Medical Coverage Policy
Policy Number – MP22-026E
Original review date – 08/01/22
Effective date – 11/27/2024

Spravato (Esketamine) nasal spray

Background

Esketamine is the S-enantiomer of ketamine. It is a Non-competitive -Methyl -Aspartate (NDMA) receptor antagonist. Evidence suggests that this receptor antagonism transiently increases the activity of glutamergic neurons, including the presynaptic release of glutamate. As a result, there is activation of downstream neurotrophic intracellular signaling pathways, leading to improved synaptic connectivity. The exact mechanism of anti-depressant activity is unclear; however, it is surmised that the increased synaptic connectivity as a result of glutamate increase, has a role to play in mood elevation.

Esketamine is administered as an intranasal spray under direct supervision of a healthcare provider. Supervision includes two hours of post-administration supervision. Spravato™ nasal spray delivers a total of 28 mg of esketamine. To deliver 56 mg of esketamine, two devices are used. Three devices are required to deliver 84 mg of esketamine.

Policy statement

Disclaimer: This policy is applicable to TRICARE Prime and Select beneficiaries and may not apply to Active Duty Service Members (ADSM) under Supplemental Health Care Program (SHCP) or TRICARE Prime Remote (TPR) in accordance with TRICARE Operations Manual (TOM) Chapter 17, Section 3. Please review TOM Chapter 17, Section 3, Paragraph 2.0 onwards, regarding SHCP coverage and any TRICARE-specific exclusions included in this coverage policy to accurately determine the benefit for ADSMs.

Esketamine nasal spray is FDA-approved for the following indications:

I. Treatment resistant depression, if the following criteria are met:
   a. Patient is at least 18 years of age
   b. Patient has a clinical diagnosis of major depressive disorder as evidenced by an appropriate depression rating scale (for e.g., PHQ-9, HAM-D). *Submission of evidence based rating scale is required to assess response to treatment*
   c. Documented evidence of adherence to treatment and patient has inadequate response from or intolerance to at least two different antidepressants of adequate dose and duration in the current depressive episode from the following groups of antidepressants:
      i. Selective Serotonin Reuptake Inhibitors (for e.g., fluoxetine, sertraline, citalopram)
      ii. Serotonin and Norepinephrine Reuptake Inhibitors (for e.g., venlafaxine, duloxetine)
      iii. Buproprion
      iv. Mirtazapine
   d. Esketamine will be used in conjunction with an oral antidepressant

e. Patient has not had vagal nerve stimulation, or deep brain stimulation in the current depressive episode
f. Patient has not had a full treatment of electroconvulsive therapy (defined as at least seven treatments) in the current depressive episode
g. No aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial, and peripheral arterial vessels)
h. No arteriovenous malformations
i. No history of intracerebral hemorrhage
j. No active psychosis
k. Patient is not pregnant or breast-feeding
l. No history of hypersensitivity to esketamine, ketamine, or any of the excipients
m. Healthcare facility is enrolled in Spravato Risk Evaluation and Mitigation Strategy Program (REMS)

II. Major depressive disorder with acute suicidal ideation, if the following criteria are met:
a. Patient is at least 18 years of age
b. Patient has a clinical diagnosis of moderate to severe major depressive disorder, as as evidenced by an appropriate depression rating scale (for e.g., PHQ-9, HAM-D). *Submission of evidence based rating scale is required to assess response to treatment*
c. Patient has active suicidal ideation and intent
d. Esketamine will be used in conjunction with an oral antidepressant
e. Patient has not had vagal nerve stimulation or deep brain stimulation in the current depressive episode
f. Patient has not had a full treatment of electroconvulsive therapy (defined as at least seven treatments) in the current depressive episode
g. No aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial, and peripheral arterial vessels)
h. No arteriovenous malformations
i. No history of intracerebral hemorrhage
j. No active psychosis
k. Patient is not pregnant or breast-feeding
l. No history of hypersensitivity to Esketamine, ketamine or any of the excipients
m. Healthcare facility is enrolled in Spravato Risk Evaluation and Mitigation Strategy Program (REMS)

Limitations of coverage

I. Esketamine may only be administered at a healthcare setting enrolled in the Esketamine Risk Evaluation and Mitigation Strategy (REMS) program
II. Esketamine must be administered intranasally under the direct supervision of a healthcare provider, along with two hours of monitoring by healthcare provider post-administration
III. Only FDA approved indications of esketamine will be covered per TRICARE policy
IV. Esketamine compounded with other medications will not be covered since it is not FDA approved
V. Ketamine, administered in any form, is not covered for the treatment of depression per TRICARE policy

Dosage

Treatment resistant depression

Induction phase:

Week	**Dosage**
Weeks one-four	56mg twice a week OR 84 mg twice a week

Evidence of therapeutic benefit should be evaluated at the end of the induction phase to determine need for continued treatment with esketamine.

Maintenance phase:

Week	**Dosage**
Weeks five-eight	56 mg once a week OR 84 mg once a week

Week nine onwards: 56mg or 84 mg once a week or once in two weeks. Dosing frequency should be individualized to the least frequent dosing to maintain remission.

Initial authorization will be given for 8 weeks. **Reauthorization for three months at a time will be based on continued need and improvement in symptoms based on an objective depression rating scale**

Major depressive disorder with acute suicidal ideation

Week	**Dosage**
Weeks one-four	84 mg (or 56 mg based on tolerability) twice a week

Dose may be reduced to 56mg twice a week based on tolerability. Continuation of treatment beyond 28 days is considered investigational due to insufficient evidence.

Coding guidelines

NOTE: G2082/G2083 codes are for the drug as well as two hours post-administration observation.

The following will be the maximum units approvable.
Treatment-resistant depression
Initial authorization for eight weeks of treatment (induction): G2082/G2083 – 12 units total
Both G2082 and G2083, in any combination of units, can be authorized for eight weeks.
Total number of units authorized (for both codes combined) for eight weeks will be 12.
Reauthorization for three months: G2082/G2083 – 12 units total

Both G2082 and G2083, in any combination of units, can be authorized for three months.
Total number of units authorized (for both codes combined) for three months weeks will be 12.

Major depressive disorder with acute suicidal ideation
G2082/G2083 – eight units total. Authorization will be for four weeks of treatment only

TRICARE Policy Manual (TPM)
Chapter 7, Section 3.8
5.2.14 Spravato™ (**Esketamine**) nasal spray (CPT codes G2082-83) for the treatment of treatment-resistant depression and other U.S. Food and Drug Administration (FDA) approved indications , which is available to providers from the FDA's Spravato™ Risk Evaluation and Mitigation Strategy (REMS) Program, may be cost-shared. Reimbursement is limited to CPT codes G2082-83 and does encompass administration of the drug and post-administration observation services. Providers shall not bill solely for Spravato™ (HCPCS code S0013), as payment for the drug is included in CPT codes G2082-83 reimbursement. Preauthorization under the medical benefit is required. See Chapter 1, Section 6.1 and TOM, Chapter 7, Section 2 . Preauthorization under the medical benefit is required. See Chapter 1, Section 6.1 and TOM, Chapter 7, Section 2
7.5 Off-label use of **Spravato**™ (esketamine) is excluded.

Tricare Policy Manual TPM Ch 1 section 6.1,
1.14 Effective March 5, 2019, Spravato™ (esketamine) nasal spray shall require preauthorization under the medical benefit in accordance with Chapter 7, Section 3.8 and TOM, Chapter 7, Section 2.

Coding information

Code	Description
G2082	Office or other outpatient visit for the evaluation and management of an established patient that requires the supervision of a physician or other qualified health care professional and provision of up to 56 mg of esketamine nasal self administration, includes two hours post administration observation
G2083	Office or other outpatient visit for the evaluation and management of an established patient that requires the supervision of a physician or other qualified healthcare professional and provision of greater than 56 mg esketamine nasal self administration, includes two hours post administration observation

References

1. TRICARE Operations Manual Chapter 7, Section 3.8 TRICARE Manuals - Display Chap 7 Sect 3.8 (Change 118, Sep 25, 2023) (health.mil)
2. MCG Health. Behavioral Health Care. 28th edition. Esketamine ORG: B-007-Rx (BHG) Last update: 03/14/2024
3. Spravato™ Label 211243Orig1s000Lbl.pdf (fda.gov)
4. Hayes Inc. Esketamine (Spravato) for Treatment Resistant Major Depressive Disorder. Annual Review 01/27/2023
5. Center for Drug Evaluation and Research. Clinical Review – Spravato 211243Orig1s000MedR.pdf (fda.gov)

Revision History

December 2023: Updated references

November 2024: Updated coding and references

Approved by:

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Chief Medical Officer

Date of approval: 11/27/2024