Reference number(s)
2889-A

Specialty Guideline Management Spravato (esketamine)

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name	Dosage Form
Spravato	esketamine	nasal spray

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1]

Spravato is indicated for the treatment of:

- Treatment-resistant depression (TRD) in adults as monotherapy or in conjunction with an oral antidepressant
- Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior in conjunction with an oral antidepressant

Limitations of Use

The effectiveness of Spravato in preventing suicide or in reducing suicidal ideation or behavior has not been demonstrated. Use of Spravato 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.

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

For initial requests:

- Pretreatment depression severity score(s) from standardized rating scale(s) that reliably measure depressive symptoms (e.g., Beck Depression Inventory [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS], etc.)
- Medical records documenting inadequate response with antidepressant and augmentation agents for the current depressive episode or evidence based psychotherapy (if applicable)

For continuation of therapy:

Current depression severity score(s) from standardized rating scale(s) that reliably measure depressive symptoms (if applicable)

Prescriber Specialties

This medication must be prescribed by or in consultation with a psychiatrist.

Exclusions

Coverage will not be provided for members with moderate or severe substance or alcohol use disorder that is not currently being treated or medically managed.

Coverage Criteria

Treatment-resistant depression (TRD)/Major Depressive Disorder (MDD) with acute suicidal ideation or behavior[1-4]

Authorization of 3 months may be granted for the treatment of TRD or 1 month for the treatment of MDD with acute suicidal ideation or behavior when all of the following criteria are met:

- Member has a confirmed diagnosis of severe major depressive disorder (single or recurrent episode), documented by standardized rating scales that reliably measure depressive symptoms (e.g., Beck Depression Inventory [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS], etc.).
- Member is 18 years of age or older.
- The requested medication will be administered under the direct supervision of a healthcare provider.
- Member will be monitored by a health care provider for at least 2 hours after administration.
- Member meets either of the following criteria:
    - For treatment-resistant depression (TRD), member must meet both of the following:
        - Member has experienced an inadequate response during the current depressive episode with two antidepressants from at least two different classes with different mechanisms of action at the maximally tolerated labeled dose, each used for at least 8 weeks within the past 5 years. For the purposes of this criteria, the current depressive episode begins with the most recent onset of acute symptoms. Examples of antidepressant classes include, but are not limited to:
            - Aminoketone (Wellbutrin/SR/XL [bupropion])
            - Monoamine oxidase inhibitors (MAOIs) (e.g., Marplan, Nardil, Parnate, phenelzine, tranylcypromine)
            - Noradrenaline and specific serotoninergic antidepressants (NASSAs) (e.g., amoxapine, maprotiline, mirtazapine/ODT, Oleptro ER, Remeron/Solutab, trazodone)
            - Selective serotonin reuptake inhibitors (SSRIs) (e.g., Celexa, citalopram, escitalopram, fluoxetine, fluvoxamine, Lexapro, Luvox/CR, paroxetine, Paxil/CR, Pexeva, Prozac/Weekly, sertraline, Zoloft)
            - Serotonin-norepinephrine reuptake inhibitors (SNRIs) (e.g., Cymbalta, desvenlafaxine/ER, duloxetine, Effexor/XR, Fetzima, Khedezla, Pristiq, venlafaxine/ER)
            - Tricyclic antidepressants (TCAs) (e.g., amitriptyline, desipramine, doxepin, Elavil, imipramine, Norpramin, nortriptyline, Pamelor, Surmontil, Tofranil, trimipramine)
            - Serotonin modulators (e.g., Trintellix, vortioxetine, Viibryd, vilazodone)
        - Member has experienced an inadequate response with an adequate trial of augmentation therapy for at least 8 weeks within the past 5 years OR evidenced based psychotherapy (i.e., cognitive behavioral therapy [CBT], interpersonal therapy [IPT], supportive therapy [ST], or psychoeducational intervention [PEI]) during the current depressive episode. For the purposes of this criteria, the current depressive episode begins with the most recent onset of acute symptoms.

        - Augmentation therapy is defined as:
            - Two antidepressants with different mechanisms of action used concomitantly
            - An antidepressant and a second-generation antipsychotic used concomitantly
            - An antidepressant and lithium used concomitantly
            - An antidepressant and thyroid hormone used concomitantly
    - For major depressive disorder (MDD) with acute suicidal ideation or behavior, member meets all of the following:
        - Member has major depressive disorder with current suicidal ideation with intent defined as both of the following:
            - Member has thoughts, even momentarily, of self-harm with at least some intent or awareness that they may die as a result, or member thinks about suicide
            - Member intends to act on thoughts of killing themselves
        - 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.
        - The requested drug will be used in combination with an oral antidepressant (e.g., duloxetine, escitalopram, sertraline, venlafaxine).

Continuation of Therapy

Treatment-resistant depression (TRD)

Authorization of 6 months may be granted for the continuation of treatment of TRD when there is improvement or sustained improvement from baseline in depressive symptoms documented by standardized rating scales that reliably measure depressive symptoms (e.g., Beck Depression Inventory [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS], etc.).

Major depressive disorder (MDD) with acute suicidal ideation or behavior

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. Member must meet all requirements in the coverage criteria section for approval.

References

1. Spravato [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; January 2025.
2. American Psychological Association. Depression Assessment Instruments. Available at: https://www.apa.org/depression-guideline/assessment. Accessed October 21, 2024.
3. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Available at: www.micromedexsolutions.com [available with subscription]. Accessed October 21, 2024.
4. Thase, M and Connolly, R (2021) Unipolar depression in adults: Choosing treatment for resistant depression, UpToDate, Available at www.uptodate.com [available with subscription]. Accessed October 21, 2024.