



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMADOC-1700519818-2039838

European Medicines Agency decision

EMA/PE/0000235857

of 15 April 2025

on the acceptance of a modification of an agreed paediatric investigation plan for bupivacaine (Exparel)
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 bupivacaine (Exparel) 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 726/2004¹,

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 Agency²,

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, the decision P/0438/2022 issued on 28 October 2022 and the decision P/0021/2024 issued on 9 February 2024,

Having regard to the application submitted by Pacira Ireland Limited on 22 November 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 28 February 2025, 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), 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 Limited, Unit 13, Dundrum Business Park, Classon House, Dublin - 14 D14 W9Y3, Ireland.



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMADOC-1700519818-1797882 Corr¹
Amsterdam, 28 February 2025

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMA/PE/0000235857

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

Suspension for injection

Prolonged-release dispersion for injection

Route(s) of administration:

Perineural use

Infiltration use

Name/corporate name of the PIP applicant:

Pacira Ireland Limited

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Pacira Ireland Limited submitted to the European Medicines Agency on 22 November 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/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

¹ 8 April 2025



issued on 9 August 2021, the decision P/0438/2022 issued on 28 October 2022 and the decision P/0021/2024 issued on 9 February 2024.

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

The procedure started on 2 January 2025.

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 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;
- dispersion for injection, suspension for injection, prolonged-release dispersion 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 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)

Dispersion for injection

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

	<p>analgesia in paediatric patients from birth to less than 6 years of age undergoing cardiac surgery (402-C-WI2)</p> <p>Study 3 (402-C-NB1) (study deleted during procedure EMA/PE/0000235857)</p> <p>Study 4 (402-C-NB2) (study deleted during procedure EMA/PE/0000235857)</p> <p>Study 5 (402-C-WI3) (New study added during modification EMEA-000877-PIP03-17-M04)</p> <p>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.</p>
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 March 2031
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):

- Adults as a brachial plexus block or femoral nerve block for treatment of post-operative pain
- 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 liposomal
 - Authorised pharmaceutical form(s): prolonged-release dispersion for injection
 - Authorised route(s) of administration: Infiltration, perineural use
 - Authorised via centralised procedure