

PRIOR AUTHORIZATION POLICY

POLICY: Psychiatry – Spravato Prior Authorization Policy

- Spravato® (esketamine nasal spray – Janssen)

REVIEW DATE: 04/20/2022

OVERVIEW

Spravato, a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist, is indicated in conjunction with an oral antidepressant for the treatment of:¹

- Depressive symptoms in adults with **major depressive disorder (MDD) with acute suicidal ideation or behavior.**
- **Treatment-resistant depression (TRD)** in adults.

Limitation 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. Spravato is not approved as an anesthetic agent. The safety and effectiveness of Spravato as an anesthetic agent have not been established.

Spravato should be administered in conjunction with an oral antidepressant.¹ For MDD with acute suicidal ideation or behavior, the recommended dosage is 84 mg twice weekly for 4 weeks. The dosage may be reduced to 56 mg twice weekly based on tolerability. After 4 weeks of treatment, evidence of therapeutic benefit should be evaluated to determine the need for continued treatment. 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. For treatment-resistant depression, the recommended dose is 56 mg intranasally on Day 1, followed by 56 mg or 84 mg intranasally twice weekly for Weeks 1 to 4. On Weeks 5 to 8, Spravato should be administered once weekly at a dose of 56 mg or 84 mg intranasally. On Week 9 and thereafter, the dosing frequency should be individualized to the least frequent dosing to maintain remission/response (either every 2 weeks or once weekly) at a dose of 56 mg or 84 mg. Spravato must be administered under the direct supervision of a healthcare provider.

Disease Overview

Major depressive disorder is a serious, life-threatening condition with high rates of morbidity and a chronic disease course.² Major depressive disorder is considered the leading cause of disability worldwide and is also associated with increased mortality rates.^{3,4} About 30% to 40% of patients with major depressive disorder fail to respond to first-line treatments including oral antidepressant medications of all classes (e.g., selective serotonin reuptake inhibitors [SSRIs], serotonin-norepinephrine reuptake inhibitors [SNRIs], tricyclic antidepressants [TCAs], bupropion) and/or psychotherapy.^{2,5} In addition, the onset of treatment response for these modalities, even when effective, often takes ≥ 4 weeks, leading to greater suffering, expense, and risk. For regulatory purposes, the FDA considers patients to have treatment-resistant depression if they have MDD and they have not responded to treatment despite trials of at least two antidepressants given at adequate doses for an adequate duration in the current episode.²

The available treatments for treatment-resistant depression are limited.² Prior to the approval of Spravato, only one medication was FDA-approved for treatment-resistant depression, Symbyax® (olanzapine and fluoxetine capsules). Symbyax is indicated for treatment-resistant depression (major depressive disorder in patients who do not respond to two separate trials of different antidepressants of adequate dose and duration in the current episode) and acute depressive episodes in bipolar I disorder.⁶

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Guidelines

According to the American Psychiatric Association practice guideline for the treatment of patients with major depressive disorder (2010), the effectiveness of antidepressants is generally comparable between classes and within classes.⁷ Therefore, the initial selection of antidepressant will largely be based on the anticipated side effects, the safety or tolerability of these side effects for the individual patient, pharmacological properties of the medication (e.g., half-life, drug interactions), and additional factors such as medication response in prior episodes, cost, and patient preference. In patients with depression who either have not responded or have had trouble tolerating one SSRI agent, a trial of another SSRI (or another antidepressant) may be effective and/or better tolerated. Patients who have had a partial response to antidepressant monotherapy can be augmented with another antidepressant from a different pharmacological class or with another non-antidepressant medication, such as lithium, thyroid hormone, an anticonvulsant, a psychostimulant, or an atypical antipsychotic.

Abuse and Misuse

Spravato contains esketamine, a Schedule III controlled substance (CIII), which may be subject to abuse and diversion.¹ Assess each patient's risk for abuse or misuse prior to prescribing Spravato. All patients receiving Spravato should be monitored for the development of these behaviors or conditions, including drug-seeking behavior, while on therapy. Patients with a history of drug abuse or dependence are at greater risk. Careful consideration should be given prior to prescribing Spravato to individuals with a history of substance use disorder.

Safety

Spravato labeling includes a Boxed Warning regarding sedation, dissociation, abuse and misuse, and suicidal thoughts and behaviors in pediatric and young adult patients.¹ The most common psychological effects of Spravato were dissociative or perceptual changes (including distortion of time, space and illusions), derealization and depersonalization (61% to 84% of patients treated with Spravato developed dissociative or perceptual changes based on the Clinician-Administered Dissociative States Scale). Given its potential to induce dissociative effects, carefully assess patients with psychosis before administering Spravato; treatment should be initiated only if the benefit outweighs the risk.

Because of the risks of serious adverse outcomes resulting from sedation, dissociation, and abuse and misuse, Spravato is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).¹ Healthcare settings must be certified in the program and ensure that Spravato is only dispensed in healthcare settings and administered to patients who are enrolled in the program, administered by patients under the direct observation of a healthcare provider, and that patients are monitored by a healthcare provider for at least 2 hours after administration of Spravato. Pharmacies must be certified in the REMS and must only dispense Spravato to healthcare settings that are certified in the program.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Spravato. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Spravato as well as the monitoring required for adverse events and efficacy, approval requires Spravato to be prescribed by a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Spravato is recommended in those who meet one of the following criteria:

FDA-Approved Indications

- 1. Major Depressive Disorder with Acute Suicidal Ideation or Behavior.** Approve for 2 months if the patient meets the following criteria (A, B, C, D, and E):
 - A) Patient is ≥ 18 years of age; AND
 - B) Patient has major depressive disorder that is considered to be severe, according to the prescriber; AND
 - C) Patient is concomitantly receiving at least one oral antidepressant; AND
Note: Antidepressants may include, but are not limited to, selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), mirtazapine, and bupropion.
 - D) Patient has one of the following (i or ii):
 - i. No history of psychosis; OR
 - ii. History of psychosis and the prescriber believes that the benefits of Spravato outweigh the risks; AND
 - E) The medication is prescribed by a psychiatrist.

- 2. Treatment-Resistant Depression.** Approve for 6 months if the patient meets the following criteria (A, B, C, D, E, and F):
 - A) Patient is ≥ 18 years of age; AND
 - B) Patient meets both of the following (i and ii):
 - i. Patient has demonstrated nonresponse ($\leq 25\%$ improvement in depression symptoms or scores) to at least two different antidepressants, each from a different pharmacologic class, according to the prescriber; AND
Note: Different pharmacologic classes of antidepressants include selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), bupropion, mirtazapine, etc.
 - ii. Each antidepressant was used at therapeutic dosages for at least 6 weeks in the current episode of depression, according to the prescriber; AND
 - C) Patient is concomitantly receiving at least one oral antidepressant; AND
Note: Antidepressants may include, but are not limited to, selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), mirtazapine, and bupropion.
 - D) Patient has one of the following (i or ii):
 - i. No history of psychosis; OR
 - ii. History of psychosis and the prescriber believes that the benefits of Spravato outweigh the risks; AND
 - E) The patient's of controlled substance prescriptions has been checked using the state prescription drug monitoring program (PDMP), unless unavailable in the state (see note below), according to the prescriber; AND
Note: As of 03/25/2020, the state of Missouri is the only state in the US that does not have a PDMP program in place.
 - F) The medication is prescribed by a psychiatrist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Spravato is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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4. Depression and Other Common Mental Disorders: Global Health Estimates. Geneva: World Health Organization; 2017. Available at: <https://apps.who.int/iris/bitstream/handle/10665/254610/WHO-MSD-MER-2017.2-eng.pdf;jsessionid=A566BCE2138CF7D2CA9F1E283F2F4E71?sequence=1>. Accessed on April 18, 2022.
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