



MEDICAL COVERAGE POLICY

SERVICE: Esketamine (Spravato)

Policy Number: 257

Effective Date: 09/01/2020

Last Review: 07/30/2020

Next Review Date: 07/31/2021

Important note:

Unless otherwise indicated, this policy will apply to all lines of business.

Even though this policy may indicate that a particular service or supply may be considered medically necessary and thus covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. You need to consult the Evidence of Coverage (EOC) or Summary Plan Description (SPD) to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and your plan of benefits, the provisions of your benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare-linked plan members, this policy will apply unless there are Medicare policies that provide differing coverage rules, in which case Medicare coverage rules supersede guidelines in this policy. Medicare-linked plan policies will only apply to benefits paid for under Medicare rules, and not to any other health benefit plan benefits. CMS's Coverage Issues Manual can be found on the CMS website. Similarly, for Medicaid-linked plans, the Texas Medicaid Provider Procedures Manual (TMPPM) supersedes coverage guidelines in this policy where applicable.

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PRIOR AUTHORIZATION: Required.

POLICY: Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for coverage details.

For Medicare plans, please refer to appropriate Medicare LCD (Local Coverage Determination). If there is no applicable LCD, use the criteria set forth below.

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid TMPPM.

SWHP/FirstCare may consider esketamine (Spravato) nasal spray medically necessary for the treatment of treatment-resistant depression (TRD) in members 18 years of age or older, when the following criteria are met:

- Member has a confirmed diagnosis of severe major depressive disorder documented by standardized rating scales (e.g., Beck Depression Scale [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS], etc.); and
- Diagnosis is verified by a psychiatrist; and
- Member does not have a current or recent history (i.e., within the last 6 months) of moderate or severe substance or alcohol use disorder; and
- There is documentation of failure of or intolerance to FOUR medication trials with adequate dose and duration for depression (examples: four antidepressant agents, including 2 different agent classes; or two antidepressant agents from different agent classes with 2 augmentation trials), during the current depressive episode; and
- Esketamine will be used in combination with an oral antidepressant (e.g., duloxetine, escitalopram, sertraline, venlafaxine); and
- Administered under the direct supervision of a healthcare provider; and
- Member will be monitored by a health care provider for at least 2 hours after administration.
- There is written confirmation that all Risk Evaluation and Mitigation Strategy (REMS) requirements have been met

Treatment continued beyond one month with esketamine may be medically necessary for members with documented improvement or sustained improvement from baseline in depressive symptoms documented by standardized rating scales as noted earlier.



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Initial authorization approval duration is 4 weeks. Authorization renewal approval duration is 1 year.

SWHP considers esketamine experimental and investigational for all other indications.

OVERVIEW: Esketamine (S-enantiomer of racemic ketamine) is a nonselective, noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist. The mechanism by which it exerts its antidepressant effect is unknown. The major circulating metabolite noresketamine demonstrated activity at the same receptor with less affinity

Major depressive disorder (MDD) is a serious and life-threatening condition with high rates of morbidity and a chronic disease course. Over 16 million people in the U.S. and over 300 million people worldwide have depression. The lifetime prevalence of MDD in the U.S. is approximately 20%. Patients with MDD may be unable to work, maintain relationships, attend to self-care, and in the most severe cases may become hospitalized or attempt or commit suicide. MDD is considered the leading cause of disability worldwide and also is associated with increased mortality rates. Approximately 30% to 40% of patients with MDD fail to respond to first-line treatments, including oral antidepressant medications of all classes and/or psychotherapy. In addition, the onset of treatment response for these modalities often takes at least 4 weeks.

Spravato will be available only via a Risk Evaluation and Mitigation Strategy (REMS), which requires the following:

- Healthcare settings must be certified in the program and ensure that Spravato is only dispensed in healthcare settings and administered to patients who are enrolled in the program;
- Spravato is administered by patients under the direct observation of a healthcare provider;
- Patients are monitored by a healthcare provider for at least 2 hours after administration of Spravato;
- Pharmacies must be certified in the REMS and must only dispense Spravato to healthcare settings that are certified in the program.
- REMS details can be found of FDA website:
https://www.accessdata.fda.gov/scripts/cder/remis/index.cfm?event=IndvRemsDetails_page&REMS=386

MANDATES:

CODES:

Important note:

CODES: Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.

CPT Codes:	
CPT Not Covered:	
HCPCS Codes	J3490 and C9399
ICD10 codes:	
ICD10 Not covered:	

CMS:



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POLICY HISTORY:

Status	Date	Action
New	07/25/2019	New policy
	06/29/2020	Logo and language changed to include FC
Reviewed	07/30/2020	Added authorization duration

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. SWHP will continue to review clinical evidence related to this policy and may modify it at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available and they are not included in the list, please forward the reference(s) to SWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. Fond G, Loundou A, Rabu C, et al. Ketamine administration in depressive disorders: A systematic review and metaanalysis. *Psychopharmacology (Berl)*. 2014;231(18):3663-3676.
2. U.S. Food and Drug Administration (FDA). Spravato (esketamine) nasal spray. Prescribing Information. Reference ID: 4399464.
3. 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;175(7):620-630.
4. Daly EJ, Singh JB, Fedgchin M, et al. Efficacy and Safety of Intranasal Esketamine Adjunctive to Oral Antidepressant Therapy in Treatment-Resistant Depression: A Randomized Clinical Trial. *JAMA Psychiatry*. 2018;75(2):139-148.
5. Lapidus KA, Levitch CF, Perez AM, et al. A randomized controlled trial of intranasal ketamine in major depressive disorder. *Biol Psychiatry*. 2014;76(12):970-6.