European Medicines Agency decision

P/0413/2019

of 6 December 2019

on the agreement of a paediatric investigation plan and on the granting of a waiver for sufentanil (citrate) / ketamine (hydrochloride) (EMEA-001739-PIP02-16) 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 Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the application submitted by Copenhagen University Hospital, Rigshospitalet on 28 November 2016 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 18 October 2019, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 13 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 waiver.

(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 waiver.

[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 sufentanil (citrate) / ketamine (hydrochloride), nasal spray, solution, intranasal use, 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 waiver for sufentanil (citrate) / ketamine (hydrochloride), nasal spray, solution, intranasal use, 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 Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, 2100 - Copenhagen Ø, Denmark.

EMA/PDCO/410627/2019
Amsterdam, 18 October 2019

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

EMEA-001739-PIP02-16

Scope of the application

Active substance(s):

Sufentanil (citrate) / ketamine (hydrochloride)

Condition(s):

Treatment of acute pain

Pharmaceutical form(s):

Nasal spray, solution

Route(s) of administration:

Intranasal use

Name/corporate name of the PIP applicant:

Copenhagen University Hospital, Rigshospitalet

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Copenhagen University Hospital, Rigshospitalet submitted for agreement to the European Medicines Agency on 28 November 2016 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 3 January 2017.

Supplementary information was provided by the applicant on 11 July 2019. 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 waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   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 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 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

1.1. Condition:

Treatment of acute pain

The waiver applies to:

- the paediatric population from birth to less than 1 year of age;
- nasal spray, solution for intranasal use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric investigation plan

2.1. Condition:

Treatment of acute pain

2.1.1. Indication(s) targeted by the PIP

Treatment of acute pain in children and adolescents from 1 to less than 18 years of age in a hospital or prehospital setting

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

From 1 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Nasal spray, solution

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable
Non-clinical studies	0	Not applicable
Clinical studies	6	**Study 1** An exploratory, nonrandomised open-label trial to investigate a paediatric formulation of intranasal sufentanil and ketamine for procedural pain and to characterize its pharmacokinetic profile (PDC 01-0201)

		Study 2 A registry study of the free combination of intranasal sufentanil and s-ketamine for treatment of procedural pain in children 1 to less than 18 years of age at a tertiary hospital in Sweden, including retrospective data from 10 years of routine clinical care (PDC 01-0203) **Study 3** Randomised cross-over study to investigate the absolute bioavailability of intranasal sufentanil/ketamine in a standardized study set-up with healthy adult volunteers (PDC 01-0204) **Study 4** Randomised, double-blind parallel-group controlled trial to investigate the concentration-effect relationship, efficacy and dose-response of intranasal (IN) sufentanil/ketamine versus IN sufentanil, IN ketamine and IN placebo in adults, using a standardised dental impaction model (PDC 01-0205) **Study 5** A pharmacokinetic study of intranasal sufentanil/ketamine fixed combination in children 1 to less than 18 years of age undergoing elective surgery to provide PK data in children aged 1-2 years and collection of supplemental PK data in children 2-18 years (PDC 01-0206) **Study 6** Open-label, prospective study to assess safety, tolerability, analgesic effect and feasibility of intranasal sufentanil/ketamine in paediatric patients with moderate to severe pain, in the prehospital setting (PDC 01-0202)
Extrapolation, modelling and simulation studies	2	**Study 7** A modelling and simulation study building a population PK model combining adult and paediatric data (including simulations of PK after administration of multiple (two) doses of intranasal sufentanil/ketamine fixed combination in children (PDC 01-0207) **Study 8** Extrapolation of efficacy between adults and children based on similar exposure (PDC 01-0208)
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 2023
Deferral for one or more measures contained in the paediatric investigation plan:	No