



5.60.033

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| <b>Section:</b>    | Prescription Drugs           | <b>Effective Date:</b>       | January 1, 2025 |
| <b>Subsection:</b> | Central Nervous System Drugs | <b>Original Policy Date:</b> | March 22, 2019  |
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**Last Review Date:** December 13, 2024

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## Spravato

### Description

#### Spravato (esketamine) nasal spray

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#### 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):

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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).

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## Related policies

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### 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 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:

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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

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## 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

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- 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)   | 12 kits per 56 days |
|                                      | 84 mg dose kit (three 28 mg nasal sprays) |                     |
| Major depressive disorder (MDD)      | 56 mg dose kit (two 28 mg nasal sprays)   | 8 kits per 28 days  |
|                                      | 84 mg dose kit (three 28 mg nasal sprays) |                     |

**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)         | Every one to two weeks | 12 kits per 84 days |
|                                      | OR<br>84 mg dose kit (three 28 mg nasal sprays) |                        |                     |
| Major depressive                     | 56 mg dose kit (two 28 mg nasal sprays)         | Twice per week         | 24 kits per 84 days |
|                                      | OR<br>84 mg dose kit (three 28 mg nasal sprays) |                        |                     |

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| disorder<br>(MDD) |  |  |  |
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**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              |
| September 2024 | Annual review   |
| December 2024  | Annual review   |

## Keywords

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**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.**