Spravato withMe

Spravato® (esketamine) CIII
28 mg nasal spray

For patients using commercial or private health insurance to pay for their medication:

SPRAVATO withMe Savings Program

If your patient is eligible, the SPRAVATO withMe Savings Program may provide savings on their out-of-pocket medication costs for SPRAVATO®. Depending on their health insurance plan, savings may apply toward co-pay, co-insurance, or deductible. Eligible commercially-insured patients **pay $10 per treatment** for SPRAVATO® medication costs, with an $8,150 maximum program benefit per calendar year. *Treatment* may include up to three devices administered on the same day. Program limits apply. There is a program benefit limit of list price of medication and a quantity limit of three devices per day or 23 devices in a 24-day period. There is a quantity limit of 24 devices in a 24-day period for one use per lifetime. Program does not cover the cost of treatment observation. Patients may participate without sharing their income information. See program requirements on next page.

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.

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).**

Express Enrollment at JanssenCarePathPortal.com/express allows you to check eligibility and, if eligible, enroll your patients in the SPRAVATO withMe Savings Program and get a Savings Program card.

The patient is responsible for submitting a rebate request to SPRAVATO withMe Savings Program or, at the patient's direction, the provider may submit the rebate request on behalf of the patient. Confirm with your patient who will submit rebate requests to the Savings Program.

If the patient is submitting a rebate request:

- Patient will need to complete, sign, and submit a Rebate Request Form, including a copy of their Explanation of Benefits (EOB) from their primary insurance provider (as well as any secondary insurance provider, if applicable) and a receipt from their treatment provider indicating proof of payment of their out-of-pocket SPRAVATO® medication costs
- Patients may submit rebate requests to the Savings Program by fax or mail

If the provider is submitting a rebate request on behalf of the patient:

- At your patient's request, you may submit rebate requests to the SPRAVATO withMe Savings Program on their behalf if your patient has a Patient Assignment of Benefits (AOB) consent on file
- Please ensure that your patient has completed an AOB form and that you have faxed the AOB form to the fax number found on the form, in order for SPRAVATO withMe to process a rebate claim. The AOB form can be found at **Assignment of Benefits** or by calling SPRAVATO withMe at 844-4S-WITHME (844-479-4846)

Submitting a primary claim:
To submit a **primary claim** on behalf of the patient, providers must follow the instructions on the back of the SPRAVATO withMe Savings Program card to submit a CMS-1500 (HICF) or Uniform Billing Form—CMS-1450 (UB-04)—**through their electronic billing system.**

Submitting a secondary claim:

1. If you have submitted a primary claim and the claim has a remaining balance of $10 or more, you may submit a secondary claim.
   - Before you get started, contact your clearinghouse to request that Payer ID# 56155 and 56165 be added to their system, if needed
2. Submit **secondary claim** to SPRAVATO withMe Savings Program using CMS-1500 or UB-04 medical claim forms or electronic versions 837P or 837I (electronic submission is preferred).
   - You will need to submit the primary payer Explanation of Benefits along with the secondary claim form
   - To complete the form, you will need to use medical claims information from the front of patient's Savings Program card
   - You will receive funds for approved claims by check, which will include information on setting up future payments via EFT, if preferred
     - NOTE: If you already receive funds via EFT, you will continue to receive payments that way

SPRAVATO withMe is limited to education for patients about SPRAVATO®, its administration, and/or their disease, and is not intended to provide medical advice, replace a treatment plan from the patient's doctor or nurse, or provide case management services.

Program Requirements

Patients may be eligible for the SPRAVATO withMe Savings Program if they:

- Are age 18 and older and currently use commercial or private health insurance that covers SPRAVATO®
- Are enrolled in the SPRAVATO® Risk Evaluation and Mitigation Strategy (REMS). Learn more at **SpravatoREMS.com**

There is no income requirement. SPRAVATO withMe Savings Program for SPRAVATO® is based on medication costs only and does not include costs of treatment observation.

Other requirements

- **This program is only available to people age 18 or older using commercial or private health insurance for their SPRAVATO® medication. This includes plans from the Health Insurance Marketplace.** This program is not for people who use any state or federal government-funded healthcare program. Examples of these programs are Medicare, Medicaid, TRICARE, Department of Defense, and Veterans Administration
- Patients may not seek payment for the value received from this program from any health plan, patient assistance foundation, flexible spending account, or healthcare savings account
- Patients must meet the program requirements every time they use the card
- Program terms will expire at the end of each calendar year. The program may change or end without notice, including in specific states
- To use this program, patients must follow any health plan requirements, including telling their health plan how much co-payment support they get from this program. By getting a Savings Program benefit, patients confirm that they have read, understood, and agree to the program requirements on this page, and they are giving permission for information about their Savings Program transactions to be shared with their healthcare provider(s). These transactions include rebates and any funds placed on the card or balance remaining on the card
- Before patients enroll in the program, they will be asked to provide personal information that may include their name, address, phone number, email address, and information related to their prescription medication insurance and treatment. This information is needed for Janssen Pharmaceuticals, Inc., the maker of SPRAVATO®, and our service providers to enroll patients in the SPRAVATO withMe Savings Program. We may also use the information they give us to learn more about the people who use SPRAVATO®, and to improve the information we give them. Janssen Pharmaceuticals, Inc., will not share patient information with anyone else except where legally allowed
- If patients use medical/primary insurance to pay for their medication, they need to submit a rebate request with an Explanation of Benefits (EOB) to get payment from the Savings Program. With the patient's permission, the provider may submit the rebate request and EOB for the patient by mail or through an electronic billing system. Please make sure the patient and you know who will submit the rebate request. Rebate requests must be submitted within 270 days of the date of service
- This program offer may not be used with any other coupon, discount, prescription savings card, free trial, or other offer. Offer good only in the United States and its territories. Void where prohibited, taxed, or limited by law

Patients may end their participation in SPRAVATO withMe Savings Program at any time by calling a Care Navigator at 844-4S-WITHME (844-479-4846).

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.

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.

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (CONTINUED)

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 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.

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IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS (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.

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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Please read full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

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