Spravato (esketamine)

Meets Primary Coverage Criteria or Is Covered for Contracts Without Primary Coverage Criteria

INITIAL AUTHORIZATION FOR 28 DAYS

Esketamine meets member benefit certificate primary coverage criteria that there be scientific evidence of effectiveness in improving health outcomes for the treatment of each indication when **ALL** the following conditions are met.

Treatment-Resistant Depression (TRD) in adults

1. Individual is 18 years of age or older; **AND**

2. Individual meets the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) criteria for a major depressive episode by a structured clinical interview for DSM-5 disorders (NIMH, 2017); **AND**

3. Individual's current depressive episode is considered severe depression based on either of the following (NIMH, 2017; Canuso, 2018):
    a. Montgomery-Asberg Depression Rating Scale (MADRS) ≥35 (see policy guidelines); **OR**
    b. Hamilton Rating Scale for Depression (HAM-D) score ≥24 (see policy guidelines); **OR**
    c. Patient Health Questionnaire (PHQ-9) score ≥20 (see policy guidelines); **OR**
    d. Other standardized clinician administered rating scale indicating severe depression.

4. Individual meets the following (FDA Spravato, 2019; Canuso, 2018):
Recently (e.g., < 2 years) and/or currently has tried and had an inadequate response to three antidepressant agents from 3 different antidepressant classes (i.e., selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, tricyclic antidepressants, bupropion, or mirtazapine). An adequate trial of an antidepressant is defined by BOTH of the following:
    a. The trial length was at least 6 weeks at generally accepted doses or of sufficient duration as determined by the treating physician at the generally accepted doses; **AND**
    b. Individual was ≥80% adherent to the agent during the trial; **AND**

5. Individual will receive esketamine nasal spray in conjunction with an oral antidepressant that is different from previous therapies (FDA Spravato, 2019; Canuso, 2018); **AND**

6. Individual does not have current substance use disorder unless in remission (complete abstinence for a month, **with a negative drug and alcohol screen**) (Canuso, 2018); **AND**

7. Individual does **NOT** have any Food and Drug Administration (FDA) labeled contraindications to the requested agent (FDA Spravato, 2019):
    a. Aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial and peripheral arterial vessels) or arteriovenous malformation.
    b. Intracerebral hemorrhage.
    c. Hypersensitivity to esketamine, ketamine, or any of the excipients; **AND**

8. Esketamine nasal spray is intended to be used consistently with the FDA approved label including meeting Spravato Risk Evaluation and Mitigation Strategy (REMS) program requirements; **AND**

9. The prescriber is a physician specialist in the area of the individual's diagnosis (e.g., psychiatrist); **AND**

10. Must be dosed in accordance with the FDA label. See dosing guidelines below.

REAUTHORIZATION for 3 months, with review then reauthorized annually

Esketamine nasal spray may be reauthorized for up to 3 months, with review. May then be approved annually if **ALL** the following conditions are met (FDA Spravato, 2019; Canuso, 2018):

1. Individual has had improvement in depression symptoms as evaluated with an appropriate depression rating scale (e.g., Patient Health Questionnaire-9, Clinically Useful Depression Outcome Scale, Quick Inventory of Depressive Symptomatology-Self Report 16 Item, MADRS, HAM-D); **AND**

2. Individual is to receive esketamine nasal spray in conjunction with an oral antidepressant; **AND**

3. Individual does not have current substance use disorder (**with a negative drug and alcohol screen); AND**

4. Individual does **NOT** develop any FDA labeled contraindications to the requested agent and esketamine nasal spray is intended to be used consistently with the FDA approved label (see policy guidelines) including meeting Spravato REMS program requirements.

Treatment of depressive symptoms in adults with major depressive disorder with acute suicidal ideation or behavior:

AUTHORIZATION FOR 28 DAYS FROM THE START OF THERAPY

1. Individual is 18 years of age or older; **AND**

2. Individual has a diagnosis of major depressive disorder; **AND**

3. Esketamine was **initiated** in the Emergency Department or inpatient facility upon diagnosis of major depressive disorder with acute suicidal ideation or behavior (documentation submitted); **AND**

4. Individual will receive esketamine nasal spray in conjunction with a new oral antidepressant or optimizing the current regimen; **AND**

5. Individual does not have current substance use disorder unless in remission (complete abstinence for a month, **with a negative drug and alcohol screen; AND**

6. Individual does **NOT** have any Food and Drug Administration (FDA) labeled contraindications to the requested agent:

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

7. Esketamine nasal spray is intended to be used consistently with the FDA approved label including meeting Spravato Risk Evaluation and Mitigation Strategy (REMS) program requirements; **AND**

8. The prescriber is a physician specialist in the area of the individual's diagnosis (e.g., psychiatrist); **AND**

9. Must be dosed in accordance with the FDA label. See dosing guidelines below.

***Montgomery-Asberg Depression Rating Scale (MADRS)**
MADRS is commonly used to evaluate the efficacy of antidepressant by assessing the severity of depression. It contains 10 items and the total score ranges from 0 to 60. The following cut-offs were proposed to classify the level of depression severity:

- 0-6: No depression (absence of symptoms)
- 7-19: Mild depression
- 20-34: Moderate depression
- 35-62: Severe depression

**** Hamilton Rating Scale for Depression (HAM-D)**
HAM-D is a 17-item rating scale to determine the severity level of depression in an individual before, during and after treatment. The total score ranges from 0 to 52, with the score corresponding to the following classifications:

- 0-7 No depression (normal)
- 8-16: Mild depression
- 17-23: Moderate depression
- ≥24: Severe depression

*****Patient Health Questionnaire (PHQ-9)**

0 to 4 points:	No depression
5 to 9 points:	Mild depression
10 to 14 points:	Moderate depression
15 to 19 points:	Moderately severe depression
20 to 27 points:	Severe depression

Dosing per FDA Guidelines

Esketamine must be administered under the direct supervision of a healthcare provider. Each treatment session consists of nasal administration of Esketamine and a 2-hour post administration observation under supervision.

Recommended Dosage for Esketamine in Treatment Resistance Depression:

Induction Phase Weeks 1 – 4: Administer twice per week
Starting dose: 56mg
Subsequent doses: 56mg or 84mg

Maintenance Phase
Weeks 5 – 8: Administer once weekly
56mg or 84mg

Week 9 and after: Administer every 2 weeks or once weekly*
56mg or 84mg

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

Recommended Dosage of Esketamine in Depressive Symptoms in Individuals with Major Depressive disorder with Acute Suicidal Ideation or Behavior:

84 mg twice per week for 4 weeks. Dosage may be reduced to 56mg twice per week based on tolerability.

Esketamine is available in nasal spray with 28 mg per device. Each nasal spray device delivers two containing a total of 28 mg of esketamine.

Quantity Limits

Treatment-Resistant Depression (TRD)

	Initial 28 days	Maintenance (starting week 5)
Spravato 56mg	8 doses (16 devices)	4 doses (8 devices) / 30 days
Spravato 84mg	7 doses (21 devices)	4 doses (12 devices) / 30 days

Major Depressive disorder with Acute Suicidal Ideation or Behavior (MDSI)*

	28 days (4 weeks)
Spravato 56mg	8 doses (24 devices)
Spravato 84mg	8 doses (16 devices)

*Maintenance dosing unavailable. Treatment beyond 4 weeks has not been systematically evaluated.

Does Not Meet Primary Coverage Criteria Or Is Investigational For Contracts Without Primary Coverage Criteria

Esketamine, for any indication or circumstance not described above, does not meet member benefit certificate primary coverage criteria that there be scientific evidence of effectiveness in improving health outcomes.

For members with contracts without primary coverage criteria, Esketamine, for any indication or circumstance not described above, is considered **investigational**. **Investigational** services are specific contract exclusions in most member benefit certificates of coverage.