

Spravato® (esketamine) (Intranasal)

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I. Length of Authorization

Initial coverage will be provided for 6 months and may be renewed annually thereafter.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

[G2082/G2083]

- **Treatment Resistant Depression (TRD)**
 - Induction (weeks 1 to 4): 1 billable unit twice weekly
 - Maintenance (weeks 5 and after): 1 billable unit weekly
- **Depressive Symptoms In Patients With Major Depressive Disorder (MDD) With Acute Suicidal Ideation/Behavior:** 1 billable unit twice weekly

[S0013]

- **Treatment Resistant Depression (TRD)**
 - Induction (weeks 1 to 4): 56 billable units on Day 1, then 84 billable units twice weekly
 - Maintenance (weeks 5 and after): 84 billable units weekly
- **Depressive Symptoms In Patients With Major Depressive Disorder (MDD) With Acute Suicidal Ideation/Behavior:** 168 billable units weekly

III. Initial Approval Criteria ^{1,15}

Coverage is provided in the following conditions:

- Patient is at least 18 years old; **AND**
- Patient must have a baseline assessment using any validated depression rating scale (e.g., Montgomery-Asberg Depression Rating Scale [MADRS], Hamilton Depression Rating Scale [HAM-D], Patient Health Questionnaire Depression Scale [PHQ-9], Beck Depression Inventory [BDI], Quick Inventory of Depressive Symptomatology [QIDS], etc.); **AND**

Universal Criteria ^{1,11}

- Patient has a diagnosis of major depressive disorder (MDD) according to the current version of the Diagnostic and Statistical Manual of Mental Disorders (e.g., DSM-5-TR); **AND**

- Patient must not have any of the following:
 - Aneurysmal vascular disease
 - Arteriovenous malformation
 - History of intracerebral hemorrhage
 - Known hypersensitivity to ketamine; **AND**
- Patient is not receiving concomitant ketamine therapy; **AND**

Treatment-Resistant Depression (TRD) †^{1,7,8,12-13,16}

- Used as monotherapy or in conjunction with an oral antidepressant; **AND**
- Patient has tried psychotherapy alone or in combination with an oral antidepressant, if psychotherapy resources are available; **AND**
- Patient is NOT receiving concomitant electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), vagus nerve stimulation (VNS), or deep brain stimulation (DBS); **AND**
- Patient has failed a trial of at least 2 antidepressants of *different* classes for a duration of at least 6 weeks each with adequate adherence at generally accepted doses in the current depressive episode, unless contraindicated or clinically significant adverse effects are experienced (*'Failed trial' is defined as less than or equal to 25% reduction in symptom severity using any validated depression rating scale*)

Depressive Symptoms In Patients With Major Depressive Disorder (MDD) With Acute Suicidal Ideation/Behavior †^{1,9,10}

- Must be used in conjunction with an oral antidepressant; **AND**
 - Patient is experiencing acute suicidal ideation or behavior; **OR**
 - Patient has recently been discharged from a hospital in which treatment with esketamine has been initiated

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Ⓢ Orphan Drug

IV. Renewal Criteria^{1,15}

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the universal and indication specific criteria as identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: sedation, dissociation, respiratory depression, signs of abuse/dependence, severe cognitive impairment, ulcerative/interstitial cystitis, suicidal thoughts/behavior, severe hypertension, etc.; **AND**
- Patient has demonstrated disease improvement and/or stabilization as evidenced by a reduction in symptom severity, compared to baseline, using any validated depression rating scale.

V. Dosage/Administration ¹

Indication	Dose
Treatment-resistant depression (TRD)	<p><u>Induction Phase:</u></p> <ul style="list-style-type: none"> Weeks 1 to 4: Administer 56 mg or 84 mg intranasally twice per week <p><u>Maintenance Phase:</u></p> <ul style="list-style-type: none"> Weeks 5 to 8: Administer 56 mg or 84 mg intranasally once weekly Weeks 9 and after: Administer 56 mg or 84 mg intranasally once every 2 weeks or once weekly* <p><i>*Dosing frequency should be individualized to the least frequent dosing to maintain remission/response.</i></p>
Depressive Symptoms in Major Depressive Disorder (MDD) with Acute Suicidal Ideation/Behavior	<p>Administer 84 mg intranasally twice per week for 4 weeks.</p> <ul style="list-style-type: none"> Dosage may be reduced to 56 mg twice per week based on tolerability. After 4 weeks of treatment with Spravato, evidence of therapeutic benefit should be evaluated to determine need for continued treatment. The use of Spravato, in conjunction with an oral antidepressant, beyond 4 weeks has not been systematically evaluated in the treatment of depressive symptoms in patients with MDD with acute suicidal ideation or behavior.
<ul style="list-style-type: none"> Spravato must be administered under the direct supervision of a healthcare provider. A treatment session consists of nasal administration of Spravato and post-administration observation under supervision. 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. 	

VI. Billing Code/Availability Information

HCPCS(s):

- J3490 – Unclassified drugs
- C9399 – Unclassified drugs or biologicals
- S0013 – Esketamine, nasal spray, 1 mg; 1 billable unit = 1 mg
- *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 health care professional and provision of up to 56 mg of esketamine nasal self-administration, includes 2 hours post-administration observation
- *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 health care professional and provision of greater than 56 mg esketamine nasal self-administration, includes 2 hours post-administration observation

** Required for Medicare part B claims. For non-Medicare, those that do not accept the G Codes, providers may continue to report separate codes for the drug and service using the unclassified drug codes (J3490 or C9399) for Spravato and the most appropriate E/M CPT® code for the service.*

NDC(s):

- 56 mg Dose Kit: Unit-dose carton containing two 28 mg nasal spray devices (56 mg total dose): 50458-0028-xx
- 84 mg Dose Kit: Unit-dose carton containing three 28 mg nasal spray devices (84 mg total dose): 50458-0028-xx

VII. References

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
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F32.0	Major depressive disorder, single episode, mild
F32.1	Major depressive disorder, single episode, moderate
F32.2	Major depressive disorder, single episode, severe without psychotic features
F32.3	Major depressive disorder, single episode, severe with psychotic features
F32.4	Major depressive disorder, single episode, in partial remission
F32.5	Major depressive disorder, single episode, in full remission
F32.9	Major depressive disorder, single episode, unspecified
F33.0	Major depressive disorder, recurrent, mild
F33.1	Major depressive disorder, recurrent, moderate
F33.2	Major depressive disorder, recurrent severe without psychotic features
F33.3	Major depressive disorder, recurrent, severe with psychotic symptoms
F33.40	Major depressive disorder, recurrent, in remission, unspecified
F33.41	Major depressive disorder, recurrent, in partial remission
F33.42	Major depressive disorder, recurrent, in full remission
F33.8	Other recurrent depressive disorders
F33.9	Major depressive disorder, recurrent, unspecified
R45.851	Suicidal ideations

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes		
Jurisdiction	NCD/LCA/LCD Document (s)	Contractor
H, L	A59249	Novitas Solutions, Inc.
N	A59250	First Coast Service Options, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC