Spravato® (esketamine) C III
28 mg nasal spray

Once a decision has been made to prescribe SPRAVATO®

PATIENT TREATMENT INITIATION CONSIDERATIONS

These personalized, step-by-step initiation considerations can help you keep track of the treatment initiation process and minimize treatment delays for your patients prescribed SPRAVATO®. Enter your patient's name and check off each step as it is completed, including date and notes for context and follow-up.

Patient Name: _____ **HCP Name:** _____

TREATMENT INITIATION STEPS	DATE	NOTES
Set expectations with the adult patient prior to treatment with SPRAVATO®: Confirm the provider has discussed the appropriate indication, dosage, and frequency for the patient: ☐ Induction dose (new patients) ☐ Maintenance dose (existing patients)	/ /	
☐ Share what to expect during treatment (scheduling, transportation, coverage and affordability options, applicable medical records)	/ /	
Consider using the SPRAVATO withMe suite of patient support resources to help navigate access and affordability challenges*:		
☐ Enroll patient in the SPRAVATO withMe program at SpravatoProviderPortal.com or fax Program Enrollment Form (PEF) to 1-844-577-7282 and, if applicable:	/ /	
☐ Inform commercially insured patients about the SPRAVATO withMe Savings Program and Observation Rebate Program†	/ /	
Note: *Patients must be REMS enrolled prior to enrollment in SPRAVATO withMe.*		

BENEFITS INVESTIGATION (BI)	DATE	NOTES
☐ Conduct the BI (check for medical and pharmacy coverage); consider using SPRAVATO withMe for BI support at SpravatoProviderPortal.com or call 1-844-479-4846	/ /	
Note: *If you are not using the SPRAVATO withMe program, the office must conduct the BI.*		

PRIOR AUTHORIZATION (PA)	DATE	NOTES
☐ Obtain PA (check options below); consider using SPRAVATO withMe for PA support at SpravatoProviderPortal.com or call 1-844-479-4846 ☐ Pharmacy ☐ Medical ☐ Medical AOB‡	/ /	
Note: *Be cognizant of approval time frames and reauthorization requirements, including baseline rating scales. If denied, verify which coverage was investigated.*		
☐ Engage Johnson & Johnson Patient Access Specialist as appropriate with any questions regarding these steps	/ /	

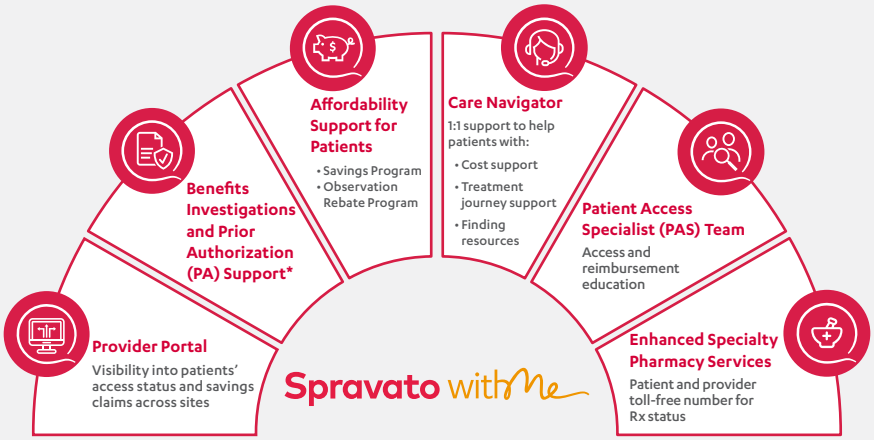
PATIENT COMMUNICATION FOR TREATMENT	DATE	NOTES
☐ Communicate coverage results to the patient and discuss affordability options	/ /	
☐ Enroll new patient in SPRAVATO® REMS at SPRAVATOrems.com or fax SPRAVATO® REMS Patient Enrollment Form to 1-877-778-0091	/ /	
☐ Schedule patient for treatment and confirm transportation	/ /	
☐ Verify product availability date (via pharmacy or buy and bill acquisition)	/ /	
Note: *Let the patient know that pharmacies will reach out to verify script.*		
☐ Inform referring provider that patient is starting SPRAVATO® therapy (if applicable)	/ /	

*Please see next page for information about the SPRAVATO withMe program.

†The SPRAVATO withMe Savings Program helps eligible, commercially insured patients save on their SPRAVATO® out-of-pocket medication costs, subject to program limits. The SPRAVATO withMe Observation Rebate Program reimburses eligible, commercially insured patients for their SPRAVATO® out-of-pocket treatment observation costs, subject to annual limit.

‡Medical AOB = Medical Assignment of Benefit; may allow patients with medical benefit design coverage to acquire SPRAVATO® through a specialty pharmacy.

SPRAVATO withMe Suite of Patient Support Resources



To learn more, visit **Spravatohcp.com/patient-support**

Provider Portal

- The SPRAVATO withMe Provider Portal is a flexible tool that offers patient-level visibility into activity progress on: Benefits Investigation, Prior Authorization, Appeals, and Coding and Reimbursement
- The portal offers: 2-way secure messaging with a Case Manager, streamlined patient enrollment, download of Savings Card upon patient enrollment in the SPRAVATO withMe Savings Program, and the ability to set up your own network in the system—where you can see savings status and add or remove patients across all sites

Benefits Coverage & Prior Authorization Support

- Once a decision has been made to prescribe SPRAVATO®, get a full view of your patients' coverage to help them get treatment quickly by minimizing delays
- Education and support for the Prior Authorization process is available‡

Affordability Support

- Eligible commercially insured patients can opt in to Savings Program and Observation Rebate Program† upon enrollment into SPRAVATO withMe
- 96% OF PATIENTS who use the SPRAVATO withMe Savings Program fill their first SPRAVATO® prescription versus 72% of patients who do not use the Savings Program‡

Care Navigator

- A Care Navigator is a healthcare professional with mental health experience who can offer one-to-one dedicated support to patients throughout their treatment journey. Care Navigators do not offer medical advice
- Care Navigators can provide cost support plus complete treatment journey support or just cost-focused support
- Patients can opt out of Care Navigator support anytime

Patient Access Specialist Team (PAS)

A Patient Access Specialist is a Johnson & Johnson representative who can support navigating the access journey in specific patient cases. To request a local representative, scan the code and select "SPRAVATO withMe" as a topic.

Data rates may apply.

Enhanced Specialty Pharmacy Services

A direct customer support line is available at contracted specialty pharmacies for addressing SPRAVATO®-related inquiries. To learn more, go to https://www.spravatohcp.com/payer-coverage-and-reimbursement/

See next page for additional information on SPRAVATO withMe support.

The patient support and resources provided by SPRAVATO withMe are not intended to give medical advice, replace a treatment plan from the patient's healthcare provider, offer services that would normally be performed by the provider's office, or serve as a reason to prescribe SPRAVATO®.
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 Johnson & Johnson product. Because the information we give you comes from outside sources, SPRAVATO withMe cannot promise the information will be complete.
*SPRAVATO withMe automatically provides Prior Authorization form assistance, including status updates. Within the Patient Enrollment Form, you may choose not to receive Prior Authorization form assistance from SPRAVATO withMe.
†We do not fill out any information that requires the medical judgment of the prescriber, and only the prescriber can determine whether to pursue a prior authorization.
‡The SPRAVATO withMe Savings Program helps eligible, commercially insured patients save on their SPRAVATO® out-of-pocket medication costs, subject to program limits. The SPRAVATO withMe Observation Rebate Program reimburses eligible, commercially insured patients for their SPRAVATO® out-of-pocket treatment observation costs, subject to annual limit.
§Source: IQVIA LAAD data for new commercial patients starting between 2019 and Sept 2023.

Indications and Important Safety Information

Indications:

SPRAVATO® (esketamine) CIII Nasal Spray is indicated for the treatment of:

- Treatment-resistant depression (TRD) in adults as monotherapy or in conjunction with an oral antidepressant.
- Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior in conjunction with an oral antidepressant.

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).**

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.

Please see additional Important Safety Information continued on next page. Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.

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 3% 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. In 1-year and 3-year, long-term, open-label clinical trials in adults, the effect of SPRAVATO® on cognitive functioning remained stable over time as evaluated by the Cogstate computerized battery and Hopkins Verbal Learning Test-Revised.

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/research/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

TRD: The most commonly observed adverse reactions in patients treated with SPRAVATO® plus oral antidepressant (incidence ≥5% and at least twice that of placebo nasal spray plus oral antidepressant) were 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: The most commonly observed adverse reactions in patients treated with SPRAVATO® plus oral antidepressant (incidence ≥5% and at least twice that of placebo nasal spray plus oral antidepressant) were dissociation, dizziness, sedation, blood pressure increased, hypoesthesia, vomiting, euphoric mood, and vertigo.

The most common adverse reactions with SPRAVATO® TRD monotherapy (≥5% and at least twice that of placebo nasal spray) were dissociation, nausea, dizziness, headache, anxiety, vomiting, feeling drunk, blood pressure increased, and sedation.

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

cp-170362v7

© Johnson & Johnson and its affiliates 2025 06/25 cp-448989v3