

EMA/828934/2018

European Medicines Agency decision P/0013/2019

of 3 January 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral for bupivacaine / meloxicam (HTX-011) (EMA-002246-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 726/2004¹,

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 Agency²,

Having regard to the application submitted by Heron Therapeutics. B.V. on 19 January 2018 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 16 November 2018, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 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.
- (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.

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 bupivacaine / meloxicam (HTX-011), solution for injection, infiltration, 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 bupivacaine / meloxicam (HTX-011), solution for injection, infiltration, 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

This decision is addressed to Heron Therapeutics, B.V., Herengracht 500, 1017CB – Amsterdam, The Netherlands.

EMA/PDCO/599940/2018
London, 16 November 2018

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

EMA-002246-PIP01-17

Scope of the application

Active substance(s):

Bupivacaine / meloxicam (HTX-011)

Condition(s):

Treatment of acute postoperative pain

Pharmaceutical form(s):

Solution for injection

Route(s) of administration:

Infiltration

Name/corporate name of the PIP applicant:

Heron Therapeutics. B.V.

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Heron Therapeutics. B.V. submitted for agreement to the European Medicines Agency on 19 January 2018 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 27 February 2018.

Supplementary information was provided by the applicant on 10 August 2018. 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.

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 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

Not applicable.

2. Paediatric investigation plan

2.1. Condition:

Treatment of acute postoperative pain

2.1.1. Indication(s) targeted by the PIP

Treatment of acute postoperative 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)

Solution for injection

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	2	Study 1: Definitive juvenile toxicity study to assess the potential general toxicity of meloxicam including the development of kidney, liver, lung, and testes in neonatal animals (HTX-011-nonclinical-2) Study 2: Definitive juvenile toxicity study to assess the potential toxicity of the dimethyl sulfoxide excipient on the CNS via histopathology, long-term functional and cognitive assessments and ophthalmic examinations (HTX-011-nonclinical-1)
Clinical studies	2	Study 3: Randomised, double-blind, active controlled, multicentre study to evaluate the PK, PD, and safety and tolerability of a single-dose administration into the surgical site of HTX-011 compared with bupivacaine HCl 0.25% (without epinephrine) in adolescents and children from 3 to less than 18 years of age undergoing unilateral open inguinal herniorrhaphy (HTX-011-clinical-1)

		Study 4: Randomised, double-blind, active controlled, multicentre study to evaluate the PK, safety and pharmacodynamics of a single-dose administration into the surgical site of HTX-011 compared with bupivacaine HCl 0.25% in children from birth to less than 3 years of age undergoing unilateral open inguinal herniorrhaphy (HTX-011-clinical-2)
Extrapolation, modelling and simulation studies	8	Study 5: Step-up (physiologically based) pharmacokinetic (PBPK) Modelling and Simulation to support dose selection for adolescents (12 to less than 18 years of age) (HTX-011-PBPK-1) Study 6: Step-up (physiologically based) PBPK Modelling and Simulation to support dose selection for children (6 to less than 12 years of age) (HTX-011-PBPK-2) Study 7: Step-up (physiologically based) PBPK Modelling and Simulation to support dose selection for children (3 to less than 6 years of age) (HTX-011-PBPK-3) Study 8: Step-up (physiologically based) PBPK Modelling and Simulation to support dose selection for neonates and infants (from birth to less than 3 years of age) (HTX-011-PBPK-4) Study 9: Step-down Population PK model (assumption: Linear PK) (HTX-011-PPK-1) Study 10: Step-down Population PK model (assumption: Linear PK) (HTX-011-PPK-2) Study 11: Step-down Population PK model (assumption: Linear PK) (HTX-011-PPK-3) Study 12: Step-down Population PK model (assumption: Linear PK) (HTX-011-PPK-4)
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 November 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes