

## Medical Coverage Policy | Intravenous Anesthetics for the Treatment of Chronic Pain and Psychiatric Disorders



**EFFECTIVE DATE:** 03|01|2025

**POLICY LAST REVIEWED:** 11|05|2025

### OVERVIEW

Intravenous (IV) infusion of lidocaine or ketamine has been investigated for the treatment of migraine and chronic daily headache, fibromyalgia, and chronic neuropathic pain. Chronic neuropathic pain disorders include phantom limb pain, post-herpetic neuralgia, complex regional pain syndrome, diabetic neuropathy, and pain related to stroke or spinal cord injuries. An IV infusion of ketamine has also been investigated for treatment-resistant depression and obsessive-compulsive disorder (OCD). For these applications, a series of IV infusions would be administered daily for up to a week.

### MEDICAL CRITERIA

Not applicable

### PRIOR AUTHORIZATION

Not applicable

### POLICY STATEMENT

#### Medicare Advantage Plans

Intravenous infusion of anesthetics (eg, ketamine or lidocaine) for the treatment of chronic pain, including, but not limited to chronic neuropathic pain, chronic daily headache, fibromyalgia, is not covered as the evidence is insufficient to determine the effects of the technology on health outcomes.

Intravenous infusion of anesthetics (eg, ketamine or lidocaine) for the treatment of psychiatric disorders, including but not limited to treatment-resistant depression obsessive-compulsive disorder, and post-traumatic stress disorder is not covered as the evidence is insufficient to determine the effects of the technology on health outcomes.

#### Commercial Products

Intravenous infusion of anesthetics (eg, ketamine or lidocaine) for the treatment of chronic pain, including, but not limited to chronic neuropathic pain, chronic daily headache, fibromyalgia, is considered not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes.

Intravenous infusion of anesthetics (eg, ketamine or lidocaine) for the treatment of psychiatric disorders, including but not limited to treatment-resistant depression ~~and~~ obsessive-compulsive disorder, and post-traumatic stress disorder is considered not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes.

### BACKGROUND

For individuals who have chronic pain syndromes (eg, neuropathic pain or fibromyalgia) who receive a course of IV anesthetics (eg, lidocaine, ketamine), the evidence includes systematic reviews, several randomized controlled trials (RCTs), and observational studies. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, quality of life (QOL), medication use, and treatment-related morbidity. Several RCTs have been performed using IV lidocaine for post-herpetic neuralgia (PHN), complex regional pain syndrome (CRPS), and diabetic neuropathy. These trials have failed to show a durable effect of lidocaine infusion on chronic pain. Two trials with a total of 100 patients provide limited evidence that courses of IV ketamine may provide temporary relief (2 to 4 weeks) to some chronic pain patients in some settings. Neither of the RCTs used an active control, raising concerns about placebo effects. A third trial found no benefit from

a single infusion of ketamine or ketamine/magnesium. Overall, the intense treatment protocols, the severity of adverse events, and the limited treatment durability raise questions about the net health benefit of this therapy. Additional clinical trials are needed to evaluate the long-term efficacy and safety of repeat courses of IV anesthetics for chronic pain. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have treatment-resistant depression who receive a course of IV ketamine, the evidence consists of systematic reviews, RCTs, and case series. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, quality of life, medication use, and treatment-related morbidity. Two publications of double-blind trials were identified that compared repeated ketamine infusion with an infusion of saline for treatment-resistant depression. Additionally, 2 open-label randomized trials comparing ketamine infusion to electroconvulsive therapy (ECT) were identified. There is a possibility of publication bias due to the lack of publication of many other small trials. Systematic reviews in patients with unipolar depression or depression related to bipolar disorder have identified numerous studies evaluating the efficacy of ketamine infusion. While the analyses indicate depression improvement in the short-term, there is limited evidence beyond a single infusion. One study with 26 patients found no significant difference in a depression scale at the end of infusion. A larger RCT (N=68) found a significantly greater improvement in a depression scale during the 4-week infusion period, but the effect diminished over 3 weeks post-infusion. The trial did not use an active control, raising the possibility of placebo effects and unblinding of patients and investigators. The open-label randomized trials comparing ketamine with ECT produced mixed results, with the first trial indicating ketamine was not noninferior to ECT in inducing remission and the second trial indicating ketamine was noninferior to ECT in inducing response. These divergent findings may be attributable to differences in the populations studied, as the first trial was conducted in severely ill inpatients and the second trial was conducted in a less severely ill, predominantly outpatient sample. Large observational studies in patients with depression indicate improvement on depression rating scales following ketamine infusions; however, these studies lack a control group, and no firm conclusions on the effectiveness or safety of serial ketamine infusions can be drawn from this evidence. Common side effects of ketamine infusion include headache, anxiety, dissociation, nausea, and dizziness. The intense treatment protocols, the severity of adverse events, and the short treatment durability limit the clinical utility of the treatment. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have other psychiatric disorders (eg, obsessive-compulsive disorder [OCD], post-traumatic stress disorder [PTSD]) who receive a course of IV ketamine, the evidence consists of RCTs and case series. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, quality of life, medication use, and treatment-related morbidity. One double-blind placebo-controlled trial and case series for OCD treatment, and 1 double-blind trial comparing multiple ketamine infusions with midazolam in one double-blind, crossover RCT in patients with serotonin reuptake inhibitor-resistant OCD (N=15) found that ketamine infusion provided a higher frequency of Yale-Brown Obsessive Compulsive Scale (YBOCS) response at day 7 compared with placebo; however, unblinding was suspected and only data from the first phase were analyzed because of a carryover effect of ketamine. A case series (N=14) identified only 1 patient who demonstrated prespecified significant YBOCS response after 2 to 3 weeks. A small RCT in patients with chronic PTSD (N=30) found that ketamine infusion produced significantly greater improvements in a PTSD symptom scale at 2 weeks compared to midazolam. Common side effects of ketamine infusion include headache, anxiety, dissociation, nausea, and dizziness. The intense treatment protocols, the severity of adverse events, and the short treatment durability limit the clinical utility of the treatment. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Courses of intravenous (IV) anesthetic agents may be given in the inpatient or outpatient setting as part of a pain management program, with the infusion of a subanesthetic dose preceded by a bolus infusion to achieve desired blood levels sooner. Treatment protocols for the initial cycle may include infusion of subanesthetic doses for 1 to 6 hours for up to 10 days.

Lidocaine, which prevents neural depolarization through effects on voltage-dependent sodium channels, is also used systemically for the treatment of arrhythmias. Adverse events for lidocaine are common, can be mild to

moderate, and include general fatigue, somnolence, dizziness, headache, periorbital and extremity numbness and tingling, nausea, vomiting, tremors, and changes in blood pressure and pulse. Severe adverse events may include arrhythmias, seizures, loss of consciousness, confusion, or even death. Lidocaine should only be given IV to patients with normal conduction on electrocardiography and normal serum electrolyte concentrations to minimize the risk of cardiac arrhythmias.

Ketamine is an antagonist of the N-methyl-d-aspartate receptor and a dissociative anesthetic. It is the sole anesthetic agent approved for diagnostic and surgical procedures that does not require skeletal muscle relaxation. Respiratory depression may occur with overdosage or too rapid a rate of administration of ketamine. Ketamine is a schedule III-controlled substance. Psychological manifestations vary in severity from pleasant, dream-like states to hallucinations and delirium; further, these manifestations can be accompanied by confusion, excitement, aggression, or irrational behavior. The occurrence of adverse events with IV anesthetics may be reduced by the careful titration of subanesthetic doses. However, the potential benefits must be carefully weighed against the potential for serious, harmful adverse events.

The IV administration of anesthetics has been reported for various conditions, including chronic headache, chronic pain of neuropathic origin, fibromyalgia, depression, and obsessive-compulsive disorders.

Chronic daily headache is defined as a headache disorder that occurs more than 15 days a month for at least 3 months. Chronic daily headache includes chronic migraine, new daily persistent headache, hemicranias continua, and chronic tension-type headache.

Neuropathic pain is often disproportionate to the extent of the primary triggering injury and may consist of thermal or mechanical allodynia, dysesthesia, and/or hyperalgesia. Allodynia is pain that occurs from a stimulus that normally does not elicit a painful response (eg, light touch, warmth). Dysesthesia is a constant or ongoing unpleasant or electrical sensation of pain. Hyperalgesia is an exaggerated response to normally painful stimuli. In the latter, symptoms may continue longer (eg,  $\geq 6$  months) than clinically expected after an illness or injury. It is proposed that chronic neuropathic pain results from peripheral afferent sensitization, neurogenic inflammation, and sympathetic afferent coupling, along with sensitization and functional reorganization of the somatosensory, motor, and autonomic circuits in the central nervous system. Therefore, treatments focus on reducing activity and desensitizing pain pathways, thought to be mediated through N-methyl-d-aspartate receptors in the peripheral and central nervous system. Sympathetic ganglion blocks with lidocaine have been used to treat sympathetically maintained chronic pain conditions, such as complex regional pain syndrome (previously known as reflex sympathetic dystrophy). Test infusion of an anesthetic has also been used in treatment planning to assess patient responsiveness to determine whether medications, such as oral mexiletine or oral ketamine, may be effective. A course of IV lidocaine or ketamine, usually at subanesthetic doses, has also been examined. This approach for treating chronic neuropathic pain differs from continuous subcutaneous or IV infusion of anesthetics for managing chronic pain conditions, such as terminal cancer pain, which is not discussed herein.

Fibromyalgia is a chronic state of widespread pain and tenderness. Although fibromyalgia is generally considered a disorder of central pain processing or central sensitization, others have proposed that the nerve stimuli causing pain originates mainly in the muscle, causing both widespread pain and pain on movement. There are focal areas of hyperalgesia, or tender points, which tend to occur at muscle-tendon junctions. Biochemical changes associated with fibromyalgia include alterations in N-methyl-d-aspartate receptors, low levels of serotonin, suppression of dopamine-releasing neurons in the limbic system, dysfunction of the hypothalamic-pituitary-adrenal axis, and elevated substance P levels. Fibromyalgia is typically treated with neuropathic pain medications such as pregabalin, non-narcotic pain relievers, or low doses of antidepressants.

The use of IV ketamine has also been reported for treatment-resistant depression, defined as depression that does not respond adequately to appropriate courses of antidepressant medications. Particularly challenging are patients with treatment-resistant depression with suicidal ideation. Several studies are ongoing to test the efficacy of IV ketamine in patients with suicidal ideation who present to the emergency department.

## Regulatory Status

IV lidocaine is approved by the U.S. Food and Drug Administration for systemic use in the acute treatment of arrhythmias and locally as an anesthetic; IV lidocaine for the treatment of chronic pain or psychiatric disorders is considered off-label use.

Ketamine hydrochloride injection is approved for diagnostic and surgical procedures that do not require skeletal muscle relaxation, for the induction of anesthesia before the administration of other general anesthetic agents, and to supplement low-potency agents, such as nitrous oxide. IV ketamine for the treatment of chronic pain or psychiatric disorders is an off-label use.

## COVERAGE

### Medicare Advantage Plans and Commercial Products

Benefits may vary between groups/contracts. Please refer to the Evidence of Coverage or Subscriber Agreement for applicable not medically necessary/not covered benefits/coverage

## CODING

### Medicare Advantage Plans and Commercial Products

There is no specific HCPCS code(s) for this service; Claims should be filed using an unlisted HCPCS drug code(s) for the treatments noted in this policy.

## RELATED POLICIES

Unlisted Procedures

## PUBLISHED

Provider Update, January 2026

Provider Update, January 2025

Provider Update, March 2022

Provider Update, August 2021

Provider Update, June 2020

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