Reference number(s)
2889-A

SPECIALTY GUIDELINE MANAGEMENT

SPRAVATO (esketamine) nasal spray

POLICY

I. 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
Spravato is indicated, in conjunction with an oral antidepressant, for the treatment of:

1. Treatment-resistant depression (TRD) in adults
2. 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 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.

II. DOCUMENTATION

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

A. For initial requests:
   1. 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.)
   2. Medical records documenting inadequate response with antidepressant and augmentation agents for the current depressive episode (if applicable)

B. For continuation of therapy:
   Current depression severity score(s) from standardized rating scale(s) that reliably measure depressive symptoms (if applicable)

III. EXCLUSION

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.

IV. CRITERIA FOR INITIAL APPROVAL

A. Treatment-resistant depression (TRD)/Major Depressive Disorder (MDD) with acute suicidal ideation or behavior

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

1. 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]).
2. The requested medication will be prescribed by or in consultation with a psychiatrist.
3. Member is 18 years of age or older.
4. Requested drug will be administered under the direct supervision of a healthcare provider.
5. Member will be monitored by a health care provider for at least 2 hours after administration.
6. Requested drug will be used in combination with an oral antidepressant (e.g., duloxetine, escitalopram, sertraline, venlafaxine).
7. Member meets either of the following criteria:
   i. Member must meet both of the following:
      a. Member has experienced inadequate response during the current depressive episode with two antidepressants (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], bupropion, mirtazapine) from at least two different classes (different mechanisms of action) at the maximally tolerated labeled dose, each used for at least 8 weeks;
         - 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, Irenka, Khedezla, Pristiq, venlafaxine/ER)
         - Tricyclic antidepressants (TCAs) (e.g., amitriptyline, desipramine, doxepin, Elavil, imipramine, Norpramin, nortriptyline, Pamelor, Surmontil, Tofranil, trimipramine)
      b. Member has experienced an inadequate response with an adequate trial of augmentation therapy OR evidenced based psychotherapy (e.g., cognitive behavioral therapy) during the current depressive episode
         - 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
           - An antidepressant and buspirone used concomitantly
   ii. Member has major depressive disorder with both of the following:
      a. Member has 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

b. 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.

V. CONTINUATION OF THERAPY

A. Treatment-resistant depression (TRD)
Authorization of 3 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]).

B. 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 initial criteria for approval.

VI. REFERENCES

1. Spravato [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; July 2020.
2. American Psychological Association. *Depression Assessment Instruments.* Available at: https://www.apa.org/depression-guideline/assessment. Accessed October 5, 2022.
3. Micromedex Solutions [database online]. Ann Arbor, MI: Truven Health Analytics Inc. Available at: www.micromedexsolutions.com [available with subscription]. Accessed October 5, 2022.
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 5, 2022.