MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-102374-PIP01-26

Scope of the Application

Active Substance(s)

KETAMINE HYDROCHLORIDE; SUFENTANIL CITRATE

Condition(s)

Treatment of acute pain

Pharmaceutical Form(s)

Nasal spray, solution

Route(s) of Administration

NASAL USE

Name / Corporate name of the PIP applicant

Proveca Pharma Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Proveca Pharma Limited submitted to the licensing authority on 02/07/2026 14:05 BST an application for a Paediatric Investigation Plan

The procedure started on 27/07/2026 12:29 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral.

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-102374-PIP01-26

Of 08/10/2026 16:34 BST

On the adopted decision for KETAMINE HYDROCHLORIDE; SUFENTANIL CITRATE (MHRA-102374-PIP01-26) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan).

This decision applies to a Paediatric Investigation Plan for KETAMINE HYDROCHLORIDE; SUFENTANIL CITRATE, Nasal spray, solution , NASAL USE .

This decision is addressed to Proveca Pharma Limited, 2 Dublin Landings North Wall Quay , Dublin, IRELAND, D01 V4A3

ANNEX I

1. Waiver

1.1 Condition:

Treatment of acute pain The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 1 year of age Pharmaceutical form(s): Nasal spray, solution Route(s) of administration: NASAL USE Reason for granting waiver: 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(s):

Treatment of acute pain.

2.2 Indication(s) targeted by the PIP:

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

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from 1 year to less than 18 years of age.

2.4 Pharmaceutical Form(s):

Nasal spray, solution

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable
Non-Clinical Studies	0	Not applicable
Clinical Studies	6	Study 1 (PDC 01-0201) 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. Study 2 (PDC 01-0203) 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. Study 3 (PDC 01-0204) Randomised cross-over study to investigate the absolute bioavailability of intranasal sufentanil/ketamine in a standardised study set-up with healthy adult volunteers. Study 4 (PDC 01-0205) 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. Study 5 (PDC 01-0206) 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. Study 6 (PDC 01-0202) 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 an acute care setting.
Extrapolation, Modeling & Simulation Studies	2	Study 7 (PDC 01-0207) 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. Study 8 (PDC 01-0208) Extrapolation of efficacy between adults and children based on similar exposure.
Other Studies	0	Not applicable
Other Measures	0	Not applicable

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	31/07/2025
Deferral of one or more studies contained in the paediatric investigation plan:	No