Generic Name: esketamine

Applicable Drugs: Spravato

Preferred: N/A

Non-preferred: N/A

Date of Origin: 8/27/2024

Date Last Reviewed / Revised: 9/25/2025

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through IV are met)

I. Documented diagnosis of one of the following conditions A or B AND must meet criteria listed under applicable diagnosis:

A. Treatment-resistant depression (TRD)

i. Minimum age requirement: 18 years old.

ii. Documented baseline scoring on at least one of the following clinical assessments:

1. Hamilton Rating Scale for Depression (HAMD17)
2. Quick Inventory of Depressive Symptomatology (QIDS-C16)
3. Montgomery-Asberg Depression Rating Scale (MADRS)
4. Patient Health Questionnaire (PHQ-9)

iii. Documented clinically significant treatment failure with five or more antidepressant medications or regimens. Treatment failure is defined as not achieving a therapeutic response despite using the medications at optimized doses for at least 8 weeks. The medications must be from at least three of the following drug categories, or the member must have contraindications to all drug categories listed:

1. Selective serotonin reuptake inhibitor (SSRIs) (e.g., escitalopram, fluoxetine, paroxetine, sertraline)
2. Serotonin-norepinephrine reuptake inhibitors (SNRIs) (e.g., duloxetine, venlafaxine)
3. Bupropion
4. Tricyclic antidepressants (TCAs) (e.g., amitriptyline, nortriptyline)
5. Mirtazapine
6. Monoamine oxidase inhibitors (MAOIs) (e.g., selegiline)

iv. Documentation that at least one of the five or more antidepressant trials (as defined in criterion iii above) included concomitant treatment with augmentation therapy at an optimized dose for a minimum of 8 weeks. Augmentation therapy is defined as the concomitant use of:

1. One or more antidepressant(s) and a second-generation antipsychotic
2. One or more antidepressant(s) and lithium
3. One or more antidepressant(s) and an anticonvulsant

B. Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior

i. Diagnosis of major depressive disorder according to current DSM criteria.

ii. Documentation that patient is experiencing acute suicidal ideation or behavior.

iii. Documentation that patient is currently taking or is newly initiated on an oral antidepressant, and that Spravato will be used in conjunction with this antidepressant.

II. Treatment must be prescribed by or in consultation with a psychiatrist, and the provider or the provider's healthcare setting is certified in the Spravato REMS program.

III. Request is for a medication with the appropriate FDA labeling, or its use is supported by current clinical practice guidelines.

IV. Refer to the plan document for the list of preferred products. If the requested agent is not listed as a preferred product, must have documented treatment failure or contraindication to the preferred product(s).

EXCLUSION CRITERIA

- Aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial and peripheral arterial vessels) or arteriovenous malformation.
- Intracerebral hemorrhage.
- Hypersensitivity to esketamine, ketamine, or any of the excipients.

OTHER CRITERIA

- Recommended dosage for treatment-resistant depression:

SPRAVATO® (esketamine) nasal spray, CIII

Table 1: Recommended Dosage for SPRAVATO for TRD

		Adults
Induction Phase	**Weeks 1 to 4:**	
	Administer twice per week	56 mg or 84 mg
Maintenance Phase	**Weeks 5 to 8:**	
	Administer once weekly	56 mg or 84 mg
	Week 9 and after:	
	Administer every 2 weeks or once weekly*	56 mg or 84 mg

* Dosing frequency should be individualized to the least frequent dosing to maintain remission/response.

- Recommended dosage for MDD with acute suicidal ideation or behavior: 84 mg twice per week for 4 weeks. Dosage may be reduced to 56 mg twice per week based on tolerability.
- Spravato is available in 56 mg or 84 mg dose kits, containing either two or three 28 mg nasal spray devices, respectively.

QUANTITY / DAYS SUPPLY RESTRICTIONS

- Treatment-resistant depression (TRD):
  - Induction (Weeks 1 to 4): two dose kits (4 to 6 devices) per 7 days
  - Weeks 5 to 8: one dose kit (2 to 3 devices) per 7 days
  - Week 9 and thereafter: one dose kit (2 to 3 devices) per 14 days, or one dose kit (2 to 3 devices) per 7 days with clinical justification of medical necessity for weekly dosing.
- MDD with acute suicidal ideation or behavior: eight dose kits (24 devices) per 28 days

APPROVAL LENGTH

- **Authorization:**
  - Treatment-resistant depression (TRD): 3 months
  - MDD with acute suicidal ideation or behavior: 4 weeks.
- **Re-Authorization:**
  - Treatment-resistant depression: 6 months, with an updated letter of medical necessity or progress notes showing that current medical necessity criteria are met and that the

medication is effective, as evidenced by score improvement from baseline on clinical assessment(s).

- MDD with acute suicidal ideation or behavior: no reauthorization.
  - The use of Spravato, in conjunction with an oral antidepressant, beyond 4 weeks has not been systematically evaluated in the treatment of depressive symptoms in patients with MDD with acute suicidal ideation or behavior.

APPENDIX

N/A

REFERENCES

1. Spravato. Prescribing Information. Janssen Pharmaceuticals Inc.; April 2025. Accessed September 25, 2025. https://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/SPRAVATO-pi.pdf.
2. American Psychiatric Association (APA). Practice guideline for the treatment of patients with major depressive disorder. 3rd ed. Arlington (VA): American Psychiatric Association (APA); 2010 Oct.
3. Canuso CM, Singh JB, Fedgchin M, 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 Jul 1;175(7):620-630. https://doi.org/10.1176/appi.ajp.2018.17060720.
4. Popova V, Daly EJ, Trivedi M, et al. Efficacy and Safety of Flexibly Dosed Esketamine Nasal Spray Combined With a Newly Initiated Oral Antidepressant in Treatment-Resistant Depression: A Randomized Double-Blind Active-Controlled Study. *Am J Psychiatry*. 2019 Jun 1;176(6):428-438. https://doi.org/10.1176/appi.ajp.2019.19020172.
5. Fu DJ, Ionescu DF, Li X, et al. Esketamine Nasal Spray for Rapid Reduction of Major Depressive Disorder Symptoms in Patients Who Have Active Suicidal Ideation With Intent: Double-Blind, Randomized Study (ASPIRE I). *J Clin Psychiatry*. 2020 May 12;81(3):19m13191. https://doi.org/10.4088/JCP.19m13191.
6. Ionescu DF, Fu DJ, Qiu X, et al. Esketamine Nasal Spray for Rapid Reduction of Depressive Symptoms in Patients With Major Depressive Disorder Who Have Active Suicide Ideation With Intent: Results of a Phase 3, Double-Blind, Randomized Study (ASPIRE II), International Journal of Neuropsychopharmacology, pyaa068