

**Addendum to Protocol for Spravato® (esketamine) Nasal Spray
April 2025**

DURB Approval Date	7/2020, 1/2022, 4/2025
Commissioners Approval Date	5/2021, 11/2022

Background:

Spravato nasal spray is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist indicated for the treatment of treatment-resistant depression (TRD) in adults as monotherapy or in conjunction with an oral antidepressant and for the treatment of depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior in conjunction with an oral antidepressant.

This protocol is being updated to add criteria to allow for monotherapy of Spravato nasal spray for the indication of treatment resistant depression.

Criteria for approval:

1. Patient is of the FDA-labeled or compendial approved age
2. Patient was assessed and determined not to be at risk for abuse and misuse of Spravato nasal spray
3. Patient does not have any of the following contraindications to therapy:
 - a) Aneurysmal vascular disease (including in the brain, chest and abdominal aorta, and peripheral arterial vessels), **OR**
 - b) Arteriovenous malformation, **OR**
 - c) History of bleeding in the brain
4. Spravato nasal spray is being administered under the supervision of a healthcare provider and the patient is going to be appropriately monitored for at least 2 hours after administration
5. Patient has ONE of the following diagnoses:
 - a) Treatment-resistant depression, **OR**
 - b) Depressive symptoms with major depressive disorder (MDD) with acute suicidal ideation or behavior
6. Treatment-resistant depression is defined by the patient having documentation demonstrating a therapeutic failure of at least two (2) different classes of antidepressants at optimal therapeutic dosages each for a minimum of 4 weeks unless the patient has contraindications to all antidepressants
7. For the diagnosis of MDD with suicidal ideation or behavior, patient is using Spravato nasal spray in conjunction with an oral antidepressant therapy

8. The medication requested is prescribed in accordance with a Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with a medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence

Continuation of therapy:

1. Patient is using Spravato nasal spray in conjunction with an oral antidepressant therapy for the treatment of MDD with suicidal ideation or behavior
2. Spravato nasal spray is being administered under the supervision of a healthcare provider and the patient is going to be appropriately monitored for at least 2 hours after administration
3. Documentation showing the patient responded to therapy is demonstrated by an improvement from baseline in a clinician-rated tool/scale (e.g., The Montgomery-Asberg Depression Rating Scale (MADRS), Beck Depression Inventory, or Hamilton Depression Rating Scale)
4. The medication requested is prescribed in accordance with a Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with a medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Lexi-Drugs, national guidelines, or other peer-reviewed evidence

Approval Durations:Initial approval:

3 months for the treatment of TRD or 1 month for the treatment of MDD with acute suicidal ideation or behavior.

Renewal approval:

- TRD: 6 months
- MDD with acute suicidal ideation or behavior: The use of Spravato beyond 4 weeks has not been systematically evaluated in the treatment of depressive symptoms in patients with MDD with acute suicidal ideation or behavior. Member must meet all requirements in the coverage criteria section for approval.

Quantity Level Limit: Reference Formulary for drug specific quantity level limits

Warning: Because of the risks of serious adverse outcomes resulting from sedation, dissociation, abuse and misuse.

References:

1. Spravato [package insert]. Janssen Pharmaceuticals, Inc., Titusville, NJ 08560. January 2025. Accessed February 4, 2025
2. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier

2025. Updated periodically

3. Canuso C, Singh J, et al: Efficacy and Safety of Intranasal Esketamine for the Rapid Reduction of Symptoms of Depression and Suicidality in Patients at Imminent Risk for Suicide: Results of a Double-Blind, Randomized, Placebo-Controlled Study. *Am J Psychiatry*. 2018. Accessed online on May 24, 2019 at: <https://adaa.org/sites/default/files/Canuso-AJP-2018.pdf>
4. Practice guideline for the treatment of patients with major depressive disorder (revision). American Psychiatric Association. *Am J Psychiatry*. 2010:1-152. URL: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf Accessed February 5, 2025