Spravato® (esketamine) C III
28 mg nasal spray

Drug and Procedure Coding Overview for SPRAVATO®

WHEN TO USE WHICH CODES:

If You Buy and Bill for SPRAVATO®

Use Combination Drug and Service G Codes for

- Medicare (required)
- Non-Medicare payers that require G Codes

56-mg dose 2 devices	G2082	1 unit
84-mg dose 3 devices	G2083	1 unit

Use Drug HCPCS and Consider Using Service CPT® Codes for

- Non-Medicare payers that do not require or accept the G Codes

56-mg dose 2 devices	S0013*	56 units
84-mg dose 3 devices	S0013*	84 units

Evaluation & Management (E/M) codes

If You Acquire SPRAVATO® Through a REMS-certified Pharmacy

Consider Using Service CPT® Codes for:

- Medicare and non-Medicare payers

Service: Evaluation & Management (E/M) codes

- 99415 – Prolonged clinical staff service (the service beyond the highest time in the range of total time of the service) during an evaluation and management service in the office or outpatient setting, direct patient contact with physician supervision; first hour (list separately in addition to code for outpatient E/M service)[1]
- 99416 – Each additional 30 minutes (list separately in addition to code for outpatient E/M service)
- 99417 – Prolonged office or other outpatient E/M service(s) beyond the minimum required time of the primary procedure that has been selected using total time, requiring total time with or without direct patient contact beyond the usual service, on the date of the primary service, each 15 minutes of total time (list separately in addition to codes 99205 or 99215 for office or other outpatient E/M services)[1]
- G2212 – When billing Medicare for Prolonged Service(s), report G2212 instead of CPT 99417 and apply only after the maximum time required to report 99205 or 99215 has been exceeded by 15 minutes
- Bundled G codes may only be billed when the product is acquired by an office through a specialty distributor. They may not be used if product is acquired from a specialty pharmacy.

Reminder: Healthcare providers (HCPs) must consult with each patient's payer since coverage will vary. Please note that HCPs are responsible for selecting appropriate codes for any particular claim based on the patient's condition, the items and services that are furnished, and any specific payer requirements. It is advisable to contact your local payer with regard to local payment policies.

CPT®=Current Procedural Terminology; HCPCS=Healthcare Common Procedure Coding System. CPT® is a registered trademark of the American Medical Association.
*S0013 – Esketamine, nasal spray, 1 mg.
Payers that do not accept the G or S Codes may continue to require J3490 (Unclassified drugs).
Medicare Advantage plans may choose to cover the product through a different benefit design. Confirm the plan's preferred benefit and the appropriate product and E/M codes that would be used.

Please see Indications and Important Safety Information, including Boxed WARNINGS, on pages 4-7.

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

SPRAVATO® REMS[2]

A Risk Evaluation and Mitigation Strategy (REMS) is a strategy to manage known or potential risks associated with a drug and is required by the US Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks

SPRAVATO® is available only through a restricted distribution program called the SPRAVATO® REMS because of the risks of serious adverse outcomes resulting from sedation, dissociation, and respiratory depression caused by SPRAVATO® administration, and abuse and misuse of SPRAVATO®. SPRAVATO® is intended for use only in a certified healthcare setting.

SPRAVATO® is intended for patient administration under the direct observation of a healthcare provider, and patients are required to be monitored by a healthcare provider for at least 2 hours. SPRAVATO® must never be dispensed directly to a patient for home use.

What are the REMS requirements?

1. **Healthcare setting certification**
   All healthcare settings must be certified in the REMS in order to receive, dispense, and/or treat patients with SPRAVATO®.
2. **Pharmacy certification**
   All pharmacies must be certified in the REMS in order to receive and dispense SPRAVATO®.
3. **Patient enrollment**
   Patients in an **outpatient** setting must be enrolled in the REMS with their prescriber in order to receive SPRAVATO® treatment.

Healthcare Settings Type*

All REMS-certified Inpatient and Outpatient Healthcare Settings must have a healthcare provider counsel patients on the safety risk of SPRAVATO® and monitor patients post-dose.

Inpatient healthcare settings

- Covers inpatient units, inpatient pharmacy, and emergency departments
- Before prescribing SPRAVATO® treatment, complete and submit the ***inpatient healthcare setting enrollment form***
- Before starting SPRAVATO® treatment, inpatient settings are not required to enroll the patient in the SPRAVATO® REMS
- During SPRAVATO® treatment, inpatient settings do not require the ***patient monitoring form***. Report all suspected adverse events to SPRAVATO® REMS

Outpatient healthcare settings

- Covers outpatient medical offices and clinics
- Before prescribing SPRAVATO® treatment, complete and submit the ***outpatient healthcare setting enrollment form***
- Before starting SPRAVATO® treatment, enroll the patient by completing and submitting the ***patient enrollment form*** to the SPRAVATO® REMS
- During SPRAVATO® treatment, submit the ***patient monitoring form*** and report all suspected adverse events to the SPRAVATO® REMS

*To get started, find more information on how to certify as a healthcare setting and/or pharmacy, and view all REMS requirements and attestations by type of REMS stakeholder, **visit SPRAVATOrems.com or call 1-855-382-6022 (8AM to 8PM ET).**

Spravato® (esketamine) CIII
28 mg nasal spray

Summary of Potential Codes for SPRAVATO® Treatment[1,3]

Site of Care	Activity	Payer	Potential Coding Options	Potentially Applicable Add-on Codes
Provider Purchases SPRAVATO® From an Authorized Distributor and Bills for Drug and Services				
Physician Office	Treatment visit and drug	Medicare	G2082 or G2083*	N/A
		Non-Medicare	G2082 or G2083*	Payer discretion
			99202-99205; 99212-99215 Drug: S0013 or J3490	Prolonged Clinical Staff Services: 99415; 99416 Prolonged Service: 99417
Hospital Outpatient Department (HOPD)	Treatment visit and drug	Medicare	G2082 or G2083*	N/A
		Non-Medicare	G2082 or G2083*	Payer discretion
			99202-99205; 99212-99215 Drug: S0013 or J3490	Prolonged Clinical Staff Services: 99415; 99416 Prolonged Service: 99417
Provider Acquires SPRAVATO® From a REMS-Certified Pharmacy† and Bills for Services				
Physician Office	Treatment visit	Medicare	99202-99205; 99212-99215	Prolonged Clinical Staff Services: 99415; 99416 Prolonged Service: G2212
		Non-Medicare		Prolonged Clinical Staff Services: 99415; 99416 Prolonged Service: 99417
Hospital Outpatient Department (HOPD)	Treatment visit	Medicare	G0463‡	N/A
		Non-Medicare	99202-99205; 99212-99215	Prolonged Clinical Staff Services: 99415; 99416 Prolonged Service: 99417

*Required for Medicare; non-Medicare payers may choose to accept the G codes but are not required to do so.
†When the HCP supervising the self-administration and observation does not also provide the drug, the provider cannot report G2082 or G2083.
‡G0463 - Hospital outpatient clinic visit for assessment and management of a patient. This code applies to all levels of E/M, for both new and established patients, billed to Medicare.

Indications and Important Safety Information for SPRAVATO® (esketamine) CIII Nasal Spray

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).**

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.

(continued on next page)

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

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.

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.

(continued on next page)

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

Increase in Blood Pressure (cont'd)

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 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.

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®.

(continued on next page)

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

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.

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

cp-170362v5

References: 1. American Medical Association. Current Procedural Terminology: CPT® 2022: Professional Edition. Chicago, IL: AMA Press; 2022. **2.** SPRAVATO® (esketamine) [Prescribing Information]. Titusville, NJ: Janssen Pharmaceuticals, Inc. **3.** Centers for Medicare & Medicaid Services. October 2021 Alpha-Numeric HCPCS file. Accessed December 1, 2023. https://www.cms.gov/Medicare/Coding/HCPCSReleaseCodeSets/HCPCS-Quarterly-Update

Janssen Neuroscience

PHARMACEUTICAL COMPANIES OF Johnson & Johnson

Spravato® (esketamine) CIII
28 mg nasal spray