Esketamine (SPRAVATO)
Criteria for Use
October 2025

VA Pharmacy Benefits Management Services and National Formulary Committee

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

Exclusion Criteria

If the answer to **ANY** item below is met, then the patient should **NOT** receive esketamine.

- ☐ Allergy or previous serious adverse effects to ketamine or esketamine
- ☐ Aneurysmal vascular disease (including thoracic and abdominal aorta, intracranial, and peripheral arterial vessels) or arteriovenous malformation
- ☐ History of intracerebral hemorrhage
- ☐ Uncontrolled seizures
- ☐ Dementia
- ☐ Current or recent (within 30 days) delirium
- ☐ Current uncontrolled hypertension (systolic blood pressure >140 mm Hg or diastolic blood pressure > 90 mm Hg)
- ☐ Severe cardiac decompensation (Class IV heart failure or unstable angina)
- ☐ Severe hepatic impairment (Child-Pugh class C)
- ☐ Current or previous interstitial or ulcerative cystitis
- ☐ Comorbid psychiatric condition is present (schizophrenia, schizoaffective disorder, bipolar disorder)
- ☐ History of non-response to ketamine or esketamine
- ☐ Current or previous abuse of ketamine or esketamine
- ☐ Clinical evidence for current substance abuse except tobacco
- ☐ Current barbiturate, cannabis, or opioid use
- ☐ Current moderate or severe substance use disorder (SUD)
- ☐ Pregnancy (known pregnancy or positive pregnancy test)
- ☐ Breastfeeding/providing breastmilk to an infant

Inclusion Criteria

One of the following must be selected to meet criteria for use

- ☐ Remission not achieved from 2 antidepressant trials including a trial of an augmentation strategy in

the current episode of depression^1 and 4 total adequate antidepressant trials in the patient's lifetime

☐ Patient is hospitalized with TRD with acute suicidal ideation/behavior

^1 One augmentation trial could be an adequate course of evidence-based psychotherapy (EBP)

Additional Inclusion Criteria

The answers to **ALL** of the following must be fulfilled to meet criteria

☐ All REMS requirements have been met

☐ Adults <65 years of age with current diagnosis of unipolar major depressive disorder by DSM-5

☐ Patient in current episode of depression is experiencing moderate to severe depressive symptomatology (i.e., PHQ-9 ≥15 within the last 30 days)

☐ Antidepressant treatment trials are considered unsuccessful if the patient has not responded to at least 6 weeks of an antidepressant at half maximum dose or greater

☐ A VA psychiatrist or a VA licensed health-care provider (i.e., CPP, NP, PA) has evaluated the patient and determined and documented in the patient's medical records that the patient qualifies for esketamine treatment

☐ The prescriber is a VA psychiatrist or a VA licensed health-care provider (i.e., CPP, NP, PA).

☐ The patient agrees to stay and be monitored after esketamine administration and agrees not to drive or operate heavy machinery and not to make critical decisions for the remainder of the day in which esketamine is administered

☐ The patient or their legal representative can provide signed informed consent

☐ The patient has an adult who can accompany him/her and assist with transportation, or another method of safe transport has been arranged and documented

Additional Inclusion Criteria: select if applicable

For women of childbearing potential

☐ Pregnancy should be excluded prior to receiving esketamine and the patient provided contraceptive counseling on potential risks vs. benefits of taking esketamine if patient were to become pregnant

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