Spravato® (esketamine)
(Intranasal)

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I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 6 months (180 days).
- Renewal: Prior authorization validity may be renewed every 12 months (365 days) 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 Major Depressive Disorder (MDD) With Acute Suicidal Ideation/Behavior:** 2 billable units weekly

[J0013]

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

III. Initial Approval Criteria [1,15]

Prior authorization validity is provided in the following conditions:

- Member is at least 18 years old; **AND**
- Member 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]

- Member 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**

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- Member does NOT have any FDA labeled contraindications to the requested agent [e.g., aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial, and peripheral arterial vessels); arteriovenous malformation; history of intracerebral hemorrhage; hypersensitivity to esketamine, ketamine, or any of the excipients]; **AND**
- Member is not receiving concomitant ketamine therapy; **AND**

Treatment-Resistant Depression (TRD) † [1,7,8,12-14,16]

- Used as monotherapy or in conjunction with an oral antidepressant; **AND**
- Member has tried psychotherapy alone or in combination with an oral antidepressant, if psychotherapy resources are available; **AND**
- Member is NOT receiving concomitant electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), vagus nerve stimulation (VNS), or deep brain stimulation (DBS); **AND**
- Member 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 Major Depressive Disorder (MDD) With Acute Suicidal Ideation/Behavior † [1,9,10]

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

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

IV. Renewal Criteria [1,15]

Prior authorization validity can be renewed based upon the following criteria:

- Member 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/dependance, severe cognitive impairment, ulcerative/interstitial cystitis, suicidal thoughts/behavior, severe hypertension, etc.; **AND**
- Member has demonstrated disease improvement and/or stabilization as evidenced by a reduction in symptom severity, compared to baseline, using any validated depression rating scale

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V. Dosage/Administration [1]

Indication	Dose
Treatment-resistant depression (TRD)	Induction Phase: • Weeks 1 to 4: Administer 56 mg or 84 mg intranasally twice per week Maintenance Phase: • 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* **Dosing frequency should be individualized to the least frequent dosing to maintain remission/response.*
Depressive Symptoms in Major Depressive Disorder (MDD) with Acute Suicidal Ideation/Behavior	Administer 84 mg intranasally twice per week for 4 weeks. • 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 members with MDD with acute suicidal ideation or behavior.
• 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):

- J0013 – 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.*

NDC(s):

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

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

VII. References

1. Spravato [package insert]. Titusville, NJ; Janssen Pharmaceuticals., Inc.; March 2026. Accessed June 2026.
2. Papakostas GI. Incidence, impact, and current management strategies for treatment-resistant major depressive disorder. Medscape. Available at: https://www.medscape.org/viewarticle/574817_1. Accessed June 30, 2026.
3. Gelenberg AJ, Freeman MP, Markowitz JC, et al. Practice Guideline for the Treatment of Patients With Major Depressive Disorder Third Edition. American Psychiatric Association; 2010. https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd-1410197717630.pdf
4. Major Depression. National Institute of Mental Health. Available at: https://www.nimh.nih.gov/health/statistics/major-depression.shtml. Accessed July 7, 2026.
5. Johnston KM, Powell LC, Anderson IM, et al. The burden of treatment-resistant depression: a systematic review of the economic and quality of life literature. J Affect Disord. 2019; 242: 195-210. DOI: 10.1016/j.jad.2018.06.045.
6. Socci C, Medda P, Toni C, et al. Electroconvulsive therapy and age: age-related clinical features and effectiveness in treatment resistant major depressive episode. J Affect Disord. 2018; 227:627-632.
7. Starr HL, Abell J, Larish A, et al. Self-reported review of the value of esketamine in patients with treatment-resistant depression: Understanding the patient experience in the STRIVE Study. Psychiatry Res. 2020 Nov;293:113376. doi: 10.1016/j.psychres.2020.113376. Epub 2020 Aug 8. PMID: 32818917.
8. Jha MK, Williamson DJ, Magharehabed G, et al. Intranasal esketamine effectively treats treatment-resistant depression in adults regardless of baseline irritability. J Affect Disord. 2023 Jan 15;321:153-160. doi: 10.1016/j.jad.2022.10.020. Epub 2022 Oct 20. PMID: 36273682.
9. Fu D-J, Ionescu DF, Li X, et al. Esketamine nasal spray for rapid reduction of major depressive disorder symptoms in patients who have active suicidal ideation with intent: double-blind, randomized study (ASPIRE I). J Clin Psychiatry. 2020;81(3):19m13191.
10. Rozjabek, H., Li, N., Hartmann, H. *et al.* Assessing the meaningful change threshold of Quality of Life in Depression Scale using data from two phase 3 studies of esketamine nasal spray. *J Patient Rep Outcomes* 6, 74 (2022). https://doi.org/10.1186/s41687-022-00453-y
11. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR), 2024.
12. Reif A, Bitter I, Buyze J, et al. Esketamine Nasal Spray versus Quetiapine for Treatment-Resistant Depression. N Engl J Med 2023; 389:1298.
13. McIntyre RS, Rosenblat JD, et al. Synthesizing the Evidence for Ketamine and Esketamine in Treatment-Resistant Depression: An International Expert Opinion on the Available Evidence and Implementation. Am J Psychiatry. 2021 May 1;178(5):383-399. doi: 10.1176/appi.ajp.2020.20081251. Epub 2021 Mar 17. PMID: 33726522; PMCID: PMC9635017.

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14. Qaseem A, Owens DK, Etxeandia-Ikobaltzeta I, et al. Nonpharmacologic and Pharmacologic Treatments of Adults in the Acute Phase of Major Depressive Disorder: A Living Clinical Guideline From the American College of Physicians (Version 1, Update Alert 4). Ann Intern Med. 2026;179. [Epub 10 March 2026]. doi:10.7326/ANNALS-26-00548
15. American Psychological Association. Depression Assessment Instruments. January 2023. Available at: https://www.apa.org/depression-guideline/assessment. Accessed on June 30, 2026.
16. Rush AJ, Thase ME. Improving Depression Outcome by Patient-Centered Medical Management. Am J Psychiatry. 2018 Dec 1;175(12):1187-1198. doi: 10.1176/appi.ajp.2018.18040398. Epub 2018 Sep 17. PMID: 30220219.
17. Janik A, Qiu X, Lane R, et al. Efficacy and Safety of Esketamine Nasal Spray as Monotherapy in Adults with Treatment-Resistant Depression: A Randomized, Double-Blind, Placebo-Controlled Study. Janssen Research & Development, LLC, San Diego, CA, USA; Janssen Research & Development, LLC, Raritan, NJ, USA; Janssen Research & Development, LLC, Titusville, NJ, USA; Janssen Pharmaceutica NV, Beerse, Belgium. efficacy-and-safety-of-esketamine-nasal-spray-as-monotherapy-in-adults-with-treatmentresistant-depre.pdf
18. Popova V, Daly EJ, Trivedi M, et al. Efficacy and Safety of Flexibly Dosed Esketamine Nasal Spray Combined With a Newly Initiated Oral Antidepressant in Treatment-Resistant Depression: A Randomized Double-Blind Active-Controlled Study. Am J Psychiatry. 2019 Jun 1;176(6):428-438. doi: 10.1176/appi.ajp.2019.19020172. Epub 2019 May 21. Erratum in: Am J Psychiatry. 2019 Aug 1;176(8):669. doi: 10.1176/appi.ajp.2019.1768correction1. PMID: 31109201.
19. Daly EJ, Trivedi MH, Janik A, et al. Efficacy of Esketamine Nasal Spray Plus Oral Antidepressant Treatment for Relapse Prevention in Patients With Treatment-Resistant Depression: A Randomized Clinical Trial. JAMA Psychiatry. 2019 Sep 1;76(9):893-903. doi: 10.1001/jamapsychiatry.2019.1189. PMID: 31166571; PMCID: PMC6551577.
20. Ionescu DF, Fu DJ, Qiu X, et al. Esketamine Nasal Spray for Rapid Reduction of Depressive Symptoms in Patients With Major Depressive Disorder Who Have Active Suicide Ideation With Intent: Results of a Phase 3, Double-Blind, Randomized Study (ASPIRE II). Int J Neuropsychopharmacol. 2021 Jan 20;24(1):22-31. doi: 10.1093/ijnp/pyaa068. PMID: 32861217; PMCID: PMC7816667.
21. Zaki N, Chen L, Lane, R et al. Safety and efficacy with esketamine in treatment-resistant depression: long-term extension study. International Journal of Neuropsychopharmacology, Volume 28, Issue 6, June 2025, pyaf027, https://doi.org/10.1093/ijnp/pyaf027

Appendix A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

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Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	Yes: Consider for PA
Potential for misuse/abuse	Yes: Consider for PA
Cost of drug	Yes: Consider for PA

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
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.

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Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

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

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