EMADOC-1700519818-1859738

European Medicines Agency decision

EMA/PE/0000224110

of 28 January 2025

on the acceptance of a modification of an agreed paediatric investigation plan for esketamine (hydrochloride), (Spravato) 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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on the acceptance of a modification of an agreed paediatric investigation plan for esketamine (hydrochloride), (Spravato) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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 Union procedures for the authorisation and supervision of medicinal products for human 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, decision P/0238/2019 issued on 16 July 2019 and the decision P/0136/2022 issued on 13 April 2022,

Having regard to the application submitted by Janssen Cilag International on 06 September 2024 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 13 December 2024, 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 and to the deferral.

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

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

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for esketamine (hydrochloride), (Spravato), including changes to the deferral, 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, Turnhoutseweg 30, 2340 - Beerse, Belgium.

EMADOC-1700519818-1848268[1]Corr
Amsterdam, 13 December 2024

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

EMA/PE/0000224110

Scope of the application

Active substance(s):

Esketamine (hydrochloride)

Invented name and authorisation status:

See Annex II

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

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Janssen Cilag International submitted to the European Medicines Agency on 6 September 2024 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, and decision P/0238/2019 issued on 16 July 2019 and the decision P/0136/2022 issued on 13 April 2022.

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

The procedure started on 14 October 2024.

[1] 14 January 2025

Scope of the modification

Some measures and timelines 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 and to the deferral in the scope set out in the Annex I of this opinion.

   The Paediatric Committee members of Liechtenstein and Norway agree 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 annexes 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 with acute suicidal ideation or behavior

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	**Description**
Quality-related studies	Not applicable.
Non-clinical studies	**Study 1:** Neurotoxicity study in juvenile rats to explore potential brain injury (TOX13050)

Clinical studies	**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:** Deleted in procedure EMA/PE/0000224110
Extrapolation, modelling and simulation studies	**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	Not applicable.
Other measures	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 December 2030
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of major depressive disorder

Authorised indication(s):

- Spravato, in combination with a SSRI or SNRI, is indicated for adults with treatment-resistant Major Depressive Disorder, who have not responded to at least two different treatments with antidepressants in the current moderate to severe depressive episode.
  - Invented name(s): Spravato
  - Authorised pharmaceutical form(s): nasal spray, solution
  - Authorised route(s) of administration: intranasal use
  - Authorised via centralised procedure
- Spravato, co-administered with oral antidepressant therapy, is indicated in adults with a moderate to severe episode of Major Depressive Disorder, as acute short-term treatment, for the rapid reduction of depressive symptoms, which according to clinical judgement constitute a psychiatric emergency.
  - Invented name(s): Spravato
  - Authorised pharmaceutical form(s): nasal spray, solution
  - Authorised route(s) of administration: intranasal use
  - Authorised via centralised procedure