Department of HUMAN SERVICES

Spravato (esketamine nasal spray)

IME-PAM-021

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	1/1/2021
Revision Number:	3	**Last Rev Date:**	4/15/2022
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	4/21/2023
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	4/16/2021

Overview

Medication:[i]	esketamine
Brand Name:	Spravato®
Pharmacologic Category:	N-methyl-D-aspartate (NMDA) receptor antagonist.
FDA-Approved Indication(s):	Indicated, in conjunction with an oral antidepressant, for the treatment of: • treatment-resistant depression (TRD) in adults. • depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior. • Limitations of use - The effectiveness of Spravato® in preventing suicide or in reducing suicidal ideation or behavior has not been demonstrated. Use does not preclude the need for hospitalization if clinically warranted, even if patients experience improvement after an initial dose of Spravato®. - Spravato® is not approved as an anesthetic agent. The safety and effectiveness of Spravato® as an anesthetic agent have not been established.
How Supplied:	Available in a stoppered glass vial within a nasal spray device. Each nasal spray device delivers two sprays containing a total of 28 mg of esketamine: • 56 mg dose kit: unit-dose carton containing two 28 mg nasal spray devices. • 84 mg dose kit: unit-dose carton containing three 28 mg nasal spray devices.
Dosage/Administration:	See tables below.
Benefit Category:	Medical

Treatment-Resistant Depression (TRD)

Treatment Phase	Time Frame	Administration Frequency	Dosage
Induction	Weeks 1 to 4	Twice per week	Day 1 starting dose: 56 mg Subsequent doses: 56 mg or 84 mg
Maintenance	Weeks 5 to 8	Once weekly	56 mg or 84 mg
Maintenance	Week 9 & after	Every 2 weeks or once weekly	56 mg or 84 mg

Major Depressive Disorder (MDD) with Acute Suicidal Ideation or Behavior			
Treatment	Weeks 1 to 4	Twice per week	Day 1 starting dose: 56 mg Subsequent doses: 56 mg or 84 mg
After 4 weeks of treatment with Spravato®, evidence of therapeutic benefit should be evaluated to determine need for continued treatment. The use of Spravato® beyond 4 weeks has not been systematically evaluated in the treatment of depressive symptoms in patients with MDD with acute suicidal ideation or behavior.			

Descriptive Narrative

Esketamine, the active ingredient in Spravato®, is an NMDA-receptor antagonist. The efficacy of esketamine for the treatment of TRD is mediated through antagonism of NMDA receptor, which produces a transient increase in glutamate release, leading to increases in postsynaptic alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors stimulation and subsequently to increases in neurotrophic signaling that restore synaptic function in these brain regions.[ii]

Black Box Warnings

- Potential for misuse and abuse. Monitor patients for signs and symptoms.
- 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 members.
- Spravato® is available only through a Risk Evaluation and Mitigation Strategy (REMS) program. Members self-administer the drug in the office and are then monitored for at least 2 hours by clinicians in the office (due to risk of sedation and dissociation after administration).

Tools for Measuring Depression

Evaluation of depression and response to treatment is accomplished utilizing a standard rating scale to survey the type and severity of symptoms. There are several standardized rating scales available including the following:

- Beck Depression Inventory (BDI).
- Geriatric Depression Scale (GDS).
- Hamilton Depression Rating Scale (HAM-D).
- Inventory of Depressive Symptomatology-Systems Review (IDS-SR).
- Montgomery-Asberg Depression Rating Scale (MADRS).
- Personal Health Questionnaire Depression Scale (PHQ-9).
- Quick Inventory of Depressive Symptomatology (QIDS).

Guidelines

Clinical practice guidelines for the treatment of depression were last updated prior to FDA-approval of Spravato® in 2019.

Criteria

Prior authorization is required.

Treatment Resistant Depression (TRD)

Spravato® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of MDD (meets DSM-5 criteria within the previous 4 weeks); **AND**
2. Member is 18 years of age or older; **AND**
3. Prescribed by, or in consultation with, a psychiatrist or a psychiatric or mental health nurse practitioner; **AND**
4. Depression has been determined to be treatment-resistant (in the current depressive episode, member has not responded adequately to at least two different antidepressants of adequate dose and duration); **AND**
5. Member has not responded to an adequate trial of augmentation therapy or cognitive behavioral therapy during the current depressive episode. Augmentation therapy includes an antidepressant drug plus one of the following, but not limited to, a second-generation antipsychotic, lithium, triiodothyronine, or buspirone; **AND**
6. Member will continue to use antidepressant therapy in addition to Spravato®; **AND**
7. The regimen/dosing prescribed is within FDA-approved labeling. If dose or schedule exceeds the FDA-approved regimen, regimen (including dosage) must be supported by clinical practice guidelines (supporting clinical documentation must be provided with any request for which the regimen or dosage prescribed does not align with FDA-approved labeling).

Spravato® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member has a diagnosis of MDD and is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Member has had at least a 50 percent reduction in symptoms of depression compared to baseline using a standard rating scale that reliably measures depressive symptoms; **AND**
3. Member will continue oral antidepressant therapy in conjunction with Spravato®; **AND**
4. Prescribed by, or in consultation with, a psychiatrist or a psychiatric or mental health nurse practitioner; **AND**
5. If there are any changes made to the dosing or therapy regimen, the new regimen (including dosage) must be within FDA-approved labeling, or supported by clinical practice guidelines. If new dose or dosing schedule exceeds the FDA-approved regimen, regimen (including dosage) must be supported by clinical practice guidelines (supporting clinical documentation must be provided with any

request for which the regimen or dosage prescribed does not align with FDA-approved labeling).

Major Depressive Disorder (MDD) with Acute Suicidal Ideation or Behavior

Spravato® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of MDD (meets DSM-5 criteria within the previous 4 weeks); **AND**
2. Member is judged to be at risk for suicide by a clinician based on consideration of suicidal behavior, expressed suicidal ideation, or overall clinical assessment consistent with significant continuing risk of suicide; **AND**
3. Prescribed by, or in consultation with, a psychiatrist or a psychiatric or mental health nurse practitioner; **AND**
4. Member is 18 years of age or older; **AND**
5. Prescribed in combination with initiation or optimization of oral antidepressant therapy; **AND**
6. The regimen/dosing prescribed is within FDA-approved labeling. If dose or schedule exceeds the FDA-approved regimen, regimen (including dosage) must be supported by clinical practice guidelines (supporting clinical documentation must be provided with any request for which the regimen or dosage prescribed does not align with FDA-approved labeling).

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.

Contraindications

Member diagnosed with **ANY** of the following:

1. Aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial and peripheral arterial vessels) or arteriovenous malformation; **OR**
2. Intracerebral hemorrhage; **OR**
3. Hypersensitivity to esketamine, ketamine, or any of the excipients.

Experimental/Investigational

The following uses are considered experimental/investigational:

1. Members younger than 18 years of age.
2. Use of ketamine as an intravenous infusion is not FDA approved and is not a covered benefit.
3. Administration of Spravato® at a site outside of a REMS program.

Approval Duration/Quantity Limits

Diagnosis	Initial	Continuation
TRD	3 months 8 kits* per first 28 days, then 4 kits per 28 days	6 months 4 kits per 28 days
MDD with acute suicidal ideation or behavior	4 weeks 8 kits for 28-day course of therapy	Not applicable

*Spravato is available in two formulations:
56 mg kit (containing two nasal spray devices, each containing 28 mg of esketamine).
84 mg kit (containing three nasal spray devices, each containing 28 mg of esketamine).

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
S0013	Esketamine, nasal spray, 1 mg.
E&M	Use appropriate evaluation and management (E&M) codes when billing for healthcare provider services required for Spravato administration and post-administration observation.

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.
F32.4	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.
F33.40	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.
F33.9	Major depressive disorder, recurrent, unspecified.

NDC	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
50458-0028-02 (56 mg kit)	Janssen Pharmaceuticals, Inc.	1 mg	1	2	56
50458-0028-03 (84 mg kit)	Janssen Pharmaceuticals, Inc.	1 mg	1	3	84

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[i] Spravato prescribing information (07/2020). Janssen Pharmaceuticals, Inc.: Titusville, NJ. Available online at www.spravato.com/. Accessed February 3, 2022.

[ii] Center for Drug Evaluation and Research (CDER): Clinical Pharmacology and Biopharmaceutics Review for Spravato (NDA 211243). Approval date March 5, 2019. Available online at www.accessdata.fda.gov/drugsatfda_docs/nda/2019/211243Orig1s000ClinPharmR.pdf. Accessed March 16, 2022.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version

Signature

Change Date	Changed By	Description of Change	Version
4/15/2022	CAC	Annual review. Rewrite.	3

Signature
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Change Date	Changed By	Description of Change	Version
2/14/2022	Medical director.	Clarifying language added to Coding section.	2

Signature
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Change Date	Changed By	Description of Change	Version
4/16/2021	CAC	Criteria implementation.	1

Signature
William (Bill) Jagiello, DO