EMA/313726/2019

European Medicines Agency decision

P/0238/2019

of 16 July 2019

on the acceptance of a modification of an agreed paediatric investigation plan for esketamine (hydrochloride) (EMEA-001428-PIP03-15-M01) 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 European Medicines Agency's decision P/0020/2017 issued on 31 January 2017,

Having regard to the application submitted by Janssen-Cilag International NV on 21 February 2019 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 29 May 2019, 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.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for esketamine (hydrochloride), nasal spray, solution, intranasal use, 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 Janssen-Cilag International NV, Turnhoutseweg 30, 2340 – Beerse, Belgium.

EMA/PDCO/170611/2019
Amsterdam, 29 May 2019

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-001428-PIP03-15-M01

Scope of the application

Active substance(s):

Esketamine (hydrochloride)

Condition(s):

Treatment of major depressive disorder

Pharmaceutical form(s):

Nasal spray, solution

Route(s) of administration:

Intranasal use

Name/corporate name of the PIP applicant:

Janssen-Cilag International NV

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Janssen-Cilag International NV submitted to the European Medicines Agency on 21 February 2019 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/0020/2017 issued on 31 January 2017.

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

The procedure started on 1 April 2019.

Scope of the modification

Some measures 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 in the scope set out in the Annex I of this opinion.

   The Norwegian Paediatric Committee member 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 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 major depressive disorder

The waiver applies to:

- the paediatric population from birth to less than 7 years of age;
- nasal spray, solution, intranasal use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

The waiver applies to:

- the paediatric population from 7 years to less than 12 years of age;
- nasal spray, solution, intranasal use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition:

Treatment of major depressive disorder

2.1.1. Indication(s) targeted by the PIP

Treatment of major depressive disorder (MDD) in adolescent patients at imminent risk for suicide

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

From 12 years 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	1	**Study 1:** Neurotoxicity study in juvenile rats to explore potential brain injury (TOX13050)

Area	Number of measures	Description
Clinical studies	3	**Study 2:** 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 post-treatment follow-up (ESKETINSUI2002) **Study 3:** 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 (54135419SUI3003) **Study 4:** 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 (54135419SUI3004)
Extrapolation, modelling and 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 PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By April 2026
Deferral for one or more measures contained in the paediatric investigation plan:	Yes