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Inland Empire Health Plan

IEHP UM Subcommittee Approved Authorization Guideline			
Guideline	Spravato, (esketamine)	**Guideline #**	UM_OTH 20
		Original Effective Date	2/12/20
Section	Other	**Revised Date**	

COVERAGE POLICY (MEDI-CAL)

A. Spravato (esketamine)

Requests may be approved if all of the following criteria are met:

1. A diagnosis of unipolar major depressive disorder (DSM-5; single-episode MDD or recurrent MDD without psychotic feature); and
2. Prescribed by or in consultation with a psychiatrist; and
3. Age of 18 years or older; and
4. No current substance use disorder in past 6 months; and
5. For the current major depressive episode, the patient has an inadequate response to ONE of the following:
    a. Four antidepressants from at least two different classes; or
    b. Three antidepressants from at least two different classes plus an augmenting agent
6. The antidepressant trial length was at adequate dosage (maximally tolerated) and adequate duration (at least 6 weeks)
7. Spravato will be used in combination with an oral antidepressant
8. Requested dosage is consistent with FDA approved labeling
9. Provider's healthcare setting is certified in the Risk Evaluation and Mitigation Strategy (REMS) program
10. Dispensing pharmacy (if applicable; when buy-and-bill is not feasible) is certified in the Risk Evaluation and Mitigation Strategy (REMS) program

B. Initial Authorization: may be approved for up to 8 weeks in duration

C. Continued Therapy

Clinical documentation (including, but not limited to chart notes) must be provided to confirm:

1. Current medical necessity criteria are met
2. Medication is providing clinical benefit evidenced by improvement or sustained improvement from baseline depression symptoms
3. Current dose and frequency of Spravato documented

Re-authorization: may be approved for up to 6 months in duration

COVERAGE LIMITATION AND EXCLUSIONS

Request for investigational indications including but not limited to treatment for chronic pain and bipolar depression that lack established clinical benefits and safety are not covered.

ADDITIONAL INFORMATION

Major depressive disorder is the leading cause of disability worldwide. It is estimated that up to 30% of patients with major depression do not achieve remission despite multiple antidepressant therapy. The onset of antidepressant effect may typically take several weeks, during which time patients may remain symptomatic and at risk of suicidal and self-harm behavior. Therefore, there has been a demand for a novel treatment that is effective at rapid onset for treatment-resistant depression (Popova, Daly, Trivedi et al., 2019).

In 2019, the U.S. Food and Drug Administration (FDA) approved Spravato (esketamine), a non-competitive N-methyl-D-aspartate receptor antagonist, indicated in conjunction with an oral antidepressant for the treatment of treatment-resistant depression (TRD) in adults.

Applicable Codes

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement policy.

HCPCS Code	Description
J3490	Unclassified drugs

CLINICAL/REGULATORY RESOURCE

A. American Psychiatric Association Practice Guideline for the Treatment of Patients with Major Depressive Disorder 2010:

1. Strategies to Address Incomplete Response
    a. For patients who have not fully responded to treatment for depression after maximizing the dose and duration of the antidepressant therapy, the following are recommended treatment options:
        i. Combine pharmacotherapy with a depression-focused psychotherapy at optimal intensity
        ii. Change to a different non-MAOI antidepressant medication from the same pharmacological class or to one from a different class
        iii. Augment antidepressant medications by adding another non-MAOI antidepressant or non-antidepressant agents (e.g. lithium, anti-convulsant, atypical antipsychotic, etc.)
        iv. Neurostimulation

B. <u>Diagnostic and Statistical Manual of Mental Disorders (DSM-5) Diagnostic Criteria for a Major Depressive Episode</u>

1. Five (or more) of the following symptoms have been present during the same two-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure:
    a. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g. feels sad, empty, hopeless) or observations made by others (e.g. appears tearful).
    b. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation)
    c. Significant weight loss when not dieting or weight gain (e.g. a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day.
    d. Insomnia or hypersomnia nearly every day
    e. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
    f. Fatigue or loss of energy nearly every day
    g. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
    h. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by their subjective account or as observed by others)
    i. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide
2. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
3. The episode is not attributable to the direct physiological effects of a substance or to another medical condition.
4. Criteria 1 through 3 represent a major depressive episode.
5. Responses to a significant loss (e.g. bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion 1, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical

judgement based on the individual's history and the cultural norms for the expression of distress in the context of loss.

6. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.
7. There has never been a manic or hypomanic episode.
    a. This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.

C. <u>Safety:</u>

1. Spravato carries four boxed warnings issued by the FDA including the risk for sedation, dissociative or perceptual changes, abuse or misuse potential, and the risk of suicidal thoughts and behavior
    a. Sedation rate: 49% to 61%
    b. Dissociation rate: 61% to 75%
    c. Esketamine, the s-enantiomer of ketamine, is a Schedule III substance with opioid properties.
    d. Antidepressants increased the risk of suicidal thoughts and behavior in pediatric and young adult patients in short-term studies. It is important to note that Spravato is not approved for use in pediatric patients.
2. Based on these warnings, Spravato is only available through the REMS program required by the FDA to mitigate the risks of serious adverse outcomes resulting from sedation and dissociation caused by Spravato administration, and abuse and misuse of Spravato by ensuring:
    a. Spravato is dispensed and administered to patients in a medically-supervised health care setting that monitors these patients
    b. Pharmacy and healthcare setting that dispense Spravato are REMS-certified
    c. Patients are informed about serious adverse outcomes and the need for monitoring
    d. All patients are enrolled in the REMS program to ensure and support safe-use conditions
3. In a REMS-certified medically-supervised health care setting, processes and procedures must be established to:
    a. Train all relevant staff involved in prescribing, dispensing and administering Spravato
    b. Have a prescriber on site during Spravato administration and monitoring
    c. Monitor patients for resolution of sedation and dissociation and changes in vital signs for a minimum of 2 hours

d. Counsel the patients on the need for REMS enrollment, monitoring and risks of sedation and dissociation
e. Must complete and submit the Patient Monitoring Form to the REMS program within 7 days after every treatment session
f. Ensure that Spravato is not dispensed for use outside the certified health care setting

DEFINITION OF TERMS

1. Risk Evaluation and Mitigation Strategies (REMS)- drug safety program that the FDA can require for certain medications with serious safety concerns to help ensure the benefits of the medication outweigh its risk.
2. Enantiomer- each of a pair of molecules that are mirror images of each other. Esketamine, the S-enantiomer of ketamine racemate, has a higher affinity for the NMDA receptor than the S-enantiomer (Caffrey 2019).

REFERENCES

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