MVP Health Care Medical Policy

Medicare Part B: Spravato® (Esketamine)

Type of Policy: **Medical Therapy**
Prior Approval Date: **N/A**
Approval Date: **11/01/2023**
Effective Date: **01/01/2024**
Related Policies: **NA**

Codes Requiring Prior Authorization covered under the medical benefit
S0013 Spravato® (Esketamine) nasal spray 1 mg

Overview/Summary of Evidence

Spravato (esketamine) is an intranasal spray that is FDA approved to treat two major depressive disorder (MDD) subpopulations of adults (≥18 years) when used in combination with an oral antidepressant: adults with "treatment resistant depression" (TRD) and adults with depressive symptoms with acute suicidal ideation or behavior. TRD is defined as a failure of at least 2 currently available antidepressants at adequate doses for 8 weeks. Spravato (esketamine) is the S-enantiomer of ketamine. It is a non-selective, non-competitive antagonist of N-methyl-D-aspartate (NMDA) receptor, an ionotropic glutamate receptor, thus causing an increase in glutamate and activation of AMPA receptors. Activation of AMPA receptors have strengthened synapses in the frontal cortex, the part of the brain which is closely associated with mood and motivation. Spravato is only available through a REMS program.

Spravato was designated by the FDA as a "breakthrough therapy," indicating a serious unmet need and compelling early evidence in favor of the drug. It was granted priority review, shortening the approval process from 12 months to 6 months.

Indications/Criteria

- Spravato is indicated for intranasal administration in adults (≥18 years) for treatment resistant major depressive disorder in conjunction with an oral

antidepressant and for the treatment of depressive symptoms in patients with MDD with suicidal thoughts or actions in conjunction with an oral antidepressant.

Criteria (must meet all criteria as listed below for the specific indication)	**TRD**	**MDD with suicidal ideation**
The patient must be diagnosed with Major Depressive Disorder based on DSM-5 criteria	x	x
Medical records must be received demonstrating: o Failure of at least 2 antidepressants from two different antidepressant medication classes at the maximally tolerated FDA-approved dose for a minimum of 8 weeks each. If an 8 week trial with two oral antidepressants is inappropriate, clinical rationale must be documented in the medical record and will be considered on a case by case basis **AND** o Medical records documenting failure of therapy optimization (trial of antidepressant medications from at least two different antidepressant medication classes concomitantly for an adequate duration (8 weeks), such as: SSRI/SNRI/TCA or any other combination of non-MAOI antidepressants), unless contraindicated or intolerable, **AND** o Inadequate response to antidepressant in the current depression episode. Claims history must demonstrate compliance with current antidepressant.	x	
Medical records must be received documenting patient has experienced acute suicidal ideation or behavior and patient is receiving standard of care (including hospitalization if clinically warranted).		x
Spravato must be prescribed **AND** administered by a certified provider who is able to properly monitor patient after administration at a REMS certified clinic.	x	x
Patient must be assessed using an appropriate diagnostic instrument such as PHQ-9 Patient Depression Questionnaire or Montgomery-Asberg Depression Rating	x	x

Scale (MADRS) at baseline prior to dose and after each week prior to dose		

Initial approval for TRD indication will be for 8 weeks. MADRS or PHQ-9 Patient Depression Questionnaire score at week 4 (after induction phase) and most current MADRS or PHQ-9 Patient Depression Questionnaire score must be submitted with the initial extension request.

Initial approval for MDD with acute suicidal ideation or behavior indication will be for 4 weeks. Continuation requests require evidence of therapeutic benefit with evaluation to determine need for continued treatment.

Subsequent extensions for 3 months will be granted if the following are met:

- The patient must have met all criteria specified in the "initiating therapy" section above
  AND
- Medical records must include current PHQ-9 Patient Depression Questionnaire or MADRS score and must demonstrate score and symptom improvement from baseline. Claims history must show compliance with concurrent oral antidepressant and Spravato therapy.

Exclusions

Spravato (esketamine) is not considered medically necessary and therefore is not covered when any of the following are true:

- Patient is not using Spravato in conjunction with an oral antidepressant
- Patient is less than 18 years of age
- Spravato is being prescribed for anesthetic use
- Spravato is being prescribed outside of the FDA approved dosing
- Patient is pregnant or planning to become pregnant
- Patient has severe hepatic impairment (Child-Pugh class C)
- Patient has history of aneurysm (e.g., aneurysmal vascular disease including thoracic and abdominal aorta, intracranial, and peripheral arterial vessels), arteriovenous malformation, and a history of intracranial bleeding (intracerebral hemorrhage).

- The patient has homicidal ideation, substance/alcohol use disorder in the past year, autism spectrum disorder, recent cannabis use, prior DSM-5 diagnosis of psychotic disorder, MDD with psychotic features, bipolar or related disorders, current OCD, intellectual disability, borderline personality disorder, antisocial personality disorder, histrionic personality disorder, or narcissistic personality disorder.

References

1. Spravato (esketamine) [prescribing information]. Jannesen Pharmaceuticals Lakewood, NJ 2019
2. FDA New Release. FDA approves new nasal spray medication for treatment-resistant depression; available only at a certified doctor's office or clinic Available from: https://www.fda.gov/news-events/press-announcements/fda-approves-new-nasal-spray-medication-treatment-resistant-depression-available-only-certified
3. Johnson & Johnson Press Release. Esketamine Receives Breakthrough Therapy Designation from U.S. Food and Drug Administration for Major Depressive Disorder with Imminent Risk for Suicide. Available at: https://www.jnj.com/media-center/press-releases/esketamine-recieves-breakthrough-therapy-designation-from-us-food-and-drug-administration-for-major-depressive-disorder-with-imminent-risk-of-suicide. Accessed June 2019
4. E Wajs, L Aluisio, R Morrison, EJ Daly, R Lane, P Lim, R Holder, G Sanacora, AH Young, S Kasper, AH Sulaiman, C Li, J Paik, H Manji, D Hough, WC Drevets, JB Singh. Long-Term Safety of Esketamine Nasal Spray Plus an Oral Antidepressant in Patients with Treatment-Resistant Depression: Phase 3, Open Label Safety and Efficacy Study (SUSTAIN-2).
5. National Institute of Mental Health. Sequenced Treatment Alternatives to Relieve Depression (STAR*D) Study. Available at: http://www.nimh.nih.gov/about/director/2011/antidepressants-a-complicated-picture.shtml#_edn2. Accessed June 2019
6. American Psychiatric Association. Practice Guidelines for the Treatment of Patients with Major Depressive Disorder: Third Edition. October 2010. Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf
7. Contraindications/precautions. Clinical Pharmacology. September 2021.