Spravato (esketamine)
Policy Number: C16762-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DUE BY OR BEFORE
5/1/2019	12/16/2020	1/26/2022
HCPCS CODING	**TYPE OF CRITERIA**	**LAST P&T APPROVAL/VERSION**
S0013- Esketamine, nasal spray, 1 mg	RxPA	Q1 2021 20210127C16762-A

PRODUCTS AFFECTED:
Spravato (esketamine)

DRUG CLASS:
NMDA receptor antagonist

ROUTE OF ADMINISTRATION:
Intranasal

PLACE OF SERVICE:
Specialty Pharmacy

AVAILABLE DOSAGE FORMS:
Spravato intranasal spray: 1 device (28 mg/0.2 mL)

FDA-APPROVED USES:
SPRAVATO is indicated, in conjunction with an oral antidepressant, for the treatment of treatment- resistant depression (TRD) in adults and depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior.
Limitations of Use:
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.

COMPENDIAL APPROVED OFF-LABELED USES:
None

COVERAGE CRITERIA: INITIAL AUTHORIZATION DIAGNOSIS:
Major depressive disorder, treatment resistant.

REQUIRED MEDICAL INFORMATION:
A. MAJOR DEPRESSIVE DISORDER, TREATMENT-RESISTANT (TR-MDD), INITIAL:
(IF PATIENT IS CONTINUING SPRAVATO (ESKATAMINE) THERAPY WITHIN 24-48 HOURS POST INPATIENT DISCHARGE, AUTHORIZATION WILL BE PROVIDED FOR 4 weeks.

1. Documented diagnosis of major depressive disorder (MDD) or recurrent MDD, without

psychotic features

2. Prescriber attestation that the member's baseline depression symptoms are measured and documented with an appropriate rating scale (such as PHQ-9, Clinically Useful Depression Outcome Scale, Quick Inventory of Depressive Symptomatology-Self Report 16 Item, MADRS, HAM-D) or Hamilton Depression Rating Scale (HDRS) as a tool for monitoring response to therapy
   AND
3. Documentation that member has had a trial (minimum of 6 consistent weeks of therapy) and failure of monotherapy treatments (or labeled contraindications to all agents in class) from TWO formulary drugs from ANY of these drug class: Selective serotonin reuptake inhibitor, Serotonin- norepinephrine reuptake inhibitor, Atypical antidepressant, Serotonin modulator, Tricyclic antidepressant OR Monoamine oxidase inhibitor
   AND
4. Documentation that member will be on a concomitant oral SSRI or SNRI for full duration of Spravato therapy OR if previous trial, failure or contraindication to SSRI/SNRI, concomitant use of ONE oral antidepressant
   AND
5. Documentation of baseline blood pressure along with history of any cardiovascular disease, aneurysmal vascular disease, stroke or intracerebral hemorrhage.
   AND
6. Provider attests to provide appropriate pre- and post-dose monitoring (at least 2 hours) for blood pressure, sedation, and dissociative symptoms in presence of healthcare provider.
   AND
7. Prescriber attestation there will be~~fore~~ appropriate monitoring for persistent worsening of depression or the emergence of suicidal thoughts and behaviors.
   AND
8. Prescriber attests that Spravato will be administered at a treatment facility that is certified through the REMS program and that the member has been enrolled in the REMS program

B. MAJOR DEPRESSIVE DISORDER, with acute suicidal ideation or behavior.:
(IF PATIENT IS CONTINUING SPRAVATO (ESKATAMINE) THERAPY WITHIN 24-28 HOURS POST INPATIENT DISCHARGE, AUTHORIZATION WILL BE PROVIDED FOR 4 weeks.

1. Documented diagnosis of major depressive disorder (MDD) or recurrent MDD, with acute suicidal ideation or behavior
   AND
2. Prescriber attestation that the member's baseline depression symptoms will be measured and documented with an appropriate rating scale (such as PHQ-9, Clinically Useful Depression Outcome Scale, Quick Inventory of Depressive Symptomatology-Self Report 16 Item, MADRS, HAM-D) or Hamilton Depression Rating Scale (HDRS) as a tool for monitoring response to therapy
   AND
3. Documentation that member is/had recently (within the last 5 days) discharged from acute or subacute inpatient care for suicidality
   AND
4. Documentation that member is prescribed in combination with initiation or optimization of oral antidepressant therapy
   AND
5. Prescriber attests to baseline blood pressure monitoring for any member with history of any cardiovascular disease, aneurysmal vascular disease, stroke or intracerebral hemorrhage AND will provide appropriate pre- and post- dose monitoring (at least 2 hours) for blood pressure, sedation, and dissociative symptoms in presence of healthcare provider AND monitoring for persistent worsening of depression or the emergence of suicidal thoughts and behaviors.
   AND
6. Prescriber attests that Spravato will be administered at a treatment facility that is certified

through the REMS program and that the member has been enrolled in the REMS program

DURATION OF APPROVAL:
Treatment-Resistant Depression: Initial authorization: 4 weeks, Continuing of therapy: 6 months

Depressive Symptoms in Patients with Major Depressive Disorder with Acute Suicidal Ideation or Behavior: Initial authorization: 4 weeks, Continuation of therapy: N/A- 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.

QUANTITY:
Treatment-Resistant Depression: 28 mg per device. Induction Phase: Week 1-4 (Dosing: Day 1 56mg THEN 56 OR 84 mg twice per week) THEN, Maintenance Phase: Weeks 5-8 (Dosing: 56 OR 84 mg once weekly); THEN Week 9 and after: 56 OR 84 mg every 2 weeks or ONCE weekly

Depressive Symptoms in Patients with Major Depressive Disorder 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.

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a psychiatrist or behavioral health specialist.

AGE RESTRICTIONS:
18 years of age and older

CONTINUATION OF THERAPY:
A. MAJOR DEPRESSIVE DISORDER TREATMENT-RESISTANT (TR-MDD):

1. Documentation of a positive response to therapy evidenced by improvement in depression symptoms measured by the same rating scale used at baseline.
   AND
2. Prescriber attests to continued appropriate monitoring for worsening of depression or emergence of suicidal thoughts and behavior and signs of potential drug abuse. AND
3. Prescriber attests to continued pre- and post-dose monitoring for blood pressure, dissociation, and sedation in presence of healthcare provider.

B. MAJOR DEPRESSIVE DISORDER WITH ACUTE SUICIDAL IDEATION OR BEHAVIOR: NA

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Spravato (esketamine) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications include hypersensitivity to Spravato, aneurysmal vascular disease, and history of intracerebral hemorrhage.

OTHER SPECIAL CONSIDERATIONS:
Spravato is a schedule III-controlled substance.

BACKGROUND:

Major depressive disorder (MDD) is a behavioral disorder defined as when an individual experiences one or more major depressive episodes without a history of manic, mixed, or hypomanic episodes. Treatment resistant depression is defined as major depressive episodes that do not respond to two adequate trials of antidepressant therapy. MDD patients are 2x at risk of developing cardiovascular disease.1st line treatment consists of psychotherapy with or without SSRI/SNRIs (take 4-8 weeks for full effect), Mirtazapine, or Bupropion (APA 2010 guidelines). 2nd line recommendations include switching to a different medication or adding on another antidepressant with a different mechanism, or an atypical antipsychotic. Add-on therapy can include TCAs, lithium, triiodothyronine. Last line treatment-resistant therapy can consist of MAOIs or ECT.

Spravato is indicated for treatment-resistant depression. It's unique mechanism of action offers an alternative to treatment-failed patients who have tried oral monotherapy. It is a schedule III- controlled substance due to potential for abuse and misuse. Two studies (short-term and long-term) were evaluated by the FDA for approval of Spravato. The short-term study was a 4-week trial with primary efficacy endpoint of improvement in MADRS (Montgomery Adams Depression Rating Scale) score, and Spravato demonstrated superiority over placebo in reduction of MADRS score. The long- term study lasted more than 80 weeks and placebo-controlled. Spravato demonstrated superiority over placebo in primary efficacy endpoint of maintaining remission in therapy. Participants relapsed in the placebo group at quicker and higher rates. In both trials, Spravato and placebo nasal spray were administered with an oral antidepressant of choice between the following: duloxetine, escitalopram, sertraline, or venlafaxine with goal of maximally titrated doses.

APPENDIX:

PHQ-9, MADRS, and HAM-D Rating Scales

The MADRS is a 10-item diagnostic questionnaire used to measure the severity of depressive episodes in patients with mood disorders.

MADRS Score Depression	**Rating**
0 – 6	Normal/symptom absent
7 – 19	Mild depression
20 – 34	Moderate depression
> 34	Severe depression

The PHQ-9 is a 9-item multiple choice questionnaire used for diagnosis, screening, monitoring and measuring the severity of depression.

PHQ-9 Score Depression	**Severity**
5 – 9	Minimal symptoms
10 – 14	Minor depression Major depression, mild
15 – 19	Major depression, moderately severe
> 20	Major depression, severe

The HAM-D17 scale is a 17-item depression assessment scale to assess severity of, and change in, depressive symptoms.

HAM-D Score	**Depression Rating**
0 – 7	Normal, absence or remission of depression
8 – 16	Mild depression
17 – 23	Moderate depression
> 24	Severe depression

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

REFERENCES:

1. Spravato (esketamine) [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc; July 2020
2. Yonkers KA, Wisner KL, Stewart DE, et al. The management of depression during pregnancy: a reportfrom the American Psychiatric Association and the American College of Obstetricians and Gynecologists. Obstet Gynecol. 2009;114(3):703-713.
3. Gelenberg AJ, Freeman MP, Markowitz JC. Practice Guideline for the Treatment of Patients with Major Depressive Disorder, Third Edition. American Psychiatric Association. 2010: pg(s) 31-40. American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder, third edition. November 2010. Available at: http://psychiatryonline.org/guidelines.aspx
4. Ochs-Ross R, Daly EJ, Zhang Y et al. Efficacy and safety of esketamine nasal spray plus an oral antidepressant in elderly patients with treatment-resistant depression TRANSFORM-3. Am J Geriatric Psychiatry. 2020 Feb;28(2):121-141