Montana Healthcare Programs
Physician Administered Drug Coverage Criteria
SPRAVATO® (esketamine)

I. Medication Description

Spravato® is a non-competitive N-methyl D-aspartate (NMDA) receptor antagonist 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.

II. 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.

III. Position Statement

Coverage is determined through a prior authorization process **that must include** supporting clinical documentation for each request.

IV. Initial Coverage Criteria

Member must meet all the following criteria:

- Member is 18 years of age or older.
- Spravato® is prescribed by a psychiatric specialist.
- Member has a Diagnostic and Statistical Manual of Mental Disorders (DSM-5) diagnosis of MDD.
- Member must have had a baseline depression assessment using a validated depression rating scale (e.g., MADRS, PHQ-9, HAM-D, etc.) within the last 2 weeks.
- Member is currently taking an oral antidepressant and will continue to take the oral antidepressant in conjunction with Spravato®.
- Member must have **one** of the following diagnoses:
    1. Treatment-resistant depression (TRD), along with **all** of the following:
        a. Insufficient treatment response after at least 6 weeks duration at an adequate dose to at least two antidepressant trials with different mechanisms of action in the last 12 months. (See **Table A** below for **allowed medications and dosages**.)
        b. Insufficient treatment response after at least 6 weeks duration at an adequate dose to augmented antidepressant therapy with an atypical antipsychotic that is FDA-approved for MDD **OR** lithium in the last 12 months. (See **Table B** below for **allowed medications and dosages**.)
        c. Actively involved in psychotherapy or inadequate response to psychotherapy.
        OR
    2. Major Depressive Disorder (MDD) with acute suicidal ideation or behavior, along with **all** of the following:
        a. Member must receive initial doses of Spravato® **inpatient** (subsequent doses will be allowed outpatient).

b. Must provide documentation of **inpatient** psychiatric assessment of suicidal ideation or behavior.

- Member does not have aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial and peripheral arterial vessels), arteriovenous malformation, or history of intracerebral hemorrhage.
- Provider attests to the following:
  - Member's risk for abuse or misuse is assessed prior to initiating treatment and will be assessed periodically while on therapy.
  - Member and facility are enrolled in the Spravato® REMS program.
  - Treatment sessions will include post-treatment observation until clinically stable for a minimum of 2 hours.

V. Renewal Coverage Criteria

Member must meet all the following criteria:

- Treatment-resistant depression:
  - Member has been compliant with an oral antidepressant and continues to meet the initial criteria.
  - Member has been compliant with Spravato® therapy.
  - Member is receiving a benefit from Spravato® therapy, as demonstrated by a reduction in symptom severity compared to the baseline depression assessment utilizing the same rating scale.
- MDD in adults with acute suicidal ideation or behavior:
  - Must provide documentation of psychiatric assessment of suicidal ideation or behavior.
  - Must provide evidence that member has not been optimized on current antidepressant therapy.

VI. Quantity Limitations

Treatment-resistant depression:

- Weeks 1 to 4: 2 kits/week
- Weeks 5 and after: 1 kit/week

MDD in adults with acute suicidal ideation or behavior:

- Weeks 1 to 4: 2 kits/week

VII. Coverage Duration

Treatment-resistant depression:

- Initial approval duration: 4 weeks
- Renewal approval duration: 6 months

MDD in adults with acute suicidal ideation or behavior:

- Initial approval duration: Initial doses ***must be administered while inpatient*** and subsequent doses will be allowed outpatient up to a combined total of 4 weeks.
- Renewal approval duration: 4 weeks (1x authorization only).

Table A: Antidepressant Medications

Medication	Dosage
Amitriptyline (Elavil®)	Initial 25-50mg/day; Max 300mg/day (usual dose 100-300mg/day)
Bupropion (Wellbutrin®)	Initial 100mg 2x/day; Max 450mg/day (usual dose 100mg 3x/day)
Bupropion Sustained-Release (Wellbutrin SR®)	Initial 150mg/day; Max 200mg 2x/day (target dose 150mg 2x/day)
Bupropion Extended-Release (Wellbutrin XL®)	Initial 150mg/day; Max 450mg/day (target dose 300-450mg/day)
Bupropion Extended-Release (Forfivo XL®)	450mg/day
Bupropion Extended-Release (Aplenzin®)	Initial 174mg/day; Max 348mg/day (target dose 348mg/day)
Citalopram (Celexa®)	Initial 20mg/day; Max of 40mg/day
Desipramine (Norpramin®)	Initial 25-50mg/day; Max of 300mg/day (usual dose 100-200mg/day)
Desvenlafaxine Extended-Release (Pristiq®)	Initial 50mg/day; Max 100mg/day
Doxepin (Silenor®)	Initial 25-50mg/day; Max 300mg/day (usual dose 100-300mg/day)
Duloxetine (Cymbalta®)	Initial 40-60mg/day; Max 120mg/day (maintenance dose 60mg/day)
Escitalopram (Lexapro®)	Initial 10mg/day; Max 20mg/day
Fluoxetine (Prozac®)	Initial 20mg/day; Max 80mg/day (usual dose 20-60mg/day)
Imipramine (Tofranil®)	Initial 25-50mg/day; Max 300mg/day (usual dose 100-300mg/day)
Levomilnacipran (Fetzima®)	Initial 20mg; Max 120mg/day (maintenance 40-120mg/day)
Mirtazapine (Remeron®)	Initial 15mg/day; Max 45mg/day
Nortriptyline (Pamelor®)	Initial 25mg/day; Max of 150mg/day (usual dose 25mg 3-4x/day)
Paroxetine (Paxil®)	Initial 20mg/day; Max 50mg/day
Paroxetine Controlled-Release (Paxil CR®)	Initial 25mg/day; Max 62.5mg/day
Sertraline (Zoloft®)	Initial 50mg/day; Max 200mg/day
Trazodone (Desyrel®)	Initial 50mg 2x/day; Max 600mg/day (target dose 200-400mg/day)
Venlafaxine (Effexor®)	Initial 37.5-75mg/day; Max 375mg/day (usual dose 75-375mg/day)
Venlafaxine Extended-Release (Effexor XR®)	Initial 37.5mg-75mg/day; Max 225mg/day (usual dose 75-225mg/day)
Vilazodone (Viibryd®)	Initial 10-20mg/day; Max 40mg/day
Vortioxetine (Trintellix®)	Initial 5-10mg/day; Max 20mg/day (target dose 20mg/day)

Table B: Augmented Antidepressant Therapy Medications

Medication	Dosage
Abilify Aripiprazole (Abilify®)	Initial 2-5mg/day; Max of 15mg/day
Brexpiprazole (Rexulti®)	Initial 0.5-1mg/day; Max of 3mg/day
Quetiapine Extended-Release (Seroquel XR®)	Initial 50mg/day; Max 300mg/day (usual dose 150-300mg/day) ***Only ER FDA-approved**
Olanzapine (Zyprexa®)	Initial 5mg/day **in combination with Fluoxetine**; Max of 20mg/day
Lithium Immediate-Release or Extended-Release (Lithobid®)	Therapeutic response generally occurs with serum concentrations between 0.5 to 0.7mEq/L

*Due to the poor level of evidence of psychostimulants, these are not included as allowable augmented antidepressant therapies.