



**Kaiser Foundation Health Plan
of Washington**

Clinical Review Criteria

Ketamine for the Treatment of Depression and Other Psychiatric Disorders

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Criteria

For Medicare Members

Source	Policy
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	None
Local Coverage Determinations (LCD)	None
Local Coverage Article (LCA)	None
Kaiser Permanente Medical Policy	Due to the absence of an active NCD, LCD, or other coverage guidance, Kaiser Permanente has chosen to use their own Clinical Review Criteria, " <i>Ketamine for the Treatment of Depression and Other Psychiatric Disorders</i> " for medical necessity determinations. Refer to the Non-Medicare criteria below.

For Non-Medicare Members

Ketamine (intranasal, intravenous, or subcutaneous) is considered experimental and investigational as its clinical value has not been established. Non-covered diagnoses include but are not limited to:

- Chronic pain
- Depression
- Generalized anxiety and social anxiety disorders
- Substance use disorder
- Suicidal ideation

*Esketamine nasal spray (Spravato) has separate criteria for pharmacy review:

<https://wa-provider.kaiserpermanente.org/static/pdf/provider/clinical-review/list-officeinject.pdf>

For non-covered criteria

If requesting review for this service please send the following documentation:

- Last 6 months of clinical notes from requesting provider &/or specialist

The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, Kaiser Permanente will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

Hayes Review

Ketamine Infusion for Treatment-Resistant Bipolar Depression

Conclusion - D²

A small body of very low-quality evidence found that ketamine infusion rapidly reduces symptoms of severe bipolar depression. Although the antidepressant effects appear to last for only a few days, this can be clinically significant if it improves the mood of severely depressed, potentially suicidal patients. In all of the studies, only a single dose of ketamine was administered; the safety and effectiveness of repeated administration of ketamine for treatment of bipolar depression is unknown. The evidence suggests that ketamine is reasonably safe. Additional large, well-designed studies with adequate follow-up are needed to evaluate the long-term effects of prolonged ketamine treatment.

Insights

- Ketamine is administered by infusion because it does not have good bioavailability via alternative routes, such as oral or intramuscular injection.
- The low oral bioavailability and potential for abuse makes ketamine an unlikely first- or second-line therapy for bipolar depression.
- Persons with bipolar disorder are more apt to seek medical attention when they are depressed; therefore, a careful medical history must be obtained to avoid misdiagnosis of the patient's disorder as major depression.
- None of the reviewed payers had policies available for the use of ketamine to treat bipolar depression.

Ketamine as Primary Therapy for Treatment-Resistant Unipolar Depression Or Posttraumatic Stress Disorder

Conclusion- C (For ketamine as a treatment for treatment-resistant unipolar depression)

D2 (For ketamine as a treatment for posttraumatic stress disorder (PTSD)).

A moderate-size body of low-quality evidence has consistently found that ketamine reduces symptoms of severe treatment-resistant unipolar depression, symptoms of PTSD, or suicidal ideation at short-term follow-up of 1 to 3 days posttreatment; however, the findings at longer-term follow-up of 1 to 4 weeks are mixed. The majority of the studies administered only a single dose of ketamine; the safety and effectiveness of repeated administration of ketamine for treatment of depression or PTSD is unknown. The evidence suggests that ketamine is reasonably safe if complications are properly managed. Additional large, well-designed studies with adequate follow-up are needed to evaluate the long-term effects of prolonged ketamine treatment, to assess simplified ketamine administration via intranasal or subcutaneous routes, to determine the efficacy and safety of ketamine for PTSD treatment, and to evaluate the efficacy and safety of ketamine relative to ECT for unipolar depression.

Insights

- The low oral bioavailability and potential for abuse makes ketamine an unlikely first- or second-line therapy for treatment-resistant unipolar depression or PTSD.
- The reviewed studies found that ketamine is consistently beneficial for 24 hours posttreatment; however, the durability of results at 1 to 4 weeks posttreatment are mixed. Thus, it is unclear whether ketamine provides durable relief of depression or PTSD symptoms.
- As the beneficial effects of ketamine may be limited to 24 hours posttreatment, it is important to establish the safety and effectiveness of repeated administration of ketamine. There is currently a paucity of studies investigating repeated administration of ketamine for unipolar depression or PTSD.
- Several representative payer organizations do not have coverage policies for ketamine monotherapy for unipolar depression or PTSD.

Applicable Codes

Considered Not Medically Necessary - experimental, investigational or unproven:

CPT® or HCPCS Codes	Description
J3490	Unclassified drugs
<i>Commonly submitted with CPT code(s) 96365, 96366, 96367, or 96368</i>	
ICD-10 Codes	Description
F01-F09	Mental disorders due to known physiological conditions
F10-F19	Mental and behavioral disorders due to psychoactive substance use
F20-F29	Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders
F30-F39	Mood [affective] disorders
F40-F48	Anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders

F50-F59	Behavioral syndromes associated with physiological disturbances and physical factors
F60-F69	Disorders of adult personality and behavior
F70-F79	Intellectual disabilities
F80-F89	Pervasive and specific developmental disorders
F90-F98	Behavioral and emotional disorders with onset usually occurring in childhood and adolescence
F99-F99	Unspecified mental disorder
T14.91XA	Suicidal behavior with attempted self-injury
R45.89	Suicidal behavior without attempted self-injury
T65.92XA	Suicidal deliberate poisoning
R45.851	Suicidal ideation
R45.851	Suicidal ideations
R45.851	Suicidal intent
T50.902A	Suicidal overdose
T50.902A	Suicidal overdose, initial encounter
T50.902S	Suicidal overdose, sequela
T50.902D	Suicidal overdose, subsequent encounter
R45.89	Suicidal risk
R45.851	Suicidal thoughts
R45.851	Feeling suicidal
T40.602A	Narcosis due to narcotic, purposeful, non-suicidal
Z71.1	Concern about becoming suicidal without diagnosis
F32.A, R45.851	Depression with suicidal ideation
Z91.52	History of non-suicidal self-harm
Z91.51	History of suicidal behavior

***Note:** Codes may not be all-inclusive. Deleted codes and codes not in effect at the time of service may not be covered.

**To verify authorization requirements for a specific code by plan type, please use the [Pre-authorization Code Check](#).

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Date Created	Date Reviewed	Date Last Revised
11/10/2021	12/07/2021 ^{MPC} ,	12/07/2021

^{MPC} Medical Policy Committee

Revision History	Description
12/07/2021	MPC approved to adopt a policy of non-coverage for IV Ketamine for mental diagnoses including chronic pain, depression, generalized anxiety and social anxiety disorders, substance use disorder and suicidal ideation.
06/21/2022	Updated the 60-day notice to 12/1/2022 and removed "oral" per Pharmacy