Medical Policy:

Spravato (esketamine hydrochloride) Nasal Spray

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.196	September 26, 2025	August 1, 2019

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The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Length of Authorization

Coverage will be provided: Initial: 3 months, Continuation: 6 months

Max Units (per dose and over time) [Medical Benefit]:

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): 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

Guideline

I. INITIAL APPROVAL CRITERIA

Coverage is provided in the following conditions:

- Patient is 18 years of age or older; **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**
- 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** meets criteria for one of the following diagnoses 1 or 2):

1. **Treatment-Resistant Depression (TRD) †**
    A. Patient has tried psychotherapy alone or in combination with an oral antidepressant, if psychotherapy resources are available; **AND**
    B. Patient is NOT receiving concomitant electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), vagus nerve stimulation (VNS), or deep brain stimulation (DBS); **AND**
    C. Patient has had an inadequate response to the maximum tolerated dose of at least **TWO** antidepressant classes (e.g., selective serotonin reuptake inhibitors [SSRIs], serotonin-norepinephrine reuptake inhibitors [SNRIs], tricyclic antidepressants [TCAs], bupropion, mirtazapine, etc.) for at least 6 weeks during the current major depressive episode (MDE) (Document medication, dose, and duration); **AND**
    D. Patient will be using Spravato as monotherapy or in conjunction with an oral antidepressant.

2. **Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior †**
    A. Must be used in conjunction with an oral antidepressant; **AND**
        1. Patient is experiencing acute suicidal ideation or behavior; **OR**
        2. Patient 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

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II. RENEWAL CRITERIA

Coverage can be renewed based upon the following criteria:

1. Patient continues to meet the initial approval criteria and specific indication **AND**
2. 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**
3. 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.

Dosing/Administration

Spravato is administered intranasally twice weekly for 4 weeks, then once weekly for four weeks, then weekly or every other week thereafter.

The recommended dosing schedule is as follows:

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 patients 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.	

Limitations/Exclusions

Spravato is not considered medically necessary for indications other than those listed above due to insufficient evidence of therapeutic value.

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Applicable Procedure Codes

Code	Description
S0013	Esketamine, nasal spray, 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 ***Medicare only***
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 ***Medicare only***

Applicable NDCs

Code	Description
50458-0028--00	Unit-dose carton containing 28 mg nasal spray device
50458-0028--02	Unit-dose carton containing 28 mg (56 mg dose) nasal spray device
50458-0028--03	Unit-dose carton containing 28 mg (84 mg dose) nasal spray device

ICD-10 Diagnoses

Code	Description
F32.0-F33.9	Major depressive disorder, recurrent
R45.851	Suicidal ideations

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	9/26/2025	Updated TRD dose From: Induction (weeks 1 to 4): 56 billable units on Day 1. To 84 billable units twice weekly. Updated name from Major depressive disorder (treatment-resistant) to Treatment-Resistant Depression (TRD). Replaced in TRD - Patient has a diagnosis of moderate to severe major depressive disorder; to Patient has tried psychotherapy alone or in combination with an oral antidepressant, if psychotherapy resources are available. Updated two different therapies to read two different classes.
EmblemHealth & ConnectiCare	9/2/2025	Updated induction and maintenance dose.
EmblemHealth & ConnectiCare	8/12/2025	Updated Dosage/Administration chart and Dosing Limits. Update universal criteria to include the following: •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

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		•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. Updated TRD – Spravato can be used as monotherapy OR in combination with an oral antidepressant. Added Patient is NOT receiving concomitant electroconvulsive therapy (ECT), transcranial magnetic stimulation (TMS), vagus nerve stimulation (VNS), or deep brain stimulation (DBS). MDD Update: Added 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. Removed The prescriber represents that, in the absence of the requested drug, within the next 24 to 48 hours the member will require confinement in an acute care psychiatric institution; AND Member has a depressive episode so acute and so severe that the member is not able to participate in self-care (e.g., washing, eating), is unable to participate at all in their usual daily activities (e.g., work), and has persistent thoughts of hopelessness and helplessness as well as anhedonia; AND Patient will be using Spravato in conjunction with an oral antidepressant. Updated renewal "Criteria and Removed patient will continue Spravato in conjunction with an oral antidepressant"
EmblemHealth & ConnectiCare	1/6/2025	Revision: Initial Criteria: removed: "(≤ 50% improvement in depression symptoms or scores) " from the statement: " Patient has had an inadequate response (≤ 50% improvement in depression symptoms or scores) to the maximum tolerated dose of at least TWO antidepressant therapies…" Renewal Criteria: removed: "a 50%" from the statement: " Patient has had at least a 50% reduction in symptoms of depression compared to baseline using a standard rating scale that reliably measures depressive symptoms;"
EmblemHealth & ConnectiCare	12/11/2024	Addition of G2082 and G2083 Procedure Codes 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 - ***Medicare only*** 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 - ***Medicare only***
EmblemHealth & ConnectiCare	1/3/2024	Annual Review: Added Max units, updated dosing chart
EmblemHealth & ConnectiCare	4/27/2023	Annual Review: no criteria changes

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EmblemHealth & ConnectiCare	1/12/2023	Transfer to New Template
EmblemHealth & ConnectiCare	7/7/2021	Updated Procedure codes
EmblemHealth & ConnectiCare	8/13/2020	Added new indication: Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior. Added criteria for new indication. Added diagnosis code R45.851 suicidal ideations.

References

1. Spravato [package insert]. Titusville, NJ; Janssen Pharmaceuticals., Inc.; January 2025. Accessed January 2025.

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