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-101342-PIP01-24-M01

Scope of the Application

Active Substance(s)

ESKETAMINE HYDROCHLORIDE

Condition(s)

Treatment of major depressive disorder (MDD)

Pharmaceutical Form(s)

Nasal spray, solution

Route(s) of Administration

INTRANASAL USE

Name / Corporate name of the PIP applicant

Janssen-Cilag Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Janssen-Cilag Ltd submitted to the licensing authority on 08/02/2024 21:31 GMT an application for a Modification

The procedure started on 08/05/2024 14:29 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-101342-PIP01-24-M01

Of 16/05/2024 07:50 BST

On the adopted decision for ESKETAMINE HYDROCHLORIDE (MHRA-101342-PIP01-24-M01) 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 Modification for ESKETAMINE HYDROCHLORIDE, Nasal spray, solution , INTRANASAL USE .

This decision is addressed to Janssen-Cilag Ltd, 50-100 Holmers Farm Way, High Wycombe, UNITED KINGDOM, HP12 4EG

ANNEX I

1. Waiver

1.1 Condition:

Treatment of major depressive disorder. The waiver applies / applied to: Paediatric Subset(s): The paediatric population from birth to less than 7 years of age. Pharmaceutical form(s): Nasal spray, solution Route(s) of administration: INTRANASAL USE Reason for granting waiver: On the grounds the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s) The waiver applies / applied to: Paediatric Subset(s): The paediatric population from 7 years to less than 12 years of age. Pharmaceutical form(s): Nasal spray, solution Route(s) of administration: INTRANASAL USE Reason for granting waiver: On the grounds the specific medicinal product is likely to be unsafe

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of major depressive disorder.

2.2 Indication(s) targeted by the PIP:

Treatment of major depressive disorder in adolescent patients with imminent risk of suicide.

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

For the paediatric population from 12 years 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	1	Study 1 (TOX13050) Neurotoxicity study in juvenile rats to explore potential brain injury.
Clinical Studies	3	Study 2 (ESKETINSUI2002) Double-blind, double-dummy, randomised dose-response study to evaluate the efficacy and safety of intranasal esketamine compared with psychoactive placebo in adolescents with major depressive disorder assessed to be at imminent risk for suicide, with an initial 8-week post-treatment follow-up as part of a full 6-month posttreatment follow-up. Study 3 (54135419SUI3003) Double-blind, double-dummy, randomised study to evaluate the efficacy and safety of intranasal esketamine compared with psychoactive placebo in adolescents with major depressive disorder assessed to be at imminent risk for suicide, with an initial 8-week post-treatment follow-up as part of a full 6-month post-treatment follow-up. Study 4 (54135419SUI3004) Open-label study to evaluate the safety of repeated doses of intranasal

		esketamine in adolescents with major depressive disorder assessed to be at risk for suicide.
Extrapolation, Modeling & Simulation Studies	1	Study 5 Population PK modelling and simulation study to identify possible covariates that have an influence on esketamine exposure after intranasal administration and to support dose selection for adolescents.
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:	30/06/2027
Deferral of one or more studies contained in the paediatric investigation plan:	Yes