Spravato® (esketamine) CIII

28 mg nasal spray

A Guide to Referring Your Patients to a SPRAVATO® REMS-Certified Treatment Center

Scan here to Find a Center

Indications:

SPRAVATO® (esketamine) CIII Nasal Spray is indicated, in conjunction with an oral antidepressant, for the treatment of:

- Treatment-resistant depression (TRD) in adults.
- 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®.
- SPRAVATO® is not approved as an anesthetic agent. The safety and effectiveness of SPRAVATO® as an anesthetic agent have not been established.

ADs=antidepressants.
REMS=Risk Evaluation and Mitigation Strategy.

Important Safety Information

WARNING: SEDATION; DISSOCIATION; RESPIRATORY DEPRESSION; ABUSE AND MISUSE; and SUICIDAL THOUGHTS AND BEHAVIORS

See full prescribing information for complete boxed warning

- **Risk for sedation, dissociation, and respiratory depression after administration. Monitor patients for at least two hours after administration (5.1, 5.2, 5.3).**
- **Potential for abuse and misuse. Consider the risks and benefits of using SPRAVATO® prior to use in patients at higher risk of abuse. Monitor for signs and symptoms of abuse and misuse (5.4).**
- **SPRAVATO® is only available through a restricted program called the SPRAVATO® REMS (5.5).**
- **Increased risk of suicidal thoughts and behaviors in pediatric and young adult patients taking antidepressants. Closely monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors. SPRAVATO® is not approved for use in pediatric patients (5.6).**

(continued on page 3)

Please see additional Important Safety Information throughout this brochure, full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

It takes 3 steps to refer to a REMS-certified SPRAVATO® treatment center, after you've identified and educated your appropriate patient on SPRAVATO®

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Your role as the Referring Provider

1 Use the Find a Center tool to locate a treatment center

2 Submit the referral directly to the treatment center

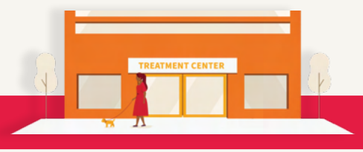
3 Continue to provide care for your patient

Patient

First consultation between the Patient & Treatment Center

Patient begins treatment on second visit to Treatment Center

Treatment Center



Treatment Center receives patient information

Treatment Center completes benefits investigation and Prior Authorization

Patient continues ongoing treatment at the treatment center

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SPRAVATO®
Dosing Considerations

Spravato withMe

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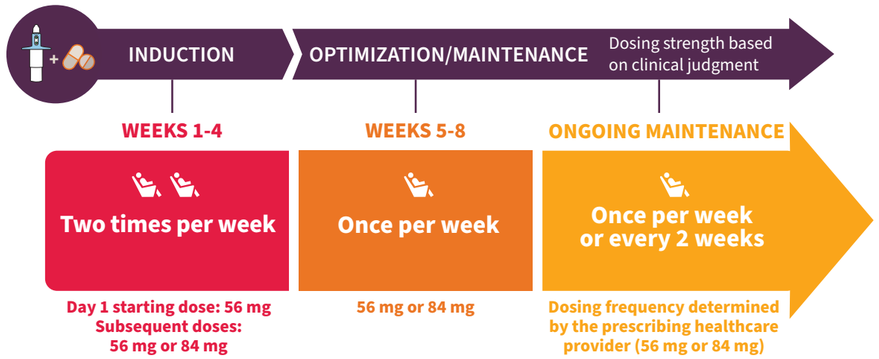


Administration

- Patient-administered under supervision of a healthcare provider (eg, a psychiatrist, nurse, or nurse practitioner)

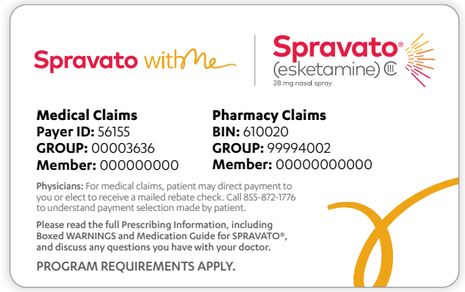
Monitoring & Discharge

- Observation by a healthcare provider will be required for at least 2 hours until the provider determines the patient is safe to leave
- Monitor patients for changes in respiratory status (including pulse oximetry) at each treatment session
- Blood pressure should be monitored prior to and 40 minutes after administration and subsequently as clinically warranted until values remain consistent at a safe level and the treatment session ends
- Patients should not drive or operate heavy machinery until the next day, following a restful sleep
- Patients should coordinate transportation after treatment

The SPRAVATO withMe Savings Program Could Help Your Eligible Patients Save

Eligible commercially insured patients could pay $10 per treatment for SPRAVATO® out-of-pocket medication costs.

- Eligible patients with commercial insurance pay as little as $10 per treatment for their SPRAVATO® medication. There are quantity limits and savings limits each year
- Program does not cover the cost of treatment observation. Patients may participate without sharing their income information. See spravatowithmeprogramrequirements.pdf



Information about your patients' insurance coverage, cost support options, and treatment support is given by service providers for SPRAVATO withMe. The information you get does not require you or your patient to use any Janssen product. Because the information we give you comes from outside sources, SPRAVATO withMe cannot promise the information will be complete. SPRAVATO withMe cost support is not for patients in the Johnson & Johnson Patient Assistance Foundation.

SPRAVATO® is covered by most insurance plans.
HCPs should consult with each patient's payer since coverage will vary.

Important Safety Information (continued)

CONTRAINDICATIONS

SPRAVATO® is contraindicated in patients with:

- Aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial and peripheral arterial vessels) or arteriovenous malformation.
- History of intracerebral hemorrhage.
- Hypersensitivity to esketamine, ketamine, or any of the excipients.

WARNINGS AND PRECAUTIONS

Sedation: SPRAVATO® may cause sedation or loss of consciousness. In some cases, patients may display diminished or less apparent breathing. In clinical trials, 48% to 61% of SPRAVATO®-treated patients developed sedation and 0.3% to 0.4% of SPRAVATO®-treated patients experienced loss of consciousness.

Because of the possibility of delayed or prolonged sedation, patients must be monitored by a healthcare provider for at least 2 hours at each treatment session, followed by an assessment to determine when the patient is considered clinically stable and ready to leave the healthcare setting.

Closely monitor for sedation with concomitant use of SPRAVATO® with CNS depressants (e.g., benzodiazepines, opioids, alcohol).

Dissociation: 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 SPRAVATO®-treated patients developed dissociative or perceptual changes). 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 dissociation, patients must be monitored by a healthcare provider for at least 2 hours at each treatment session, followed by an assessment to determine when the patient is considered clinically stable and ready to leave the healthcare setting.

Respiratory Depression: In postmarketing experience, respiratory depression was observed with the use of SPRAVATO®. In addition, there were rare reports of respiratory arrest.

Because of the risks of respiratory depression, patients must be monitored for changes in respiratory status by a healthcare provider for at least 2 hours (including pulse oximetry) at each treatment session, followed by an assessment to determine when the patient is considered clinically stable and ready to leave the healthcare setting.

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Please see additional Important Safety Information throughout this brochure, full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

It takes 3 steps to refer to a REMS-certified SPRAVATO® treatment center, after you've identified and educated your appropriate patient about SPRAVATO®

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1 Find a SPRAVATO® treatment center

2 Submit the referral directly to the treatment center

3 Continue to provide care for your patient

1 Find a SPRAVATO® treatment center

Establish a relationship with local treatment centers

- **Use the Find a Center tool** on spravatohcp.com to find a local REMS-certified treatment center that accepts your patient's insurance

Pro Tip: When using the Find a Center tool, you can filter by insurance plans

- **Connect with the treatment center** to understand their referral process, and confirm if the treatment center is accepting new patients for SPRAVATO®
- **Understand the treatment center logistics,** including what days of the week they offer SPRAVATO® and other amenities (such as extended hours)

Scan here to access the SPRAVATO® Find-a-Center tool

Important Safety Information (continued)

Abuse and Misuse: SPRAVATO® contains esketamine, a Schedule III controlled substance (CIII), and may be subject to abuse and diversion. Assess each patient's risk for abuse or misuse prior to prescribing and monitor all patients for the development of these behaviors or conditions, including drug-seeking behavior, while on therapy. Individuals with a history of drug abuse or dependence are at greater risk; therefore, use careful consideration prior to treatment of individuals with a history of substance use disorder and monitor for signs of abuse or dependence.

SPRAVATO® Risk Evaluation and Mitigation Strategy (REMS): SPRAVATO® is available only through a restricted program called the SPRAVATO® REMS because of the risks of serious adverse outcomes from sedation, dissociation, respiratory depression, and abuse and misuse.

Important requirements of the SPRAVATO® REMS include the following:

- Healthcare settings must be certified in the program and ensure that SPRAVATO® is:
  - Only dispensed and administered in healthcare settings.
  - Patients treated in outpatient settings (e.g., medical offices and clinics) must be 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.

Further information, including a list of certified pharmacies, is available at www.SPRAVATOrems.com or 1-855-382-6022.

Suicidal Thoughts and Behaviors in Adolescents and Young Adults: In pooled analyses of placebo-controlled trials of antidepressant drugs (SSRIs and other antidepressant classes) that included adult and pediatric patients, the incidence of suicidal thoughts and behavior in patients age 24 years and younger was greater than in placebo-treated patients. SPRAVATO® is not approved in pediatric (<18 years of age) patients.

There was considerable variation in risk of suicidal thoughts and behaviors among drugs, but there was an increased risk identified in young patients for most drugs studied.

Monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy and at times of dosage changes. Counsel family members or caregivers of patients

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It takes 3 steps to refer to a REMS-certified SPRAVATO® treatment center, after you've identified and educated your appropriate patient on SPRAVATO® (continued)

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2 Submit the referral directly to the treatment center

Refer your patients

- You do not have to complete the benefits investigation and prior authorization in order to get your patients started
- **Provide all patient information,** so the treatment center can complete the benefits investigation and prior authorization, including:
  - Insurance information
  - Medication history
  - Past treatment failures

Pro Tip: Based on the insurance plan, your patient may have 2 insurance cards for pharmacy and/or medical benefit

- The treatment center you refer to may already have a referral process in place
  - If not, use the **Patient Referral for SPRAVATO® Treatment Form** to fax the needed information

3 Continue to provide care for your patient

Continue to provide care to your patients

- You can be confident that your patients are supported throughout their treatment experience with SPRAVATO® when you:
  - **Continue follow-up and ongoing appointments** with your patients as appropriate
  - **Ask your patient** about their progress on SPRAVATO®
  - **Stay connected with the treatment center** to receive progress updates on your patients

Important Safety Information (continued)

Suicidal Thoughts and Behaviors in Adolescents and Young Adults: (continued)
to monitor for changes in behavior and to alert the healthcare provider. Consider changing the therapeutic regimen, including possibly discontinuing SPRAVATO® and/or the concomitant oral antidepressant, in patients whose depression is persistently worse, or who are experiencing emergent suicidal thoughts or behaviors.

Increase in Blood Pressure: SPRAVATO® causes increases in systolic and/or diastolic blood pressure (BP) at all recommended doses. Increases in BP peak approximately 40 minutes after SPRAVATO® administration and last approximately 4 hours.

Approximately 8% to 19% of SPRAVATO®-treated patients experienced an increase of more than 40 mmHg in systolic BP and/or 25 mmHg in diastolic BP in the first 1.5 hours after administration at least once during the first 4 weeks of treatment. A substantial increase in blood pressure could occur after any dose administered even if smaller blood pressure effects were observed with previous administrations. SPRAVATO® is contraindicated in patients for whom an increase in BP or intracranial pressure poses a serious risk (e.g., aneurysmal vascular disease, arteriovenous malformation, history of intracerebral hemorrhage). Before prescribing SPRAVATO®, patients with other cardiovascular and cerebrovascular conditions should be carefully assessed to determine whether the potential benefits of SPRAVATO® outweigh its risk.

Assess BP prior to administration of SPRAVATO®. In patients whose BP is elevated prior to SPRAVATO® administration (as a general guide: >140/90 mmHg), a decision to delay SPRAVATO® therapy should take into account the balance of benefit and risk in individual patients.

BP should be monitored for at least 2 hours after SPRAVATO® administration. Measure blood pressure around 40 minutes post-dose and subsequently as clinically warranted until values decline. If BP remains high, promptly seek assistance from practitioners experienced in BP management. Refer patients experiencing symptoms of a hypertensive crisis (e.g., chest pain, shortness of breath) or hypertensive encephalopathy (e.g., sudden severe headache, visual disturbances, seizures, diminished consciousness, or focal neurological deficits) immediately for emergency care.

Closely monitor blood pressure with concomitant use of SPRAVATO® with psychostimulants (e.g., amphetamines, methylphenidate, modafinil, armodafinil) or monoamine oxidase inhibitors (MAOIs).

In patients with a history of hypertensive encephalopathy, more intensive monitoring, including more frequent blood pressure and symptom assessment, is warranted because these patients are at increased risk for developing encephalopathy with even small increases in blood pressure.

Cognitive Impairment

Short-Term Cognitive Impairment: In a study in healthy volunteers, a single dose of SPRAVATO® caused cognitive performance decline 40 minutes post-dose. Compared to placebo-treated subjects, SPRAVATO®-treated subjects required a greater effort to complete the cognitive tests at 40 minutes post-dose. Cognitive performance and mental effort were comparable between SPRAVATO® and placebo at 2 hours post-dose. Sleepiness was comparable after 4 hours post-dose.

Long-Term Cognitive Impairment: Long-term cognitive and memory impairment have been reported with repeated ketamine misuse or abuse. No adverse effects of SPRAVATO® nasal spray on cognitive functioning were observed in a one-year open-label safety study; however, the long-term cognitive effects of SPRAVATO® have not been evaluated beyond one year.

(continued on page 6)

Please see additional Important Safety Information throughout this brochure, full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

For your patients with treatment-resistant depression (TRD)
Choose SPRAVATO® as the 1st-line augmentation therapy, and refer your appropriate patient to a treatment center today

LOCATE treatment centers near you using the QR code (above)

CALL selected centers and ask for information (detailed in grid on page 3)

RECORD answers in the appropriate fields

Information on pages 2 and 3 is intended to be filled out by the physician or office staff.

Call the treatment center for:

- ☐ Insurance plans accepted
- ☐ Whether patient insurance information is required before or during the first consult
- ☐ Days and hours SPRAVATO® treatment is offered
- ☐ Availability for new SPRAVATO® patients
- ☐ Intake form needed, if any
- ☐ Best method of receiving patient updates from treatment centers

Important Safety Information (continued)

Impaired Ability to Drive and Operate Machinery: Before SPRAVATO® administration, instruct patients not to engage in potentially hazardous activities requiring complete mental alertness and motor coordination, such as driving a motor vehicle or operating machinery, until the next day following a restful sleep. Patients will need to arrange transportation home following treatment with SPRAVATO®.

Ulcerative or Interstitial Cystitis: Cases of ulcerative or interstitial cystitis have been reported in individuals with long-term off-label use or misuse/abuse of ketamine. In clinical studies with SPRAVATO® nasal spray, there was a higher rate of lower urinary tract symptoms (pollakiuria, dysuria, micturition urgency, nocturia, and cystitis) in SPRAVATO®-treated patients than in placebo-treated patients. No cases of esketamine-related interstitial cystitis were observed in any of the studies, which involved treatment for up to a year.

Monitor for urinary tract and bladder symptoms during the course of treatment with SPRAVATO® and refer to an appropriate healthcare provider as clinically warranted.

PREGNANCY, EMBRYO-FETAL TOXICITY, AND LACTATION

SPRAVATO® is not recommended during pregnancy. SPRAVATO® may cause fetal harm when administered to pregnant women. Advise pregnant women of the potential risk to an infant exposed to SPRAVATO® *in utero*. Advise women of reproductive potential to consider pregnancy planning and prevention.

(continued on back cover)

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SPRAVATO® Treatment Centers

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Name of Treatment Center			
SPRAVATO® Coordinator's Name			
Location			
Phone, Email, or Fax			
Insurance Plans Accepted			
Insurance Policy Considerations			
Insurance Information Needed	☐ Before 1st consult ☐ During 1st consult	☐ Before 1st consult ☐ During 1st consult	☐ Before 1st consult ☐ During 1st consult
SPRAVATO® Treatment Days	Days Hours	Days Hours	Days Hours

Watch stories told by real patients and caregivers about how SPRAVATO® has helped make them feel like themselves again

Scan the QR code below:

These are real patients or caregivers of patients with treatment-resistant depression. They have been compensated for their time by Janssen Pharmaceuticals, Inc.

Important Safety Information (continued)

PREGNANCY, EMBRYO-FETAL TOXICITY, AND LACTATION (continued)

There are risks to the mother associated with untreated depression in pregnancy. If a woman becomes pregnant while being treated with SPRAVATO®, treatment with SPRAVATO® should be discontinued and the patient should be counseled about the potential risk to the fetus.

Pregnancy Exposure Registry: There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to antidepressants, including SPRAVATO®, during pregnancy. Healthcare providers are encouraged to register patients by contacting the National Pregnancy Registry for Antidepressants at 1-844-405-6185 or online at https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/antidepressants/.

SPRAVATO® is present in human milk. Because of the potential for neurotoxicity, advise patients that breastfeeding is not recommended during treatment with SPRAVATO®.

SELECT USE IN SPECIFIC POPULATIONS

Geriatric Use: No overall differences in the safety profile were observed between patients 65 years of age and older and patients younger than 65 years of age. At the end of a 4-week, randomized, double-blind study, there was no statistically significant difference between groups on the primary efficacy endpoint.

Hepatic Impairment: SPRAVATO®-treated patients with moderate hepatic impairment may need to be monitored for adverse reactions for a longer period of time.

SPRAVATO® has not been studied in patients with severe hepatic impairment (Child-Pugh class C). Use in this population is not recommended.

ADVERSE REACTIONS

The most common adverse reactions with SPRAVATO® plus oral antidepressant (incidence ≥5% and at least twice that of placebo nasal spray plus oral antidepressant) were:

TRD: dissociation, dizziness, nausea, sedation, vertigo, hypoesthesia, anxiety, lethargy, blood pressure increased, vomiting, and feeling drunk.

Treatment of depressive symptoms in adults with MDD with acute suicidal ideation or behavior: dissociation, dizziness, sedation, blood pressure increased, hypoesthesia, vomiting, euphoric mood, and vertigo.

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