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Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	March 22, 2019
Subject:	Spravato	**Page:**	1 of 6

Last Review Date: December 8, 2023

Spravato

Description

Spravato (esketamine) nasal spray

Background
Spravato (esketamine) is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist. Esketamine, the S-enantiomer of racemic ketamine, is a non-selective, non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor, an ionotropic glutamate receptor. The mechanism by which Spravato exerts its antidepressant effect is unknown (1).

Regulatory Status
FDA-approved indications: Spravato is indicated, in conjunction with an oral antidepressant, for the treatment of: (1)

- Treatment-resistant depression (TRD) in adults.
- Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior.

Limitations of Use: (1)

- The effectiveness of Spravato in preventing suicide or in reducing suicidal ideation or behavior has not been demonstrated. Use of Spravato does not preclude the need for hospitalization if clinically warranted, even if patients experience improvement after an initial dose of Spravato.
- Spravato is not approved as an anesthetic agent. The safety and effectiveness of Spravato as an anesthetic agent have not been established.

Spravato has a boxed warning regarding (1):

1. Risk for sedation, dissociation, and respiratory depression after administration. Patients should be monitored for at least two hours after administration.
2. Potential for abuse and misuse. Consider the risks and benefits of prescribing Spravato prior to using in patients at higher risk of abuse. Patients should be monitored for signs and symptoms of abuse and misuse.
3. Spravato is only available through a restricted program called the Spravato REMS.
4. Increased risk of suicidal thoughts and behaviors in pediatric and young adult patients taking antidepressants. Antidepressant-treated patients should be closely monitored for clinical worsening and emergence of suicidal thoughts and behaviors.

Evidence of therapeutic benefit should be evaluated after 4 weeks to determine need for continued treatment (1).

Spravato may cause fetal harm when administered to pregnant women. Pregnant women should be advised of the potential risk to an infant exposed to Spravato in utero. Women of reproductive potential should be advised to consider pregnancy planning and prevention (1).

The safety and effectiveness of Spravato in pediatric patients less than 18 years of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Spravato may be considered **medically necessary** if the conditions indicated below are met.

Spravato therapy may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Treatment-resistant depression
    a. Inadequate treatment response, intolerance, or contraindication to at least **TWO** different antidepressants
2. Major depressive disorder (MDD) with acute suicidal ideation or behavior

AND ALL of the following:

a. Depression was diagnosed using an approved scoring tool, such as the PHQ-9 (e.g., https://www.mdcalc.com/phq-9-patient-health-questionnaire-9)
b. Used in conjunction with an oral antidepressant
c. Administered under the supervision of a healthcare provider
d. Blood pressure will be assessed prior to and after each administration
e. Prescriber agrees to monitor for sedation, dissociation, and respiratory depression for at least two hours after administration
f. Healthcare setting, pharmacy, and patient are registered with the REMS program
g. Prescriber agrees to monitor for clinical worsening and emergence of suicidal thoughts and behaviors
h. Prescriber agrees to advise pregnant females and females of reproductive potential about the risks for fetal harm

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Treatment-resistant depression
2. Major depressive disorder (MDD) with acute suicidal ideation or behavior

AND ALL of the following:

a. Patient has been evaluated for a positive response to therapy
b. Used in conjunction with an oral antidepressant
c. Administered under the supervision of a healthcare provider
d. Blood pressure will be assessed prior to and after each administration
e. Prescriber agrees to monitor for sedation, dissociation, and respiratory depression for at least two hours after administration

f. Prescriber agrees to monitor for clinical worsening and emergence of suicidal thoughts and behaviors
g. Prescriber agrees to advise pregnant females and females of reproductive potential about the risks for fetal harm

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Diagnosis	Strength	Quantity
Treatment-resistant depression (TRD)	56 mg dose kit (two 28 mg nasal sprays) 84 mg dose kit (three 28 mg nasal sprays)	12 kits per 56 days
Major depressive disorder (MDD)	56 mg dose kit (two 28 mg nasal sprays) 84 mg dose kit (three 28 mg nasal sprays)	8 kits per 28 days

Duration 56 days for TRD
28 days for MDD

Prior – Approval *Renewal* Limits

Quantity

Diagnosis	Strength	Dosing Interval	Quantity
Treatment-resistant depression (TRD)	56 mg dose kit (two 28 mg nasal sprays) **OR** 84 mg dose kit (three 28 mg nasal sprays)	Every one to two weeks	12 kits per 84 days
Major depressive	56 mg dose kit (two 28 mg nasal sprays) **OR** 84 mg dose kit (three 28 mg nasal sprays)	Twice per week	24 kits per 84 days

disorder (MDD)			

Duration 12 months

Rationale

Summary
Spravato (esketamine) is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist. Esketamine, the S-enantiomer of racemic ketamine, is a non-selective, non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor, an ionotropic glutamate receptor. The mechanism by which Spravato exerts its antidepressant effect is unknown. The safety and effectiveness of Spravato in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Spravato while maintaining optimal therapeutic outcomes.

References
1. Spravato [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; October 2023.

Policy History

Date	Action
March 2019	Addition to PA
June 2019	Annual review. Added requirement of scoring tool such as PHQ-9 per SME
August 2020	Addition of indication: major depressive disorder (MDD) with acute suicidal ideation or behavior. Updated PHQ-9 scoring tool link
September 2020	Annual review
September 2021	Annual review
September 2022	Annual review
September 2023	Annual review
December 2023	Annual editorial review and reference update. Per PI update, added requirement to monitor for respiratory depression

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.