controlled study to evaluate the safety and efficacy of Exparel for postoperative analgesia in paediatric patients from birth to less than 6 years of age undergoing cardiac surgery.
Extrapolation, modelling and simulation studies	Not applicable
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:	No
Date of completion of the paediatric investigation plan:	By September 2026
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 postsurgical analgesia

Authorised indication(s):

- EXPAREL liposomal is indicated:

  in adults as a brachial plexus block or femoral nerve block for treatment of post-operative pain.

  in adults and children aged 6 years or older as a field block for treatment of somatic post-operative pain from small- to medium-sized surgical wounds.

- Invented name(s): Exparel
- Authorised pharmaceutical form(s): Prolonged-release dispersion for injection
- Authorised route(s) of administration: Infiltration, perineural use
- Authorised via centralised procedure