UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2022 P 2168-7
Program	Prior Authorization/Medical Necessity
Medication	Spravato™ (esketamine)
P&T Approval Date	6/2019, 9/2019, 2/2020, 12/2020, 4/2021, 4/2022, 12/2022
Effective Date	3/1/2023; Oxford only: 3/1/2023

1. Background:

Spravato™ (esketamine) 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 and depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior.

Because of the risks of serious adverse outcomes resulting from sedation, dissociation, and abuse and misuse, Spravato is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Spravato REMS

For the purposes of this program, a trial and failure of a given antidepressant is defined as the patient unable to achieve a clinical meaningful improvement of the maximally tolerated dose(s) for at least 8 weeks in the current depressive episode.[2,3]

2. Coverage Criteria [a]:

A. Major depressive disorder (treatment-resistant)

1. **Initial Authorization**

a. **Spravato** will be approved based on **all** of the following criteria

(1) Diagnosis of major depressive disorder (treatment-resistant), according to the current DSM (i.e., DSM-5) criteria, by a mental health professional.

-AND-

(2) Prescribed by or in consultation with a psychiatrist

-AND-

(3) Submission of medical records (e.g., chart notes, laboratory values) documenting baseline scoring (prior to starting Spravato) on at least **one** of the following clinical assessments has been completed:

(a) Baseline score on the 17-item Hamilton Rating Scale for Depression (HAMD17)
(b) Baseline score on the 16-item Quick Inventory of Depressive Symptomatology (QIDS-C16)
(c) Baseline score on the 10-item Montgomery-Asberg Depression Rating Scale (MADRS)

-AND-

(4) History of a trial, failure, and/or contraindication of **three** different antidepressant medications or treatment regimens at the maximally tolerated dose(s) for at least 8 weeks in the current depressive episode.

An antidepressant or treatment regimen would include any of the following classes or combinations (document medication, dose, and duration):

(a) Selective serotonin reuptake inhibitors (e.g., citalopram, fluoxetine, paroxetine, sertraline)
(b) Serotonin norepinephrine reuptake inhibitors (e.g., duloxetine, venlafaxine, etc.)
(c) Bupropion
(d) Tricyclic antidepressants (e.g, amitriptyline, clomipramine, nortriptyline, etc.)
(d) Mirtazapine
(e) Monoamine oxidase inhibitors (e.g., selegiline, tranylcypromine, etc.)
(f) Serotonin modulators (e.g., nefazodone, trazodone, etc.)
(e) Augmentation with lithium, Cytomel (liothyronine), antipsychotics, or anticonvulsants

-AND-

(5) Spravato will be used in combination with an oral antidepressant (one that the patient has not previously failed).

-AND-

(6) Provider and/or the provider's healthcare setting is certified in the Spravato REMS program

Authorization will be issued for 3 months

2. **Reauthorization**

a. **Spravato** will be approved based on **all** of the following criteria:

(1) Documentation of remission or a positive clinical response to Spravato therapy

-AND-

(2) Submission of medical records (e.g., chart notes, laboratory values) documenting baseline and recent (within the last month) scoring on at least **one** of the following assessments demonstrating remission or clinical response (e.g., score reduction from baseline) as defined by the:

(a) Hamilton Rating Scale for Depression (HAMD17; remission defined as a score of ≤ 7)

(b) Quick Inventory of Depressive Symptomatology (QIDS-C16; remission defined as a score of ≤ 5)
(c) Montgomery-Asberg Depression Rating Scale (MADRS; remission defined as a score of ≤ 12)

-AND-

(3) Spravato will be used in combination with an oral antidepressant

-AND-

(4) Provider and/or the provider's healthcare setting is certified in the Spravato REMS program

-AND-

(5) Prescribed by or in consultation with a psychiatrist

Authorization will be issued for 6 months

B. Depressive symptoms in adults with major depressive disorder (MDD) with acute suicidal ideation or behavior

1. **Authorization**

a. **Spravato** will be approved based on **all** of the following criteria:

(1) Diagnosis of major depressive disorder according to the current DSM (i.e., DSM-5) criteria, by a mental health professional.

-AND-

(2) Patient is experiencing an acute suicidal ideation or behavior

-AND-

(3) Patient receiving newly initiated or optimized oral antidepressant

-AND-

(4) Provider and/or the provider's healthcare setting is certified in the Spravato REMS program

Authorization will be issued for 1 month

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Spravato [prescribing information]. Lakewood, NJ; Janssen Pharmaceuticals, Inc.; July 2020.
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3. American Psychiatric Association (APA). Practice guideline for the treatment of patients with major depressive disorder. 3rd ed. Arlington (VA): American Psychiatric Association (APA); 2010 Oct.
4. Psychopharmacologic Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee Meeting. FDA Briefing Document. February 12, 2019. https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PsychopharmacologicDrugsAdvisoryCommittee/UCM630970.pdf. (Accessed on March 11, 2019)
5. Thase M, Connolly KR. Unipolar depression in adults: Treatment of resistant depression. Solomon D, ed. UpToDate. Waltham, MA: UpToDate Inc. https://www.uptodate.com (Accessed on March 11, 2019)
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7. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23:56–61.
8. Rush AJ, Bernstein IH, Trivedi MH, et al. An evaluation of the Quick Inventory of Depressive Symptomatology and the Hamilton Rating Scale for Depression: a Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial report. Biol Psychiatry 2006; 59:493–501.
9. Trivedi MH1, Rush AJ, Wisniewski SR, et al. Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. Am J Psychiatry. 2006 Jan;163(1):28-40.
10. Trivedi MH, Rush AJ, Gaynes BN, et al. Maximizing the adequacy of medication treatment in controlled trials and clinical practice: STAR*D measurement-based care. Neuropsychopharmacology. 2007 Dec;32(12):2479-89.
11. Canuso CM, Singh JB, Fedgchin M, et al. Efficacy and Safety of Intranasal Esketamine for the Rapid Reduction of Symptoms of Depression and Suicidality in Patients at Imminent Risk for Suicide: Results of a Double-Blind, Randomized, Placebo-Controlled Study. Am J Psychiatry. 2018 Jul 1;175(7):620-630.
12. Popova V, Daly EJ, Trivedi M, et al. Efficacy and Safety of Flexibly Dosed Esketamine Nasal Spray Combined With a Newly Initiated Oral Antidepressant in Treatment-Resistant Depression: A Randomized Double-Blind Active-Controlled Study. Am J Psychiatry. 2019 Jun 1;176(6):428-438.
13. Fu DJ, Ionescu DF, Li X, et al. Esketamine Nasal Spray for Rapid Reduction of Major Depressive Disorder Symptoms in Patients Who Have Active Suicidal Ideation With Intent: Double-Blind, Randomized Study (ASPIRE I). J Clin Psychiatry. 2020 May 12;81(3):19m13191.
14. Ionescu DF, Fu DJ, Qiu X, et al. Esketamine Nasal Spray for Rapid Reduction of Depressive Symptoms in Patients With Major Depressive Disorder Who Have Active Suicide Ideation With Intent: Results of a Phase 3, Double-Blind, Randomized Study (ASPIRE II), International Journal of Neuropsychopharmacology, pyaa068

Program	Prior Authorization/Medical Necessity – Spravato (esketamine)
Change Control	
6/2019	New program.
9/2019	Updated coverage criteria.
2/2020	Updated coverage criteria to require submission of baseline validated provider administered assessments.
12/2020	Updated background and coverage criteria for new indication for MDD with acute suicidal ideation or behavior. Updated references.
4/2021	Clarified submission of clinical assessments to include medical record submission.
4/2022	Annual review with no change to clinical criteria.
12/2022	Updated coverage criteria for treatment-resistant depression with clarification of requirement for combination with "new" oral antidepressant to be an agent that has not been previously failed.