Access & Reimbursement Guide

Information to Support the Access & Reimbursement Process for SPRAVATO®.

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).

Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39.
Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
Table of Contents

Introduction

How to Use This Guide

Introduction to SPRAVATO®

SPRAVATO® Coding With G Codes

SPRAVATO® Coding With HCPCS and CPT Codes

Important Safety Information

Appendices
Introduction

Janssen Pharmaceuticals, Inc., is pleased to provide you and your office staff with information to assist you in requesting reimbursement for SPRAVATO® (esketamine) CIII Nasal Spray on behalf of your patients. We have developed this Access and Reimbursement Guide to provide coding information, a list of authorized SPRAVATO® distributors, and important product information that we hope will be helpful to you and your practice.

- This document is presented for informational purposes only and is not intended to provide reimbursement or legal advice
- There is no International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) code for treatment-resistant depression. Payer requirements for diagnosis codes will vary. It is essential to verify correct diagnosis coding with each payer
- For 2020, Centers for Medicare and Medicaid Services (CMS) requires new, dose-specific Healthcare Common Procedure Coding System (HCPCS) codes to the drug and associated services. For non-Medicare payers that choose not to adopt these codes, there is currently no unique designated code to describe the observation and monitoring of SPRAVATO® administration. 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
- Laws, regulations, and policies concerning reimbursement are complex and updated frequently
  - While we have made an effort to be current as of the issue date of this document, the information may not be as current or comprehensive when you view it
  - Similarly, all Current Procedural Terminology (CPT®) and HCPCS codes are supplied for informational purposes only, and this information does not represent any statement, promise, or guarantee by Janssen Pharmaceuticals, Inc., about coverage, levels of reimbursement, payment, or charge
  - Please consult with your payer organizations for local or actual coverage and reimbursement policies and with your internal reimbursement specialist for any reimbursement or billing questions

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**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).

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How to Use This Guide

1. **Review the “Introduction to SPRAVATO®”**
   This introductory information provides an overview of SPRAVATO® usage, indications, dosage and administration, as well as a summary of the Risk Evaluation and Mitigation Strategy (REMS) requirements for all uses of SPRAVATO®. General coverage considerations are also presented, including a review of medical necessity and a summary of SPRAVATO® coverage by site of care and payer.

2. **Select the Applicable Coding Section**
   There are changes to the 2020 Medicare coding for SPRAVATO®. The new codes and reporting requirements may differ from those of other payers. To simplify use of this SPRAVATO® Access & Reimbursement Guide, SPRAVATO® coding guidelines are separated into 2 distinct sections:
   - **Coding for SPRAVATO® With G Codes**
   - **Coding for SPRAVATO® With HCPCS and CPT® Codes**

   The chart on the next page will help guide your selection of the applicable coding section. If you purchase and bill for SPRAVATO®, payer policy will dictate how the drug and associated services are coded. If you acquire SPRAVATO® through a REMS-certified pharmacy, the pharmacy will bill the drug and the payer policy will dictate appropriate service codes.

3. **Check the Appendices for Helpful Tools**
   For information on product ordering, sample letters for medical necessity and formulary exception requests, please see Appendix A and Appendix B.
How to Use This Guide (continued)

Select the Applicable Coding Section

<table>
<thead>
<tr>
<th>If You Purchase and Bill for SPRAVATO®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use Combination Drug and Service G Codes for:</td>
</tr>
<tr>
<td>- Medicare (required)</td>
</tr>
<tr>
<td>- Non-Medicare payers that require G Codes</td>
</tr>
<tr>
<td>G2082 56-mg dose 2 units</td>
</tr>
<tr>
<td>G2083 84-mg dose 3 units</td>
</tr>
</tbody>
</table>

FOR CODING INFORMATION, PLEASE SEE: SPRAVATO® Coding With G Codes

| Use Drug HCPCS and Consider Using Service CPT® Codes for: |
| - Non-Medicare payers that do not require or accept the G Codes |
| J3490* 56-mg dose 2 units |
| J3490* 84-mg dose 3 units |

*J3490 - Unclassified drugs; bill 1 unit; identify drug and total dosage in “Remarks” field

<table>
<thead>
<tr>
<th>If You Acquire SPRAVATO® Through a REMS-certified Pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider using Service CPT® Codes for:</td>
</tr>
<tr>
<td>- Medicare and non-Medicare payers</td>
</tr>
<tr>
<td>Consider using Evaluation &amp; Management (E/M) codes</td>
</tr>
</tbody>
</table>

Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39. Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
SPRAVATO® Indication and Usage¹

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

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

REMS (Risk Evaluation and Mitigation Strategy) Information for SPRAVATO®

The goal of the REMS is to mitigate the risks of serious adverse outcomes resulting from sedation and dissociation caused by SPRAVATO® administration, and abuse and misuse of SPRAVATO®, by:

- Ensuring that SPRAVATO® is only dispensed and administered to patients in a medically supervised healthcare setting that monitors these patients
- Ensuring pharmacies and healthcare settings that dispense SPRAVATO® are certified
- Ensuring that each patient is informed about the serious adverse outcomes resulting from sedation and dissociation and the need for monitoring
- Enrollment of all patients in the REMS (registry) to further characterize the risks and support safe use

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 after SPRAVATO® administration. SPRAVATO® must never be dispensed directly to a patient for home use.

SPRAVATO® Dosage and Administration

Dosage – Adult¹

SPRAVATO® requires a 2-phase dosing regimen: induction and maintenance. A treatment session consists of nasal administration of SPRAVATO® and post-administration observation under the supervision of a healthcare provider. The dosage recommendations for SPRAVATO® are shown in Table 1. Dose adjustments should be made based on efficacy and tolerability to the previous dose.

Table 1: Recommended Dosage for SPRAVATO®¹

<table>
<thead>
<tr>
<th></th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Induction Phase</strong></td>
<td></td>
</tr>
<tr>
<td>Weeks 1-4:</td>
<td>Day 1 starting dose: 56 mg</td>
</tr>
<tr>
<td>Administer twice per week</td>
<td>Subsequent doses: 56 mg or 84 mg</td>
</tr>
<tr>
<td><strong>Maintenance Phase</strong></td>
<td></td>
</tr>
<tr>
<td>Weeks 5 to 8:</td>
<td>56 mg or 84 mg</td>
</tr>
<tr>
<td>Administer once weekly</td>
<td></td>
</tr>
<tr>
<td><strong>Weeks 9 and after:</strong></td>
<td>56 mg or 84 mg</td>
</tr>
<tr>
<td>Administer every 2 weeks</td>
<td></td>
</tr>
<tr>
<td>or once weekly*</td>
<td></td>
</tr>
</tbody>
</table>

¹Dosing frequency should be individualized to the least frequent dosing to maintain remission/response.
SPRAVATO® is for nasal use only. The nasal spray device delivers a total of 28 mg of esketamine. To prevent loss of medication, do not prime the device before use. Use 2 devices (for a 56-mg dose) or 3 devices (for an 84-mg dose), with a 5-minute rest between use of each device.

SPRAVATO® must be self-administered under the direct supervision of a healthcare provider. A treatment session consists of nasal administration of SPRAVATO® and post-administration observation under supervision.

Blood Pressure Assessment

- Assess blood pressure prior to dosing with SPRAVATO®
- If baseline blood pressure is elevated, consider the risks of short-term increases in blood pressure and benefit of SPRAVATO® treatment
- Do not administer SPRAVATO® if an increase in blood pressure or intracranial pressure poses a serious risk
- After dosing with SPRAVATO®, reassess blood pressure at approximately 40 minutes and subsequently as clinically warranted
- If blood pressure is decreasing and the patient appears clinically stable for at least 2 hours, the patient may be discharged at the end of the post-dose monitoring period; if not, continue to monitor

Food and Liquid Intake Recommendations Prior to Administration

- Because some patients may experience nausea and vomiting after administration of SPRAVATO®, advise patients to avoid food for at least 2 hours before administration and to avoid drinking liquids at least 30 minutes prior to administration

Nasal Corticosteroid or Nasal Decongestant

- Patients who require a nasal corticosteroid or nasal decongestant on a dosing day should administer these medications at least 1 hour before SPRAVATO®

Post-Administration Observation

During and after SPRAVATO® administration at each treatment session, observe the patient for at least 2 hours until the patient is safe to leave. Before SPRAVATO® administration, instruct patients not to engage in potentially hazardous activities, such as driving a motor vehicle or operating machinery, until the next day after a restful sleep.

Missed Treatment Session(s)

If a patient misses treatment sessions and there is worsening of depression symptoms, per clinical judgment, consider returning to the patient’s previous dosing schedule (i.e., every 2 weeks to once weekly, weekly to twice weekly; see Table 1).
SPRAVATO® Coverage Considerations

Factors That Influence Coverage

Third-party payers (e.g., commercial insurers, Medicare, Medicaid) may cover drugs that require HCP management for their approved U.S. Food and Drug Administration (FDA) indications, and the associated administration services. However, benefits may vary depending on the payer and the specific plan (“insurance product”) in which a patient is enrolled.

Medical Necessity

When third-party payers review drug claims, they will first determine if the type of service provided is covered under their policies. Next, payers will look for evidence supporting the medical necessity of the therapy. This evidence may include:

- Information about the patient’s medical condition and history
- A physician’s statement or letter of medical necessity
- Supporting literature (e.g., peer-reviewed studies and compendia monographs)
- Prescribing information
- Availability of other treatment alternatives

Medical necessity refers to a decision by a health plan that a treatment, test, or procedure is necessary for health or to treat a diagnosed medical problem. Health insurance companies provide coverage only for health-related services that they define or determine to be medically necessary. Commercial insurers, Medicaid program coverage policies, Medicare National Coverage Determinations and Medicare Administrative Contractors’ Local Coverage Determinations define medical necessity requirements. These documents contain guidance on covered diagnoses, required documentation, and limitations of coverage for specific medical services or items. Reimbursement policies and guidelines may vary by payer.

Administrative Considerations

Other considerations may be involved in a payer’s decision to cover a product or service:

- **Site of care:** Does the payer contract specifically indicate the sites of care that may bill for the drug and its administration? Payers may have site-specific coverage rules. For example, does the plan require that the drug be administered only in a physician practice setting and restrict coverage if provided in a hospital outpatient setting?
- **Participating providers:** Is the billing provider a “participating” member of, or “in-network” provider for, that specific plan? Payers contract with providers to deliver services to the plan’s members. Providers are thus participating within that plan’s network, requiring them to abide by the contract charge structure when providing care for that plan’s members. Services provided by non-participating providers may not be covered in the absence of an approved exception request or other pre-approval from a health plan.
- **Prior authorization:** If required by the plan, has the appropriate referral or prior authorization been obtained? Many plans require that nonemergency services be pre-approved or that a primary care physician make the referral for specialty care. Failing to obtain appropriate referrals or pre-authorization can result in nonpayment by the plan.
**SPRAVATO® Coverage Considerations (continued)**

**Coverage for SPRAVATO®**

Coverage for SPRAVATO® will vary by payer, individual contracts, and treatment setting. When provided under the supervision of an HCP in an authorized site of care, the drug will often be covered under the payer’s medical benefit. Alternatively, the drug may be covered under the pharmacy benefit and delivery to the site of care will be through a REMS-certified pharmacy distributor.

**Table 2: SPRAVATO® Coverage Summary**

<table>
<thead>
<tr>
<th>Site of Care</th>
<th>Medicare Part A</th>
<th>Medicare Part B</th>
<th>Medicare Part D</th>
<th>Commercial Insurance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient Hospital (Acute Care)</td>
<td>IPPS</td>
<td>N/A</td>
<td>N/A</td>
<td>Payer reimbursement policies</td>
</tr>
<tr>
<td></td>
<td>• Covered within the MS-DRG</td>
<td></td>
<td></td>
<td>Typically covered within the DRG</td>
</tr>
<tr>
<td>Inpatient Psychiatric Facility</td>
<td>IPF-PPS</td>
<td>N/A</td>
<td>N/A</td>
<td>Payer reimbursement policies</td>
</tr>
<tr>
<td></td>
<td>• Covered within the MS-DRG</td>
<td></td>
<td></td>
<td>Typically covered within the DRG</td>
</tr>
<tr>
<td>Hospital Outpatient Department (HOPD)</td>
<td></td>
<td>N/A</td>
<td></td>
<td>Payer reimbursement policies</td>
</tr>
<tr>
<td></td>
<td>OPPS</td>
<td></td>
<td></td>
<td>Typically covered as a medical benefit, separately or as a combination service</td>
</tr>
<tr>
<td></td>
<td>• Drug and management covered together as a single service (i.e., G Code)</td>
<td></td>
<td></td>
<td>May be covered as a pharmacy benefit, with REMS-certified pharmacy distribution</td>
</tr>
<tr>
<td></td>
<td>Local Coverage Determinations may apply</td>
<td></td>
<td></td>
<td>May be covered as a pharmacy benefit, with REMS-certified pharmacy distribution</td>
</tr>
<tr>
<td>Physician Practice</td>
<td></td>
<td></td>
<td></td>
<td>Payer reimbursement policies</td>
</tr>
<tr>
<td></td>
<td>PFS</td>
<td></td>
<td></td>
<td>Typically covered as a medical benefit, separately or as a combination service</td>
</tr>
<tr>
<td></td>
<td>• Drug and management covered together as a single service (i.e., G Code)</td>
<td></td>
<td></td>
<td>May be covered as a pharmacy benefit, with REMS-certified pharmacy distribution</td>
</tr>
<tr>
<td></td>
<td>Local Coverage Determinations may apply</td>
<td></td>
<td></td>
<td>May be covered as a pharmacy benefit, with REMS-certified pharmacy distribution</td>
</tr>
</tbody>
</table>

*Prior authorization, step therapy, quantity limits, etc.

**Key**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPPS</td>
<td>Inpatient Prospective Payment System</td>
</tr>
<tr>
<td>MS-DRG</td>
<td>Medicare Severity Diagnosis-Related Group</td>
</tr>
<tr>
<td>IPF-PPS</td>
<td>Inpatient Psychiatric Facility Prospective Payment System</td>
</tr>
<tr>
<td>OPPS</td>
<td>Outpatient Prospective Payment System</td>
</tr>
<tr>
<td>PDP</td>
<td>Prescription Drug Plan</td>
</tr>
<tr>
<td>PFS</td>
<td>Physician Fee Schedule</td>
</tr>
</tbody>
</table>

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Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
2020 Medicare G Codes for SPRAVATO® (esketamine) and Observation and Monitoring of SPRAVATO® Administration Under HCP Supervision Consistent With REMS Requirements

As part of the calendar year 2020 Physician Fee Schedule, the CMS released an interim final rule, establishing coding and payment rules for the evaluation and management, observation, and provision of self-administered SPRAVATO® under Medicare Part B. This rule established 2 new dose-specific HCPCS codes (G2082 and G2083) for the provision of drug and professional services associated with SPRAVATO® therapy. Effective January 1, 2020, these codes are required for billing Medicare on both physician office (CMS-1500) and hospital outpatient (CMS-1450) claims. Non-Medicare payers may choose to accept the G Codes but are not required to do so.

Because the new G Codes describe both drug and service, beginning January 1, 2020, SPRAVATO® will no longer be coded separately on Medicare claims or on claims for non-Medicare payers that require G Codes. For payers that do not accept the G Codes, providers will continue to report separate codes for the drug and service: the miscellaneous drug code (J3490 – unclassified drug) for SPRAVATO® and the most appropriate E/M CPT® Code for the service. For more information, please see the other section of this guide: “SPRAVATO® Coding With HCPCS and CPT® Codes”.

The following table describes the G Codes. Selection of the appropriate code is dose dependent. G2082 is used to report SPRAVATO® doses of 56 mg or less, and G2083 is used to report doses greater than 56 mg (i.e., 84 mg, 3 units/devices). The 2-hour post-administration period is consistent with REMS requirements and remains the same for both doses.

Table 3: Codes to Report SPRAVATO®, Effective January 1, 2020

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Descriptor</th>
</tr>
</thead>
<tbody>
<tr>
<td>G2082</td>
<td>Office or other outpatient visit for the evaluation and management of an established patient that requires the supervision of a physician or other qualified healthcare professional and provision of up to 56 mg of esketamine nasal self-administration, includes 2 hours post-administration observation.</td>
</tr>
<tr>
<td>G2083</td>
<td>Office or other outpatient visit for the evaluation and management of an established patient that requires the supervision of a physician or other qualified healthcare professional and provision of greater than 56 mg of esketamine nasal self-administration, includes 2 hours post-administration observation.</td>
</tr>
</tbody>
</table>
Combination Coding for SPRAVATO® (esketamine) and Observation and Monitoring of SPRAVATO® Administration Under HCP Supervision Consistent With REMS Requirements (continued)

ICD-10-CM Diagnosis Codes

ICD-10-CM diagnosis codes use 3 to 7 alpha and numeric characters to achieve the greatest level of specificity. Codes with 3 characters are included in ICD-10-CM as the heading of a category of codes that may be further subdivided by use of additional characters to provide greater detail. A 3-character code is to be used only if it is not further subdivided. A code is invalid if it has not been coded to the full number of characters required for that code, including the 7th character, if applicable.4

There is no ICD-10-CM code for treatment-resistant depression. Payer requirements for ICD-10-CM codes will vary. It is essential to verify the correct diagnosis coding with each payer. The codes below are provided for your consideration, since our clinical trials included patients with major depressive disorder (MDD) who failed at least 2 treatments of adequate dose and duration.

Table 4: ICD-10-CM Diagnosis Codes for Consideration*5

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>F32.0</td>
<td>Major depressive disorder, single episode, mild</td>
</tr>
<tr>
<td>F32.1</td>
<td>Major depressive disorder, single episode, moderate</td>
</tr>
<tr>
<td>F32.2</td>
<td>Major depressive disorder, single episode, severe without psychotic features</td>
</tr>
<tr>
<td>F32.9</td>
<td>Major depressive disorder, single episode, unspecified</td>
</tr>
<tr>
<td>F33.0</td>
<td>Major depressive disorder, recurrent, mild</td>
</tr>
<tr>
<td>F33.1</td>
<td>Major depressive disorder, recurrent, moderate</td>
</tr>
<tr>
<td>F33.2</td>
<td>Major depressive disorder, recurrent, severe without psychotic features</td>
</tr>
<tr>
<td>F33.9</td>
<td>Major depressive disorder, recurrent, unspecified</td>
</tr>
<tr>
<td>F32.4</td>
<td>Major depressive disorder, single episode, in partial remission</td>
</tr>
<tr>
<td>F32.5</td>
<td>Major depressive disorder, single episode, in full remission</td>
</tr>
<tr>
<td>F33.40</td>
<td>Major depressive disorder, recurrent, in remission, unspecified</td>
</tr>
<tr>
<td>F33.41</td>
<td>Major depressive disorder, recurrent, in partial remission</td>
</tr>
<tr>
<td>F33.42</td>
<td>Major depressive disorder, recurrent, in full remission</td>
</tr>
</tbody>
</table>

*These codes are not intended to be promotional or to encourage or suggest a use of drug that is inconsistent with FDA-approved use. The codes provided are not exhaustive and additional codes may apply.
Other Coding Considerations

Place of Service (POS) Codes

The POS code set provides setting information necessary to appropriately pay professional service claims. The place of service is the location of the provider’s face-to-face encounter with the beneficiary. POS codes are required on all claims for professional services (billed on CMS-1500). The physician practice setting is indicated with POS code 11. To differentiate between on-campus and off-campus provider-based departments (PBDs), CMS created a new POS code (19) and revised the description for outpatient hospitals (22). Professional services delivered in outpatient hospital settings must specifically include the off-campus or on-campus POS on the claim form.

Table 5: Place of Service Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Name</th>
<th>Descriptor</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Office</td>
<td>Location, other than a hospital, skilled nursing facility, military treatment facility, community health center, state or local public health clinic, or intermediate care facility, where the health professional routinely provides health examinations, diagnosis, and treatment of illness or injury on an ambulatory basis.</td>
</tr>
<tr>
<td>19</td>
<td>Off Campus – Outpatient Hospital</td>
<td>A portion of an off-campus hospital provider-based department that provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization.</td>
</tr>
<tr>
<td>22</td>
<td>On Campus – Outpatient Hospital</td>
<td>A portion of a hospital’s main campus that provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization.</td>
</tr>
<tr>
<td>53</td>
<td>Community Mental Health Center</td>
<td>A facility that provides the following services: outpatient services, including specialized outpatient services for children, the elderly, individuals who are chronically ill, and residents of the center’s mental health services area who have been discharged from inpatient treatment at a mental health facility; 24-hour-a-day emergency care services; day treatment, other partial hospitalization services, or psychosocial rehabilitation services; screening for patients being considered for admission to state mental health facilities to determine the appropriateness of such admission; and consultation and education services.</td>
</tr>
</tbody>
</table>

Revenue Codes

Many payers require use of American Hospital Association revenue codes to bill for services provided in hospital outpatient departments. Revenue codes consist of a leading zero followed by 3 other digits and are used on claim forms to assign costs to broad categories of hospital revenue centers. Codes used for Medicare claims are available from Medicare contractors. The following revenue code may be applicable to CMS-1450 claims for SPRAVATO®:

- **0510 – Clinic, General**

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Other Coding Considerations (continued)

**Code Modifiers**

Modifiers are used to indicate that a service or procedure has been altered by some specific circumstance but not changed in its definition or code. They add more information and help to eliminate the appearance of duplicate billing and unbundling. Appropriately used, modifiers increase coding and reimbursement accuracy. The following table summarizes modifiers that may be applicable to SPRAVATO® coding and billing in physician offices and hospital outpatient departments.

**Table 6: Summary of Code Modifiers**

<table>
<thead>
<tr>
<th>Modifier</th>
<th>Description</th>
<th>Indication and Placement</th>
<th>CMS-1500 (Item 24D)</th>
<th>CMS-1450 (Box 44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO*</td>
<td>Services, procedures, and/or surgeries furnished at excepted off-campus provider-based outpatient departments</td>
<td>• To be reported with every HCPCS code for all hospital items and services furnished in an excepted off-campus, PBD of a hospital</td>
<td>N/A</td>
<td>Required by Medicare</td>
</tr>
<tr>
<td>PN*</td>
<td>Nonexcepted service provided at an off-campus, outpatient, PBD of a hospital</td>
<td>• To be reported on each claim line with each nonexcepted item and service furnished in a nonexcepted, off-campus, PBD of a hospital</td>
<td>N/A</td>
<td>Required by Medicare</td>
</tr>
</tbody>
</table>

*The PO and PN modifiers are NOT to be reported for dedicated emergency departments, remote locations, or satellite facilities of a hospital, or a PBD that is “on campus.”

Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39. Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
Modifiers PO and PN: Excepted and Nonexcepted Items and Services

Medicare rules now require that services furnished in off-campus PBDs of a hospital that began billing under the OPPS on or after November 2, 2015, are no longer paid under the OPPS. These services are referred to as “nonexcepted” and paid under the Medicare Physician Fee Schedule (MPFS). CMS established a new modifier: “PN” (nonexcepted service provided at an off-campus, outpatient, PBD of a hospital) to identify and pay nonexcepted items and services billed on an institutional claim. Nonexcepted off-campus PBDs of a hospital are required to report this modifier on each claim line with a HCPCS for nonexcepted items and services. The use of modifier “PN” will trigger a payment rate under the MPFS. CMS expects the PN modifier to be reported with each nonexcepted line item and service including those for which payment will not be adjusted, such as separately payable drugs, clinical laboratory tests, and therapy services.8

Excepted off-campus PBDs of a hospital must continue to report the existing modifier: “PO” (services, procedures, and/or surgeries provided at excepted off-campus provider-based outpatient departments) for all excepted items and services with a HCPCS. This modifier should not be reported for remote locations of a hospital, satellite facilities of a hospital, or services furnished in an emergency department.8 Neither the PN nor the PO modifier is to be reported by the following hospital departments:

- A dedicated emergency department
- A PBD that is “on the campus,” or within 250 yards, of the hospital or a remote location of the hospital9

Drugs Supplied at No Cost to Provider

Payers, including Medicare Part D, may cover a drug under the patient’s pharmacy benefit. Under this model, SPRAVATO® may be delivered to the administering site via a REMS-certified pharmacy (“white bagging”). When the drug is supplied by a REMS-certified pharmacy, it cannot be billed by the administering provider. However, the HCP observation and monitoring of the drug’s administration is a billable service.10

When reporting drug administration services associated with pharmacy-supplied drugs, consider reporting the services with the relevant E/M codes (see page 25 in the “SPRAVATO® Coding With HCPCS and CPT® Codes” section).

If You Acquire SPRAVATO® Through a REMS-certified Pharmacy

Consider Using Service CPT® Codes for:

- Medicare and non-Medicare payers

Service: Consider using Evaluation & Management (E/M) Codes

Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39. Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
Filing Healthcare Claims

Physician Office Claims (CMS-1500)
The Form CMS-1500 is the basic form prescribed by CMS for the Medicare and Medicaid programs for claims from suppliers and noninstitutional providers that qualify for a waiver from the Administrative Simplification Compliance Act requirement for electronic submission of claims. It has also been adopted by the TRICARE Program. For detailed guidance on completing the CMS-1500 items, please see the Medicare Claims Processing Manual, Pub. 100-04, Chapter 26, available at:

The CMS-1500 claims form is designed to capture the data elements required by Medicare Administrative Contractors (MACs) and other third-party payers. It includes a standard set of items that must be included on all claims, as well as additional items that may be required by specific payers.

The 837P (Professional) is the standard format used by healthcare providers and suppliers to transmit healthcare claims electronically. The American National Standards Institute (ANSI) Accredited Standards Committee (ASC) X12N 837P (Professional) Version 5010A1 is the current electronic claim version. Data elements in the CMS uniform electronic billing specifications are consistent with the hard copy data set to the extent that 1 processing system can handle both. Medicare Administrative Contractors may include a crosswalk between the ASC X12N 837P and the CMS-1500 on their websites.

Hospital Outpatient Claims (CMS-1450)
The Form CMS-1450, also known as the UB-04, is a uniform institutional provider bill suitable for use in billing multiple third-party payers. It is the basic form prescribed by CMS for the Medicare and Medicaid programs for claims from hospitals, including HOPDs. Because it serves many payers, a particular payer may not need some data elements. For detailed guidance on completing the CMS-1450 items, please see the Medicare Claims Processing Manual, Pub. 100-04, Chapter 25, available at:

The 837I (Institutional) is the standard format used by institutional providers to transmit healthcare claims electronically. The ANSI ASC X12N 837I (Institutional) Version 5010A2 is the current electronic claim version. Data elements in the uniform electronic billing specifications are consistent with the hard copy data set to the extent that 1 processing system can handle both. Medicare Administrative Contractors may include a crosswalk between the ASC X12N 837I and the CMS-1450 on their websites.

For more information on electronic claims, please see the CMS website at:
### Sample CMS-1500 Claim Form: Coding for Medicare and Other Payers That Accept the G Codes

**SPRAVATO® (esketamine): 2020 Physician Office Sample Claim**

<table>
<thead>
<tr>
<th>Item</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Item 21</td>
</tr>
<tr>
<td>2</td>
<td>Item 24D</td>
</tr>
<tr>
<td></td>
<td>For Medicare claims, and non-Medicare payers that require the G Codes, enter the applicable code based on the dose of SPRAVATO®:</td>
</tr>
<tr>
<td>For 56 mg or less</td>
<td>G2082 – Office or other outpatient visit for the evaluation and management of an established patient that requires the supervision of a physician or other qualified healthcare professional and provision of up to 56 mg of esketamine nasal self-administration, includes 2 hours post-administration observation.</td>
</tr>
<tr>
<td>For more than 56 mg (i.e., 84 mg)</td>
<td>G2083 – Office or other outpatient visit for the evaluation and management of an established patient that requires the supervision of a physician or other qualified healthcare professional and provision of greater than 56 mg of esketamine nasal self-administration, includes 2 hours post-administration observation.</td>
</tr>
<tr>
<td></td>
<td>Payer requirements for coding may vary.*</td>
</tr>
<tr>
<td>3</td>
<td>Item 24E</td>
</tr>
<tr>
<td>4</td>
<td>Item 24G</td>
</tr>
</tbody>
</table>

*Contact your local payer or Janssen CarePath at 844-777-2828, Monday to Friday, 8:00 AM to 8:00 PM. E-mail: Submit questions via our askjanssenmedinfo.com site.

Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39. Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
Coping for Medicare and Other Payers That Accept the G Codes

Sample CMS-1500 Claim Form: 56-mg Dose of SPRAVATO®

Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39.

Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
Sample CMS-1450 Claim Form: Coding for Medicare and Other Payers That Accept the G Codes

SPRAVATO® (esketamine): 2020 HOPD Sample Claim

1. **Locator Box 42** List revenue code.

2. **Locator Box 43** Enter narrative description for corresponding revenue code (e.g., clinic visit).

3. **Locator Box 44** For Medicare claims, and non-Medicare payers that require the G Codes, enter the applicable code based on the dose of SPRAVATO®:

   **For 56 mg or less**
   G2082 – Office or other outpatient visit for the evaluation and management of an established patient that requires the supervision of a physician or other qualified healthcare professional and provision of up to 56 mg of esketamine nasal self-administration, includes 2 hours post-administration observation.²

   **For more than 56 mg (i.e., 84 mg)**
   G2083 – Office or other outpatient visit for the evaluation and management of an established patient that requires the supervision of a physician or other qualified healthcare professional and provision of greater than 56 mg of esketamine nasal self-administration, includes 2 hours post-administration observation.²

   **Modifiers:**
   - PO or PN modifiers must be reported by all off-campus HOPDs. The PO modifier is to be reported with every HCPCS code for all items and services furnished in an excepted, off-campus, PBD of a hospital. The PN modifier is to be reported on each claim line for all items and services furnished in a nonexcepted, off-campus, PBD of a hospital.⁸

4. **Locator Box 46** Enter 1 unit for the G Code as it describes both drug and related services.

5. **Locator Box 67** Indicate diagnosis using appropriate ICD-10-CM codes. Code to the highest level of specificity for the date of service and enter diagnoses in priority order.

*Contact your local payer or Janssen CarePath at 844-777-2828, Monday to Friday, 8:00 AM to 8:00 PM. E-mail: Submit questions via our askjanssenmedinfo.com site.

Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39. Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
Coding for Medicare and Other Payers That Accept the G Codes
Sample CMS-1450 Claim Form: 84-mg Dose of SPRAVATO®

Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39.
Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
Coding for SPRAVATO® (esketamine)

ICD-10-CM Diagnosis Codes

ICD-10-CM diagnosis codes use 3 to 7 alpha and numeric characters to achieve the greatest level of specificity. Codes with 3 characters are included in ICD-10-CM as the heading of a category of codes that may be further subdivided by use of additional characters to provide greater detail. A 3-character code is to be used only if it is not further subdivided. A code is invalid if it has not been coded to the full number of characters required for that code, including the 7th character, if applicable.4

There is no ICD-10-CM code for treatment-resistant depression. Payer requirements for ICD-10-CM codes will vary. It is essential to verify correct diagnosis coding with each payer. The codes below are provided for your consideration, since our clinical trials included patients with MDD who failed at least 2 treatments of adequate dose and duration.

Table 7: ICD-10-CM Diagnosis Codes for Consideration5

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>F32.0</td>
<td>Major depressive disorder, single episode, mild</td>
</tr>
<tr>
<td>F32.1</td>
<td>Major depressive disorder, single episode, moderate</td>
</tr>
<tr>
<td>F32.2</td>
<td>Major depressive disorder, single episode, severe without psychotic features</td>
</tr>
<tr>
<td>F32.9</td>
<td>Major depressive disorder, single episode, unspecified</td>
</tr>
<tr>
<td>F33.0</td>
<td>Major depressive disorder, recurrent, mild</td>
</tr>
<tr>
<td>F33.1</td>
<td>Major depressive disorder, recurrent, moderate</td>
</tr>
<tr>
<td>F33.2</td>
<td>Major depressive disorder, recurrent, severe without psychotic features</td>
</tr>
<tr>
<td>F33.9</td>
<td>Major depressive disorder, recurrent, unspecified</td>
</tr>
<tr>
<td>F32.4</td>
<td>Major depressive disorder, single episode, in partial remission</td>
</tr>
<tr>
<td>F32.5</td>
<td>Major depressive disorder, single episode, in full remission</td>
</tr>
<tr>
<td>F33.40</td>
<td>Major depressive disorder, single episode, in remission, unspecified</td>
</tr>
<tr>
<td>F33.41</td>
<td>Major depressive disorder, recurrent, in partial remission</td>
</tr>
<tr>
<td>F33.42</td>
<td>Major depressive disorder, recurrent, in full remission</td>
</tr>
</tbody>
</table>

*These codes are not intended to be promotional or to encourage or suggest a use of drug that is inconsistent with FDA-approved use. The codes provided are not exhaustive and additional codes may apply.
Coding for SPRAVATO® (esketamine) (continued)

National Drug Code (NDC)

The NDC is a unique number that identifies a drug's labeler, product, and trade package size. The NDC is most often used on pharmacy claims, including drugs provided for home infusion. However, the NDC is also required on Medicare claims for dual-eligible beneficiaries (Medicaid cross-over claims), Medicaid fee-for-service claims, and by some private payers. Although the FDA uses a 10-digit format when registering NDCs, payer requirements regarding the use of the 10- or 11-digit NDC may vary. Electronic data exchange generally requires use of the 11-digit NDC. To convert the 10-digit format to the 11-digit format, insert a leading zero into the middle sequence, as illustrated below:

Table 8: SPRAVATO® NDC

<table>
<thead>
<tr>
<th>10-Digit NDC</th>
<th>11-Digit NDC</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>50458-028-02</td>
<td>50458-0028-02</td>
<td>56-mg Dose Kit: Unit-dose carton containing two 28-mg nasal spray devices (56-mg total dose)</td>
</tr>
<tr>
<td>50458-028-03</td>
<td>50458-0028-03</td>
<td>84-mg Dose Kit: Unit-dose carton containing three 28-mg nasal spray devices (84-mg total dose)</td>
</tr>
</tbody>
</table>

Payer requirements for NDC use and format can vary widely. Please contact your payers for specific coding policies and more information on correct billing and claims submission.

NDC Units

The NDC unit of measure is determined by how the drug is supplied. GR (gram) applies to drugs measured by weight and is typically used for ointments, creams, or inhalers. The number of NDC units dispensed is based on the packaging and numeric quantity administered to the patient. Here are examples for 56-mg and 84-mg doses of SPRAVATO®:

Table 9: SPRAVATO® NDC Units

<table>
<thead>
<tr>
<th>Dose to Be Billed</th>
<th>11-Digit NDC</th>
<th>Packaging</th>
<th>NDC Unit of Measure</th>
<th>NDC Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>56-mg</td>
<td>50458-0028-02</td>
<td>56-mg Dose Kit</td>
<td>GR</td>
<td>0.056</td>
</tr>
<tr>
<td>84-mg</td>
<td>50458-0028-03</td>
<td>84-mg Dose Kit</td>
<td>GR</td>
<td>0.084</td>
</tr>
</tbody>
</table>

Accurate NDC coding typically requires the following components:

- Reporting the NDC with 11 digits in a 5-4-2 configuration (this may require converting a 10-digit NDC to an 11-digit NDC)
- Reporting the correct NDC unit of measure
- Reporting the number of NDC units dispensed
- Reporting the qualifier, N4, in front of the NDC

For a 56-mg dose, use the 56-mg Dose Kit (NDC 50458-028-02) containing two 28-mg nasal spray devices. This is how the NDC coding format will appear:

N450458002802 GR0.056

For an 84-mg dose, use the 84-mg Dose Kit (NDC 50458-028-03) containing three 28-mg nasal spray devices. This is how the NDC coding format will appear:

N450458002803 GR0.084

Payer policies for NDC entries may vary.

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Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39. Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
Coding for SPRAVATO® (esketamine) (continued)

**HCPCS Level II Codes**

Drugs are typically reported using permanent, product-specific HCPCS codes (e.g., J Codes) assigned by CMS. Miscellaneous or “unclassified” codes allow physician offices and HOPDs to begin billing immediately for a service or item as soon as the FDA allows it to be marketed and until assignment of a permanent code. At this time, there is no date by which a permanent code for SPRAVATO® is anticipated, thus, the drug, when separately reported, will continue to be coded with J3490 in both the physician office and HOPDs.

**Table 10: Continue to Use J3490 to Separately Report SPRAVATO®**

<table>
<thead>
<tr>
<th>Site of Care</th>
<th>Payer</th>
<th>Claims Following FDA Approval up to the Assignment of a Permanent HCPCS Code</th>
<th>Permanent National Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician Office</td>
<td>Non-Medicare</td>
<td>J3490 – unclassified drug12</td>
<td>Unknown</td>
</tr>
<tr>
<td>Hospital Outpatient Department</td>
<td>Non-Medicare</td>
<td>J3490 – unclassified drug12</td>
<td></td>
</tr>
</tbody>
</table>

When using the unclassified drug code, you will usually be required to submit additional information:

- Drug name
- Strength
- Dose administered
- Route of administration
- NDC

Some payers may require that you include the drug purchase invoice, prescribing information, documentation of medical necessity, or other support for the claim. Because requirements may vary by payer, it is advisable to check local requirements before submitting claims using unclassified codes. Unclassified codes are not drug-specific and, thus, are always reported as 1 unit. When billing on the CMS-1500, enter the unclassified drug code in Item 24D and report additional information in item 19.6 (Please see sample claims beginning on page 33.)
Coding for Observation and Monitoring of SPRAVATO® Administration Under HCP Supervision Consistent With REMS Requirements

Evaluation and Management (E/M)

The type and level of E/M service for office/outpatient settings is selected first based on the key components of history, examination, and complexity of medical decision making. Time, although included in the code descriptors, is an average of the intra-service time typically required for each level and is considered an adjunct – not the sole determinant – of the appropriate E/M level.¹³

For office and outpatient visits, E/M time is defined as only that time the physician spends face-to-face with the patient and family performing tasks such as obtaining a history, examining the patient, or counseling. Measurement of time does not include pre/post-time spent in activities such as reviewing records or tests.¹³
Coding for Observation and Monitoring of SPRAVATO® Administration Under HCP Supervision Consistent With REMS Requirements (continued)

There is currently no unique, designated code to describe the observation and monitoring of SPRAVATO® administration as required by REMS. HCPs must consult with each patient’s payer since coverage will vary. Please note that healthcare providers 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.

The following table summarizes the E/M Codes to consider for SPRAVATO® administration:

### Table 11: SPRAVATO® Administration – E/M Code Considerations*

<table>
<thead>
<tr>
<th>E/M Code</th>
<th>Key Components</th>
<th>Typical Face-to-Face Time</th>
<th>Usual Severity of Presenting Problem(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>New Patients (codes require all 3 key components)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 99201    | • Problem-focused history  
• Problem-focused examination  
• Straightforward medical decision making | 10 minutes | Self-limited or minor |
| 99202    | • Expanded problem-focused history  
• Expanded problem-focused examination  
• Straightforward medical decision making | 20 minutes | Low to moderate |
| 99203    | • Detailed history  
• Detailed examination  
• Low complexity medical decision making | 30 minutes | Moderate |
| 99204    | • Comprehensive history  
• Comprehensive examination  
• Moderate complexity medical decision making | 45 minutes | Moderate to high |
| 99205    | • Comprehensive history  
• Comprehensive examination  
• High complexity medical decision making | 60 minutes | Moderate to high |
| **Established Patients† (codes require at least 2 of the 3 key components)** |
| 99212    | • Problem-focused history  
• Problem-focused examination  
• Straightforward medical decision making | 10 minutes | Self-limited or minor |
| 99213    | • Expanded problem-focused history  
• Expanded problem-focused examination  
• Low complexity medical decision making | 15 minutes | Low to moderate |
| 99214    | • Detailed history  
• Detailed examination  
• Moderate complexity medical decision making | 25 minutes | Moderate to high |
| 99215    | • Comprehensive history  
• Comprehensive examination  
• High complexity medical decision making | 40 minutes | Moderate to high |

**Medicare E/M Code for the Hospital Outpatient Site of Care**

G0463 – Hospital outpatient clinic visit for assessment and management of a patient

This code is used exclusively for coding E/M services provided to Medicare beneficiaries in the hospital outpatient setting. It applies to all levels of E/M for both new and established patients.

*Payer requirements for SPRAVATO® administration coding may vary. Please contact your payers for specific coding policies.

†CPT® code 99211 (sometimes called a “nurse visit”) is not applicable to SPRAVATO® administration. This code does not require the presence of a physician or other qualified HCP, as presenting problems are usually minimal and services are typically performed in 5 minutes.
Coding for Observation and Monitoring of SPRAVATO® Administration Under HCP Supervision Consistent With REMS Requirements (continued)

Note that under Medicare, all levels of E/M services provided in the hospital outpatient department, for both new and established patients, are to be reported with a single HCPCS code (G0463). Other payer policies may vary. Table 11a summarizes E/M coding options by payer:

### Table 11a: SPRAVATO® Administration – E/M Code Considerations by Payer*

<table>
<thead>
<tr>
<th>Site of Care</th>
<th>Medicare*</th>
<th>Commercial</th>
<th>Medicaid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician Practice</td>
<td>CPT® 99201-99205</td>
<td>CPT® 99201-99205</td>
<td>CPT® 99201-99205</td>
</tr>
<tr>
<td></td>
<td>CPT® 99212-99215</td>
<td>CPT® 99212-99215</td>
<td>CPT® 99212-99215</td>
</tr>
<tr>
<td>Hospital Outpatient Department (HOPD)</td>
<td>G0463</td>
<td>CPT® 99201-99205</td>
<td>CPT® 99201-99205</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CPT® 99212-99215</td>
<td>CPT® 99212-99215</td>
</tr>
</tbody>
</table>

*The E/M Codes only apply to Medicare when SPRAVATO® is obtained via SPP and the HCP provides the associated services. If the drug is purchased and billed by the provider, Medicare requires the new G Codes (combined drug and service).
Coding for Observation and Monitoring of SPRAVATO®
Administration Under HCP Supervision Consistent With
REMS Requirements (continued)

Prolonged Clinical Staff Services*  

Prolonged clinical staff service codes may be used when an E/M service involves prolonged clinical staff face-to-face time beyond the typical face-to-face time of the E/M service, as stated in the code description.\(^{13}\) The physician must be present to provide direct supervision of the clinical staff and the prolonged service(s) is reported in addition to the designated E/M service. The Prolonged Clinical Staff Services codes are:

- **99415** – Prolonged clinical staff service (beyond the typical staff service time) during an evaluation and management service in the office or outpatient setting, direct patient contact with physician supervision; first hour\(^{13}\)
- **99416** – Each additional 30 minutes\(^{13}\)

These codes are used to report the total duration of face-to-face time spent by clinical staff on a given date providing prolonged service, even if the time spent by the clinical staff on that date is not continuous. Prolonged service of fewer than 45 minutes' total duration on a given date is not separately reported because the clinical staff time involved is included in the E/M Codes. The typical face-to-face time of the primary service is used in defining when the prolonged service time begins. For example, prolonged clinical staff services for 99214 begin after 25 minutes, and 99415 is not reported until at least 70 minutes' total face-to-face clinical staff time has been performed.\(^{13}\) Time spent with the patient must be clearly documented in the medical record.

**Note:** the prolonged clinical staff services codes cannot be used with the SPRAVATO® G codes (G2082 and G2083).

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*Payer requirements for SPRAVATO® administration coding may vary. Please contact your payers for specific coding policies.

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Coding for Observation and Monitoring of SPRAVATO® Administration Under HCP Supervision Consistent With REMS Requirements (continued)

Prolonged Service With Direct Patient Contact (physician-patient face-to-face time)*

In the uncommon event that a physician finds it medically necessary to directly provide the services for a SPRAVATO® encounter, the codes for prolonged service with direct patient contact may apply. These codes are reported in addition to the primary procedure and may be used when an E/M service involves prolonged physician direct patient contact beyond the usual time of the primary service. The Prolonged Service With Direct Patient Contact codes are:

- **99354** – Prolonged evaluation and management (beyond the typical service time of the primary procedure) in the office or other outpatient setting requiring direct patient contact beyond the usual service; first hour
- **99355** – Each additional 30 minutes

These codes are used to report the total duration of face-to-face time spent by the physician on a given date providing prolonged service in the office or other outpatient setting, even if the time spent by the physician on that date is not continuous. **Prolonged service of less than 30 minutes’ total duration on a given date is not separately reported because the work involved is included in the total work of the E/M Codes.** The use of the time-based add-on codes requires that a primary E/M service have a typical or specified time published in the CPT® code book. Time spent with the patient must be clearly documented in the medical record.

The following table illustrates the correct reporting of prolonged physician or other qualified HCP service with direct patient contact in the office setting beyond the usual service time:

**Table 12: Use of Prolonged Service Codes**

<table>
<thead>
<tr>
<th>Total Duration of Prolonged Services</th>
<th>Code(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 30 minutes</td>
<td>Not reported separately</td>
</tr>
<tr>
<td>30-74 minutes (30 min. – 1 hr. 14 min.)</td>
<td>99354 x 1</td>
</tr>
<tr>
<td>75-104 minutes (1 hr. 15 min. – 1 hr. 44 min.)</td>
<td>99354 x 1 AND 99355 x 1</td>
</tr>
<tr>
<td>105 minutes or more (1 hr. 45 min. or more)</td>
<td>99354 x 1 AND 99355 x 2 OR more for each additional 30 minutes</td>
</tr>
</tbody>
</table>

**Note:** the prolonged clinical staff services codes cannot be used with the SPRAVATO® G codes (G2082 and G2083).

*Payer requirements for SPRAVATO® administration coding may vary. Please contact your payers for specific coding policies.
Other Coding Considerations

POS Codes

The POS code set provides setting information necessary to appropriately pay professional service claims. The place of service is the location of the provider’s face-to-face encounter with the beneficiary. POS codes are required on all claims for professional services (billed on CMS-1500). The physician practice setting is indicated with POS code 11. To differentiate between on-campus and off-campus PBDs, CMS created a new POS code (19) and revised the description for outpatient hospitals (22). Professional services delivered in outpatient hospital settings must specifically include the off-campus or on-campus POS on the claim form.

Table 13: Place of Service Codes

<table>
<thead>
<tr>
<th>Code</th>
<th>Name</th>
<th>Descriptor</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Office</td>
<td>Location, other than a hospital, skilled nursing facility, military treatment facility, community health center, state or local public health clinic, or intermediate care facility, where the health professional routinely provides health examinations, diagnosis, and treatment of illness or injury on an ambulatory basis.</td>
</tr>
<tr>
<td>19</td>
<td>Off Campus – Outpatient Hospital</td>
<td>A portion of an off-campus hospital provider-based department that provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization.</td>
</tr>
<tr>
<td>22</td>
<td>On Campus – Outpatient Hospital</td>
<td>A portion of a hospital's main campus that provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization.</td>
</tr>
<tr>
<td>53</td>
<td>Community Mental Health Center</td>
<td>A facility that provides the following services: outpatient services, including specialized outpatient services for children, the elderly, individuals who are chronically ill, and residents of the center’s mental health services area who have been discharged from inpatient treatment at a mental health facility; 24-hour-a-day emergency care services; day treatment, other partial hospitalization services, or psychosocial rehabilitation services; screening for patients being considered for admission to state mental health facilities to determine the appropriateness of such admission; and consultation and education services.</td>
</tr>
</tbody>
</table>

Revenue Codes

Many payers require use of American Hospital Association revenue codes to bill for services provided in hospital outpatient departments. Revenue codes consist of a leading zero followed by 3 other digits and are used on claim forms to assign costs to broad categories of hospital revenue centers. Codes used for Medicare claims are available from Medicare contractors. The following revenue codes may be applicable to CMS-1450 claims for drugs and their administration:

- 0510 – Clinic, General
- 0636 – Pharmacy, drugs requiring detailed coding
Other Coding Considerations (continued)

HCPCS and CPT® Modifiers

Modifiers are used to indicate that a service or procedure has been altered by some specific circumstance but not changed in its definition or code. They add more information and help to eliminate the appearance of duplicate billing and unbundling. Appropriately used, modifiers increase coding and reimbursement accuracy. The following table summarizes modifiers that may be applicable to SPRAVATO® coding and billing in physician offices and hospital outpatient departments.

Table 14: Summary of Code Modifiers

<table>
<thead>
<tr>
<th>Modifier</th>
<th>Description</th>
<th>Indication and Placement</th>
<th>CMS-1500 (Item 24D)</th>
<th>CMS-1450 (Box 44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO*</td>
<td>Services, procedures, and/or surgeries furnished at excepted off-campus provider-based outpatient departments&lt;br&gt;• To be reported with every HCPCS code for all hospital items and services furnished in an excepted off-campus, PBD of a hospital⁸</td>
<td></td>
<td>N/A</td>
<td>Required by Medicare</td>
</tr>
<tr>
<td>PN*</td>
<td>Nonexcepted service provided at an off-campus, outpatient, PBD of a hospital&lt;br&gt;• To be reported on each claim line with each nonexcepted item and service furnished in a nonexcepted, off-campus, PBD of a hospital⁸</td>
<td></td>
<td>N/A</td>
<td>Required by Medicare</td>
</tr>
</tbody>
</table>

*The PO and PN modifiers are NOT to be reported for dedicated emergency departments, remote locations, or satellite facilities of a hospital, or a PBD that is “on campus.”⁸
Modifiers PO and PN: Excepted and Nonexcepted Items and Services

Medicare rules now require that services furnished in off-campus PBDs of a hospital that began billing under the OPPS on or after November 2, 2015, are no longer paid under the OPPS. These services are referred to as “nonexcepted” and paid under the Medicare Physician Fee Schedule (MPFS). CMS established a new modifier:

“PN” (nonexcepted service provided at an off-campus, outpatient, PBD of a hospital)

to identify and pay nonexcepted items and services billed on an institutional claim. Nonexcepted off-campus PBDs of a hospital are required to report this modifier on each claim line with a HCPCS for nonexcepted items and services. The use of modifier “PN” will trigger a payment rate under the MPFS. CMS expects the PN modifier to be reported with each nonexcepted line item and service including those for which payment will not be adjusted, such as separately payable drugs, clinical laboratory tests, and therapy services.8

Excepted off-campus PBDs of a hospital must continue to report the existing modifier:

“PO” (services, procedures, and/or surgeries provided at excepted off-campus provider-based outpatient departments) for all excepted items and services with an HCPCS.

This modifier should not be reported for remote locations of a hospital, satellite facilities of a hospital, or services furnished in an emergency department.6 Neither the PN nor the PO modifier is to be reported by the following hospital departments:

- A dedicated emergency department
- A PBD that is “on the campus,” or within 250 yards, of the hospital or a remote location of the hospital9

Drugs Supplied at No Cost to Provider

Payers, including Medicare Part D, may cover a drug under the patient’s pharmacy benefit. Under this model, SPRAVATO® may be delivered to the administering site via a REMS-certified pharmacy (“white bagging”). When the drug is supplied by a REMS-certified pharmacy, it cannot be billed by the administering provider. However, the HCP observation and monitoring of the drug’s administration is a billable service.10 When reporting drug administration services associated with pharmacy-supplied drugs, consider reporting the services with the relevant evaluation and management codes. Payer policies may vary.

If You Acquire SPRAVATO® Through a REMS-certified Pharmacy

Consider Using Service CPT® Codes for:

- Medicare and non-Medicare payers

Service: Consider using Evaluation & Management (E/M) Codes
Filing Healthcare Claims

**Physician Office Claims (CMS-1500)**

The Form CMS-1500 is the basic form prescribed by CMS for the Medicare and Medicaid programs for claims from suppliers and noninstitutional providers that qualify for a waiver from the Administrative Simplification Compliance Act requirement for electronic submission of claims. It has also been adopted by the TRICARE Program. For detailed guidance on completing the CMS-1500 items, please see the Medicare Claims Processing Manual, Pub. 100-04, Chapter 26, available at:


The 837P (Professional) is the standard format used by healthcare providers and suppliers to transmit healthcare claims electronically. The ANSI ASC X12N 837P (Professional) Version 5010A1 is the current electronic claim version. Data elements in the CMS uniform electronic billing specifications are consistent with the hard copy data set to the extent that 1 processing system can handle both. Medicare Administrative Contractors may include a crosswalk between the ASC X12N 837P and the CMS-1500 on their websites.

**Hospital Outpatient Claims (CMS-1450)**

The Form CMS-1450, also known as the UB-04, is a uniform institutional provider bill suitable for use in billing multiple third-party payers. It is the basic form prescribed by CMS for the Medicare and Medicaid programs for claims from hospitals, including HOPDs. Because it serves many payers, a particular payer may not need some data elements. For detailed guidance on completing the CMS-1450 items, please see the Medicare Claims Processing Manual, Pub. 100-04, Chapter 25, available at:


The 837I (Institutional) is the standard format used by institutional providers to transmit healthcare claims electronically. The ANSI ASC X12N 837I (Institutional) Version 5010A2 is the current electronic claim version. Data elements in the uniform electronic billing specifications are consistent with the hard copy data set to the extent that one processing system can handle both. Medicare Administrative Contractors may include a crosswalk between the ASC X12N 837I and the CMS-1450 on their websites.

For more information on electronic claims, please see the CMS website at:
Sample CMS-1500 Claim Form: Coding for Non-Medicare Payers That Do Not Accept the G Codes

**SPRAVATO® (esketamine): 2020 Physician Office Sample Claim**

1. **Item 19**
   
   When submitting a claim for a Not Otherwise Classified drug, enter the drug’s name, dose, route of administration and NDC (11-digit format). Payer requirements for information and codes may vary.*

2. **Item 21**
   
   Indicate diagnosis using appropriate ICD-10-CM codes. Use diagnosis codes to the highest level of specificity for the date of service and enter the diagnoses in priority order.

3. **Item 24A**
   
   If line item NDC information is required, it will be entered in the shaded portion of Item 24A. For example:

<table>
<thead>
<tr>
<th>DRG</th>
<th>MVR</th>
<th>MODIFIER</th>
<th>DIAGNOSIS POINTER</th>
<th>CHARGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>J3490</td>
<td>A</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

   Payer requirements for NDC entries may vary.*

4. **Item 24D**
   
   Indicate appropriate CPT, HCPCS codes, and modifiers, if required.
   
   **SPRAVATO®**
   
   J3490 – unclassified drug

   **Observation and Monitoring for SPRAVATO® Administration**

   99201-99205 – Office or other outpatient visit for the evaluation and management of a new patient

   99212-99215 – Office or other outpatient visit for the evaluation and management of an established patient

   Payer requirements for observation and monitoring coding may vary.*

5. **Item 24E**
   
   Refer to the diagnosis for this service (see box 21). Enter only 1 diagnosis pointer per line.

6. **Item 24G**
   
   **Drug**

   J3490 – Enter 1 unit and enter additional information in Item 19

   **Observation and Monitoring for SPRAVATO® Administration**

   Report appropriate E&M code; enter 1 unit

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*Contact your local payer or Janssen CarePath at 844-777-2828, Monday to Friday, 8:00 AM to 8:00 PM. E-mail: Submit questions via our askjanssenmedinfo.com site.

Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39. Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
**Sample CMS-1500 Claim Form: 56-mg Dose of SPRAVATO®**

**CPT/HCPCS**

**SPRAVATO® Coding With HCPCS and CPT Codes**

1. **HEALTH INSURANCE CLAIM FORM**

   **APPROVED BY NATIONAL UNIFORM CLAIM COMMITTEE (NUCC) 2012**

<table>
<thead>
<tr>
<th>Field</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. MEDICARE</td>
<td>Medicare ID or Medicare Number</td>
</tr>
<tr>
<td>2. TRICARE</td>
<td>TRICARE ID or PPO Number</td>
</tr>
<tr>
<td>3. CHAMPVA</td>
<td>CHAMPVA ID</td>
</tr>
<tr>
<td>4. ADMINISTRIER</td>
<td>Medicaid ID</td>
</tr>
<tr>
<td>5. PATIENT'S ADDRESS (No., Street)</td>
<td>3914 Spruce Street</td>
</tr>
<tr>
<td>6. PATIENT'S OR AUTHORIZED PERSON'S SIGNATURE</td>
<td>I authorize the release of any medical or other information necessary to process this claim.</td>
</tr>
<tr>
<td>7. INSURED'S ADDRESS (No., Street)</td>
<td>3914 Spruce Street</td>
</tr>
<tr>
<td>8. ZIP CODE</td>
<td>01010</td>
</tr>
<tr>
<td>9. TELEPHONE (Include Area Code)</td>
<td>(203) 555-1234</td>
</tr>
<tr>
<td>10. CLAIM PAYEE</td>
<td>Name of individual or entity to receive payment of medical benefits to the undersigned physician or supplier for services described below.</td>
</tr>
<tr>
<td>11. INSURED'S OR AUTHORIZED PERSON'S SIGNATURE</td>
<td>Name of individual or entity to receive payment of medical benefits to the undersigned physician or supplier for services described below.</td>
</tr>
<tr>
<td>12. ADDED CLAIM INFORMATION (Designated by NUCC)</td>
<td>SPRAVATO® (esketamine) 56 mg (2 units of 28 mg), intranasally. NDC 50458-0028-02</td>
</tr>
</tbody>
</table>

2. **CPT/HCPCS**

   **SPRAVATO® Coding With HCPCS and CPT Codes**

<table>
<thead>
<tr>
<th>Procedure/CPT/HCPCS</th>
<th>Modifier</th>
<th>NPI</th>
<th>Provider ID</th>
<th>CHARGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>J3490</td>
<td>A</td>
<td>123 456 7890</td>
<td>John Doe</td>
<td>1000</td>
</tr>
<tr>
<td>J3490</td>
<td>A</td>
<td>123 456 7890</td>
<td>John Doe</td>
<td>1000</td>
</tr>
</tbody>
</table>

3. **Billings Provider Info & Ph #**

<table>
<thead>
<tr>
<th>Field</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>26. BILLING PROVIDER INFO &amp; PH #</td>
<td>(203) 987-6543</td>
</tr>
<tr>
<td>27. SIGNATURE OF PROVIDER OR SUPPLIER</td>
<td>Signature of provider or supplier</td>
</tr>
<tr>
<td>28. BILLING PROVIDER NAME</td>
<td>Dr. Johns</td>
</tr>
<tr>
<td>29. BILLING PROVIDER ADDRESS</td>
<td>4231 Center Road Anytown, AS 01010</td>
</tr>
<tr>
<td>30. BILLING PROVIDER PHONE</td>
<td>(203) 987-6543</td>
</tr>
</tbody>
</table>

**PLEASE PRINT OR TYPE**

**CMB APPROVAL PENDING**
Sample CMS-1450 Claim Form: Coding for Non-Medicare Payers That Do Not Accept the G Codes

**SPRAVATO® (esketamine): 2020 HOPD Sample Claim**

1. **Locator Box 42** List revenue codes in ascending order.

2. **Locator Box 43** Enter narrative description for corresponding revenue code (e.g., clinic visit). If line item NDC information is required, enter it in the unshaded portion of Locator Box 43. Payer requirements for NDC entries may vary.*

3. **Locator Box 44** SPRAVATO® J3490 – Unclassified drug

   **Observation and Monitoring for SPRAVATO® Administration**

   99201-99205 – Office or other outpatient visit for the evaluation and management of a new patient

   99212-99215 – Office or other outpatient visit for the evaluation and management of an established patient

   NOTE: When drug is acquired via REMS-certified pharmacy channels, and the claim is to report the service only, Medicare requires G0463 (Hospital outpatient clinic visit for assessment and management of a patient) in lieu of the E/M CPT® Codes.

   Payer requirements for observation and monitoring coding may vary.*

   **Modifiers:**

   • PO or PN modifiers must be reported by all off-campus HOPDs. The PO modifier is to be reported with every HCPCS code for all items and services furnished in an excepted, off-campus, PBD of a hospital. The PN modifier is to be reported on each claim line for all items and services furnished in a nonexcepted, off-campus, PBD of a hospital.*

4. **Locator Box 46** Enter the number of HCPCS units.

   **Drug**

   J3490 – enter 1 unit and enter additional information in Locator Box 80 ("Remarks")

   **Observation and Monitoring for SPRAVATO® Administration**

   Report appropriate E&M code; enter 1 unit.

5. **Locator Box 67** Indicate diagnosis using appropriate ICD-10-CM codes. Code to the highest level of specificity for the date of service and enter diagnoses in priority order.

6. **Locator Box 80** When submitting a claim for an unclassified drug, enter the drug's name, dose, route of administration, and NDC (11-digit format). Payer requirements for information and codes may vary.*

---

*Contact your local payer or Janssen CarePath at 844-777-2828, Monday to Friday, 8:00 AM to 8:00 PM. E-mail: Submit questions via our askjanssenmedinfo.com site.

Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39. Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
### Coding for Non-Medicare Payers That Do Not Accept the G Codes

**Sample CMS-1450 Claim Form: 84-mg Dose of SPRAVATO®**

<table>
<thead>
<tr>
<th>Admission/Consultation Code</th>
<th>Date of Occurrence</th>
<th>Date of Occurrence Through</th>
<th>Amount</th>
<th>Total Charges</th>
</tr>
</thead>
<tbody>
<tr>
<td>0510 Clinic visit</td>
<td>01-01-20</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>0636 SPRAVATO (esketamine)</td>
<td>01-01-20</td>
<td></td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

**Remarks:**
- F33.2
- SPRAVATO® (esketamine) 84 mg intranasally.
- NDC 50458-0028-03

---

Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39. Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
Important Safety Information

**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®.

(continued on next page)

Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
Important Safety Information for SPRAVATO® (esketamine) CIII Nasal Spray (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](http://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®.

(continued on next page)
Ulcereative 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 1 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 Cmax 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,

(continued on next page)
Important Safety Information

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 ≥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®.

cp-79821v2
Janssen CarePath can help make it simple for you to help your patients

Your one source for Access, Affordability and Treatment Support for your patients

Access support to help navigate payer processes
Janssen CarePath helps verify insurance coverage for your patients taking SPRAVATO® and provides reimbursement information.

Affordability support to help your patients start and stay on the treatment you prescribe
Janssen CarePath can help you find out what affordability assistance may be available for your patients taking SPRAVATO®.

Janssen CarePath Savings Program
Eligible commercially insured patients pay $10 per treatment for SPRAVATO® medication costs.*

Treatment support to help your patients get informed and stay on prescribed Janssen treatment
Janssen CarePath provides additional support to your patients, including patient education, web-based resources, and assistance finding a location that offers SPRAVATO® treatment.

* $7,150 maximum program benefit per calendar year. Treatment may include up to three devices administered on the same day. Not valid for patients using Medicare, Medicaid, or other government-funded programs to pay for SPRAVATO® medication. Terms expire at the end of each calendar year and may change. There is no income requirement. Program does not cover the cost to give patients their treatment. See full eligibility requirements at Spravato.JanssenCarePathSavings.com.

Need help? Call 844-777-2828 Monday to Friday, 8:00 AM to 8:00 PM

Visit www.JanssenCarePath.com/hcp/Spravato

Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39. Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
APPENDIX A: Tools for Working With Payers

A sample format letter of medical necessity is shown below. You can also download editable letter templates at www.JanssenCarePath.com/hcp/Spravato.

Sample Format: Letter of Medical Necessity

[Insert Physician Letterhead]

RE: Member Name: [Insert Member Name]
Member Number: [Insert Member Number]
Group Number: [Insert Group Number]

REQUEST: Authorization for treatment with SPRAVATO™ (esketamine) Nasal Spray CIII

DIAGNOSIS: [Insert Diagnosis] [Insert ICD]

DOSE AND FREQUENCY: [Insert Dose & Frequency]

REQUEST TYPE: ☐ Standard ☐ EXPEDITED

Dear [Insert name of Medical Director or name of individual responsible for prior authorization]:

I am writing to support my request for an authorization for the above-mentioned patient to receive treatment with SPRAVATO™ for [Insert Indication], dosed concomitant with [insert oral antidepressant]. My request is supported by the following:

Summary of Patient’s Diagnosis
[Insert patient’s diagnosis, date of diagnosis, lab results and date, current condition]

Summary of Patient’s History
[Insert:
- Previous therapies/procedures, including dose and duration, response to those interventions
- Description of patient’s recent symptoms/condition
- Site of medical service—include appropriate site type: inpatient, hospital outpatient, outpatient clinic, private practice, or other
- Rationale for not using drugs that are on the plan’s formulary
- Summary of your professional opinion of the patient’s likely prognosis or disease progression without treatment with SPRAVATO™.

Note: Exercise your medical judgment and discretion when providing a diagnosis and characterization of the patient’s medical condition.]

Rationale for Treatment
[Insert summary statement for rationale for treatment such as: Considering the patient’s history, condition, and the full Prescribing Information supporting uses of SPRAVATO™, I believe treatment with SPRAVATO™ at this time is medically necessary, and should be a covered and reimbursed service.]

[You may consider including documents that provide additional clinical information to support the recommendation for SPRAVATO™ for this patient, such as the full Prescribing Information, peer-reviewed journal articles, or clinical guidelines.]

[Given the urgent nature of this request, please provide a timely authorization. Contact my office at [Insert Phone Number] if I can provide you with any additional information.]

Sincerely,

[Insert Physician Name and Participating Provider Number]

Enclosures [Include full Prescribing Information and the additional support noted above]
APPENDIX A: Tools for Working With Payers (continued)

A sample format letter to request a formulary exception is shown below. You can also download editable letter templates at www.JanssenCarePath.com/hcp/Spravato.

Sample Format: Formulary Exception Request

[Insert Physician Letterhead]

[Insert Name of Medical Director] RE: Member Name: [Insert Member Name]
[Insert Payer Name] Member Number: [Insert Member Number]
[Insert Address] Group Number: [Insert Group Number]
[Insert City, State Zip]

REQUEST: Authorization for treatment with SPRAVATO™ (esketamine) Nasal Spray CIII

DIAGNOSIS: [Insert Diagnosis] [Insert ICD]

DOSE AND FREQUENCY: [Insert Dose & Frequency]

REQUEST TYPE: ☐ Standard ☐ EXPEDITED

Dear [Insert Name of Medical Director]:

I am writing to request a formulary exception for the above-mentioned patient to receive treatment with SPRAVATO™ for [insert indication], dosed concomitant with [insert oral antidepressant]. My request is supported by the following:

Summary of Patient’s Diagnosis
[Insert patient's diagnosis, date of diagnosis, lab results and date, current condition]

Summary of Patient’s History
[Insert:
   Previous therapies/procedures, including dose and duration, response to those interventions
   Description of patient’s recent symptoms/condition
   Site of medical service—include appropriate site type: Inpatient, hospital outpatient, outpatient clinic, private practice, or other
   Rationale for not using drugs that are on the plan’s formulary
   Summary of your professional opinion of the patient’s likely prognosis or disease progression without treatment with SPRAVATO™.

Note: Exercise your medical judgment and discretion when providing a diagnosis and characterization of the patient’s medical condition.]

Rationale for Treatment
[Insert summary statement for rationale for treatment such as: Considering the patient’s history, condition, and the full Prescribing Information supporting uses of SPRAVATO™, I believe treatment with SPRAVATO™ at this time is medically necessary, and should be a covered and reimbursed service.]

[You may consider including documents that provide additional clinical information to support the recommendation for SPRAVATO™ for this patient, such as the full Prescribing Information, peer-reviewed journal articles, or clinical guidelines.]

[Given the urgent nature of this request, please provide a timely authorization. Contact my office at [Insert Phone Number] if I can provide you with any additional information.]

Sincerely,

[Insert Physician Name and Participating Provider Number]

Enclosures [Include full Prescribing Information and the additional support noted above]

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Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39. Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
APPENDIX B: Ordering Information

The following specialty distributors are authorized to sell SPRAVATO®:

<table>
<thead>
<tr>
<th>Specialty Distributor</th>
<th>Phone Number</th>
<th>Fax</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>Besse Medical</td>
<td>1-800-543-2111</td>
<td>1-800-543-8695</td>
<td><a href="http://www.besse.com">www.besse.com</a></td>
</tr>
<tr>
<td>CuraScript Specialty Distribution</td>
<td>1-877-599-7748</td>
<td>1-800-862-6208</td>
<td><a href="http://www.curascriptsd.com">www.curascriptsd.com</a></td>
</tr>
<tr>
<td>McKesson Specialty Health</td>
<td>1-855-477-9800</td>
<td>—</td>
<td><a href="http://www.mckessonspecialtyhealth.com">www.mckessonspecialtyhealth.com</a></td>
</tr>
</tbody>
</table>

This list is provided for informational purposes only. Janssen Pharmaceuticals, Inc., does not endorse the use of any particular distributor. This information was current at time of publication.

The following are authorized SPRAVATO® full-line wholesalers:

<table>
<thead>
<tr>
<th>Full-line Wholesalers</th>
<th>Phone Number</th>
<th>Fax</th>
<th>Website</th>
</tr>
</thead>
<tbody>
<tr>
<td>AmerisourceBergen</td>
<td>1-844-222-2273</td>
<td>1-888-292-9774</td>
<td><a href="http://www.amerisourcebergen.com">www.amerisourcebergen.com</a></td>
</tr>
<tr>
<td>Cardinal Health</td>
<td>1-800-926-3161</td>
<td>—</td>
<td><a href="http://www.cardinalhealth.com">www.cardinalhealth.com</a></td>
</tr>
<tr>
<td>McKesson Pharmaceutical Distribution</td>
<td>1-855-625-7385</td>
<td>—</td>
<td><a href="http://www.mckesson.com">www.mckesson.com</a></td>
</tr>
</tbody>
</table>
References


2. Medicare program; CY 2020 revisions to payment policies under the Physician Fee Schedule and other changes to Part B payment policies final rule; and coding and payment for evaluation and management, observation and provision of self-administered esketamine interim final rule. Fed Regist. 2019;84:62568. 42 CFR §403.


Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39. Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.
To contact Janssen Medical Information Center
Call: 1-800-JANSSEN (1-800-526-7736)
Monday to Friday, 9:00 am to 8:00 pm ET
E-mail: Submit questions via our askjanssenmedinfo.com site.

Visit www.JanssenCarePath.com/hcp/Spravato

To contact Janssen Medical Information Center
Call: 1-800-JANSSEN (1-800-526-7736)
Monday to Friday, 9:00 am to 8:00 pm ET
E-mail: Submit questions via our askjanssenmedinfo.com site.

Please see Important Safety Information, including Boxed WARNINGS, on pages 36-39.
Please see full Prescribing Information, including Boxed WARNINGS, and Medication Guide for SPRAVATO®.