

Benefit Design May Impact Your Pathway for Acquiring SPRAVATO[®]



Medical benefit access options include

- 1 **Medical assignment of benefit (AOB) through a REMS-certified pharmacy***
Pharmacies with specialty product experience may be able to complete the medical AOB.
- 2 **Buy and bill**



Pharmacy benefit access options include

- 1 **REMS-certified pharmacy**
- 2 **Pharmacy that may be mandated or preferred by the payer**

Approximately 90% of payers mandate or prefer the use of a specific pharmacy.^{1*†}



Confirm the patient's drug coverage and identify pharmacy options by calling the payer directly or by working with Janssen CarePath

*The AOB is specific to a patient's health plan and the pharmacy's capability. The use of mandated or preferred specialty pharmacy may vary by health plan.

†From Janssen Market Research (January 2020) based on a review of publicly available data for 102 payers selected from the largest nationwide payers (according to lives covered) who provide coverage for SPRAVATO[®]. Of these 102 payers, 93 were determined to mandate or prefer the use of a specialty pharmacy.

Indication

SPRAVATO[®] (esketamine) CIII Nasal Spray is indicated, in conjunction with an oral antidepressant (AD), for the treatment of treatment-resistant depression (TRD) in adults.

SPRAVATO[®] is not approved as an anesthetic agent. The safety and effectiveness of SPRAVATO[®] as an anesthetic agent have not been established.

Important Safety Information²

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

See full prescribing information for complete boxed warning

- **Risk for sedation and dissociation after administration. Monitor patients for at least two hours after administration (5.1, 5.2).**
- **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 (5.3).**
- **SPRAVATO[®] is only available through a restricted program called the SPRAVATO[®] REMS (5.4).**
- **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 (5.5).**

Please see Important Safety Information, including Boxed WARNINGS, on pages 4-7. Please see full [Prescribing Information](#), including Boxed WARNINGS, and [Medication Guide](#) for SPRAVATO[®]. Provide the Medication Guide to your patients and encourage discussion.

Acquiring SPRAVATO® Through the Pharmacy Pathway

Acquiring SPRAVATO® through a pharmacy may depend on a variety of payer factors, such as the patient's benefit design and the mandated use of a specific pharmacy. While each situation is unique and based on the patient's specific plan, consider the following information when determining your pathway to acquiring SPRAVATO®.

1 Confirm coverage

- Determine whether SPRAVATO® is covered under medical or pharmacy benefit
 - If SPRAVATO® is covered under the medical benefit, confirm that AOB is allowed
- Confirm prior authorization requirements, if any

2 Identify pharmacy

- Determine whether the health plan mandates or prefers a specific pharmacy
- Ensure the designated pharmacy is REMS certified

3 Prescribe SPRAVATO®

- Establish prescription process with the designated pharmacy



Confirm the patient's drug coverage and identify pharmacy options by calling the payer directly or by working with Janssen CarePath

For additional pharmacy options available for SPRAVATO®, please see page 3 of this resource.

Janssen CarePath Janssen CarePath is your one source for access, affordability, and treatment support for your patients

Janssen CarePath helps verify insurance coverage for your patients, provides reimbursement information, helps find financial assistance options for eligible patients, and provides ongoing support to help patients start and stay on SPRAVATO® treatment that you prescribed.



Need help?

Call a Janssen CarePath Care Coordinator at 844-777-2828
Monday–Friday 8:00 AM to 8:00 PM ET
Visit www.JanssenCarePath.com

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Spravato®
(esketamine) 
nasal spray 

Specialty Pharmacy Options Are Available for SPRAVATO®

The following specialty pharmacies are REMS certified and were selected for inclusion on this list because of their geographic coverage, health plan coverage, and ability to fulfill and dispense Schedule III Controlled Substances.

REMS-certified Specialty Pharmacies Contact Details*		
Pharmacy Name (Parent Company)	Phone/Fax Number	Website
AllianceRX (Walgreens/Prime)	P: 1-855-244-2555 F: 1-877-231-8302	www.alliancerxwp.com
CVS Specialty Customer Care (CVS Caremark)	P: 1-800-237-2767 F: 1-800-323-2445	www.cvsspecialty.com
Humana Specialty Pharmacy (Humana)	P: 1-800-486-2668 F: 1-877-405-7940	www.humanaspecialty.com

SPRAVATO® has a controlled distribution network that ensures SPRAVATO® is distributed only to Risk Evaluation and Mitigation Strategy (REMS)-certified pharmacies and REMS-certified settings. SPRAVATO® will not be delivered or dispensed directly to patients.

Specialty pharmacies may be able to support medical AOB and may be mandated or preferred by your patient's health plan. It is important to check with the health plan and pharmacy on these requirements.

When working with any specialty pharmacy, the specialty pharmacy may call your practice to:

- Verify prescription
- Coordinate information with you to complete prescription processing, such as collecting missing information, completing prior authorization, and coordinating medical shipments
- Confirm patient has follow-up appointment at treatment center



Remind the patient to expect a call from the specialty pharmacy to verify prescription, confirm follow-up treatment appointments, and collect co-pay

*This represents a partial list of REMS-certified pharmacies supplying SPRAVATO®. It is not intended to serve as a comprehensive list. Janssen Neuroscience, Inc., does not endorse the use of any of the listed pharmacies in particular. These pharmacies were selected for inclusion on this list because of their geographic coverage, health plan coverage, and ability to fulfill and dispense Schedule III Controlled Substances. The information provided represents no statement, promise, or guarantee of Janssen Neuroscience, Inc., concerning levels of reimbursement, payment, or charge. Please consult the health plan with regard to local or actual coverage, reimbursement policies, and determination processes. For a list of additional REMS-certified pharmacies, please contact the SPRAVATO® REMS Program at 1-855-382-6022.

Information listed is valid as of April 2020.

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Important Safety Information for SPRAVATO® (esketamine) CIII Nasal Spray²

Indication

SPRAVATO® (esketamine) CIII Nasal Spray is indicated, in conjunction with an oral antidepressant (AD), for the treatment of treatment-resistant depression (TRD) in adults.

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

Important Safety Information

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

See full prescribing information for complete boxed warning

- **Risk for sedation and dissociation after administration. Monitor patients for at least two hours after administration (5.1, 5.2).**
- **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 (5.3).**
- **SPRAVATO® is only available through a restricted program called the SPRAVATO® REMS (5.4).**
- **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 (5.5).**

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: In clinical trials, 49% to 61% of SPRAVATO®-treated patients developed sedation and 0.3% 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 [see *Drug Interaction (7.1)*].

SPRAVATO® is available only through a restricted program under a REMS.

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 75% 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.

SPRAVATO® is available only through a restricted program under a REMS.

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® is available only through a restricted program under a REMS.

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, 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 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®.

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Please see full [Prescribing Information](#), including [Boxed WARNINGS](#), and [Medication Guide](#) for SPRAVATO®.



Important Safety Information for SPRAVATO® (esketamine) CIII Nasal Spray² (continued)

- 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 behaviors 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 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 dosages. Increases in BP peak approximately 40 minutes after SPRAVATO® administration and last approximately 4 hours.

Approximately 8% to 17% 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, 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 be taken into account to balance the 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 or monoamine oxidase inhibitors (MAOIs) [see *Drug Interactions* (7.2, 7.3)].

In patients with 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. 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.

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®.

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Spravato®
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Important Safety Information for SPRAVATO® (esketamine) CIII Nasal Spray² (continued)

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.

Embryo-fetal Toxicity: 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.

DRUG INTERACTIONS

CNS depressants (e.g., benzodiazepines, opioids, alcohol): Concomitant use may increase sedation. Closely monitor for sedation with concomitant use of CNS depressants.

Psychostimulants (e.g., amphetamines, methylphenidate, modafinil, armodafinil): Concomitant use may increase blood pressure. Closely monitor blood pressure with concomitant use of psychostimulants.

Monoamine oxidase inhibitors (MAOIs): Concomitant use may increase blood pressure. Closely monitor blood pressure with concomitant use of MAOIs.

USE IN SPECIFIC POPULATIONS

Pregnancy: 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*. 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/>.

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

Females and Males of Reproductive Potential: SPRAVATO® may cause embryo-fetal harm when administered to a pregnant woman. Consider pregnancy planning and prevention for females of reproductive potential during treatment with SPRAVATO®.

Pediatric Use: The safety and effectiveness of SPRAVATO® in pediatric patients have not been established.

Geriatric Use: Of the total number of patients in Phase 3 clinical studies exposed to SPRAVATO®, 12% were 65 years of age and older, and 2% were 75 years of age and older. 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.

The mean esketamine C_{max} and AUC values were higher in elderly patients compared with younger adult patients.

The treatment of TRD in geriatric patients was evaluated in a 4-week, randomized, double-blind study comparing flexibly-dosed intranasal SPRAVATO® plus a newly initiated oral antidepressant compared to intranasal placebo plus a newly initiated oral antidepressant in patients ≥ 65 years of age. At the end of four weeks, there was no statistically significant difference between groups on the primary efficacy endpoint of change from baseline to Week 4 on the Montgomery-Åsberg Depression Rating Scale (MADRS).

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.

DRUG ABUSE AND DEPENDENCE

Controlled Substance: SPRAVATO® contains esketamine hydrochloride, the (S)-enantiomer of ketamine and a Schedule III controlled substance under the Controlled Substances Act.

Abuse: Individuals with a history of drug abuse or dependence may be at greater risk for abuse and misuse of SPRAVATO®. Abuse is the intentional, non-therapeutic use of a drug, even once, for its psychological or physiological effects. Misuse is the intentional use,

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Important Safety Information for SPRAVATO® (esketamine) CIII Nasal Spray² (continued)

for therapeutic purposes, of a drug by an individual in a way other than prescribed by a healthcare provider or for whom it was not prescribed. Careful consideration is advised prior to use of individuals with a history of substance use disorder, including alcohol.

SPRAVATO® may produce a variety of symptoms including anxiety, dysphoria, disorientation, insomnia, flashback, hallucinations, and feelings of floating, detachment and to be “spaced out.” Monitoring for signs of abuse and misuse is recommended.

ADVERSE REACTIONS

The most common adverse reactions with SPRAVATO® plus oral AD (incidence $\geq 5\%$ and at least twice that of placebo nasal spray plus oral AD) were dissociation, dizziness, nausea, sedation, vertigo, hypoesthesia, anxiety, lethargy, blood pressure increased, vomiting, and feeling drunk.

Please see full [Prescribing Information](#), including **Boxed WARNINGS**, and [Medication Guide](#) for SPRAVATO®.

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References:

1. Data on file. Janssen Pharmaceuticals, Inc. Titusville, NJ.
2. SPRAVATO® [Prescribing Information]. Titusville, NJ: Janssen Pharmaceuticals, Inc. February 2020.