EMA/36031/2017

European Medicines Agency decision

P/0020/2017

of 31 January 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for esketamine (hydrochloride) (EMEA-001428-PIP03-15) 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 Janssen-Cilag International NV on 18 December 2015 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 16 December 2016, in accordance with Article 18 of Regulation (EC) No 1901/2006 and Article 21 of said Regulation 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 deferral 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 deferral.

(4) 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 esketamine (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 deferral for esketamine (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

A waiver for esketamine (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 4

This decision is addressed to Janssen-Cilag International NV, Turnhoutseweg 30, 2340 – Beerse, Belgium.

EMA/PDCO/652305/2016
London, 16 December 2016

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

EMEA-001428-PIP03-15

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 16(1) of Regulation (EC) No 1901/2006 as amended, Janssen-Cilag International NV submitted for agreement to the European Medicines Agency on 18 December 2015 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 2 February 2016.

Supplementary information was provided by the applicant on 23 September 2016. The applicant proposed modifications to the paediatric investigation plan.

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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 18 of said Regulation;
   - to grant a deferral in accordance with Article 21 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)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population; and Article 11(1)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population.

   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 major depressive disorder

The waiver applies to:

- the paediatric population from birth to less than 7 years of age;
- nasal spray, solution, for 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 to less than 12 years of age;
- nasal spray, solution, for 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 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

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 follow-up and a full 25-week 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 follow-up and a full 25-week 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