

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



EFFECTIVE DATE: 05 | 23 | 2011

POLICY LAST UPDATED: 01 | 19 | 2022

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 depression and obsessive-compulsive 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 depression and obsessive-compulsive disorder, is considered not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes.

BACKGROUND

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, ≥ 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

Not applicable

PUBLISHED

Provider Update, March 2022

Provider Update, August 2021

Provider Update, June 2020

Provider Update, August 2019

Provider Update, May 2018

REFERENCES

1. Wertli MM, Kessels AG, Perez RS, et al. Rational pain management in complex regional pain syndrome 1 (CRPS 1)-a network meta-analysis. *Pain Med.* Sep 2014; 15(9): 1575-89. PMID 25234478
2. Schwartzman RJ, Alexander GM, Grothusen JR, et al. Outpatient intravenous ketamine for the treatment of complex regional pain syndrome: a double-blind placebo-controlled study. *Pain.* Dec 15 2009; 147(1-3): 107-15. PMID 19783371
3. Sigtermans MJ, van Hilten JJ, Bauer MCR, et al. Ketamine produces effective and long-term pain relief in patients with Complex Regional Pain Syndrome Type 1. *Pain.* Oct 2009; 145(3): 304-311. PMID 19604642
4. O'Connell NE, Wand BM, McAuley J, et al. Interventions for treating pain and disability in adults with complex regional pain syndrome. *Cochrane Database Syst Rev.* Apr 30 2013; (4): CD009416. PMID 23633371
5. Kim YC, Castaneda AM, Lee CS, et al. Efficacy and Safety of Lidocaine Infusion Treatment for Neuropathic Pain: A Randomized, Double-Blind, and Placebo-Controlled Study. *Reg Anesth Pain Med.* May 2018; 43(4): 415-424. PMID 29381569
6. Liu H, Lu F, Zhou D, et al. The Analgesic and Emotional Response to Intravenous Lidocaine Infusion in the Treatment of Postherpetic Neuralgia: A Randomized, Double-Blinded, Placebo-controlled Study. *Clin J Pain.* Nov 2018; 34(11): 1025-1031. PMID 29698250
7. Moulin DE, Morley-Forster PK, Pirani Z, et al. Intravenous lidocaine in the management of chronic peripheral neuropathic pain: a randomized-controlled trial. *Can J Anaesth.* Jul 2019; 66(7): 820-827. PMID 31098961
8. Amr YM. Multi-day low dose ketamine infusion as adjuvant to oral gabapentin in spinal cord injury related chronic pain: a prospective, randomized, double blind trial. *Pain Physician.* May-Jun 2010; 13(3): 245-9. PMID 20495588

9. Pickering G, Pereira B, Morel V, et al. Ketamine and Magnesium for Refractory Neuropathic Pain: A Randomized, Double-blind, Crossover Trial. *Anesthesiology*. Jul 2020; 133(1): 154-164. PMID 32384291
10. Patil S, Anitescu M. Efficacy of outpatient ketamine infusions in refractory chronic pain syndromes: a 5-year retrospective analysis. *Pain Med*. Feb 2012; 13(2): 263-9. PMID 21939497
11. Przeklasa-Muszynska A, Kocot-Kepska M, Dobrogowski J, et al. Intravenous lidocaine infusions in a multidirectional model of treatment of neuropathic pain patients. *Pharmacol Rep*. Oct 2016; 68(5): 1069-75. PMID 27552062
12. Mangnus TJP, Dirckx M, Bharwani KD, et al. Effect of intravenous low-dose S-ketamine on pain in patients with Complex Regional Pain Syndrome: A retrospective cohort study. *Pain Pract*. Nov 2021; 21(8): 890-897. PMID 34233070
13. Noppers I, Niesters M, Swartjes M, et al. Absence of long-term analgesic effect from a short-term S-ketamine infusion on fibromyalgia pain: a randomized, prospective, double blind, active placebo-controlled trial. *Eur J Pain*. Oct 2011; 15(9): 942-9. PMID 21482474
14. Vlainich R, Issy AM, Sakata RK. Effect of intravenous lidocaine associated with amitriptyline on pain relief and plasma serotonin, norepinephrine, and dopamine concentrations in fibromyalgia. *Clin J Pain*. May 2011; 27(4): 285-8. PMID 21178598
15. Rodriguez CI, Kegeles LS, Levinson A, et al. Randomized controlled crossover trial of ketamine in obsessive-compulsive disorder: proof-of-concept. *Neuropsychopharmacology*. Nov 2013; 38(12): 2475-83. PMID 23783065
16. Singh JB, Fedgchin M, Daly EJ, et al. A Double-Blind, Randomized, Placebo-Controlled, Dose-Frequency Study of Intravenous Ketamine in Patients with Treatment-Resistant Depression. *Am J Psychiatry*. Aug 01 2016; 173(8): 816-26. PMID 27056608
17. Feder A, Costi S, Rutter SB, et al. A Randomized Controlled Trial of Repeated Ketamine Administration for Chronic Posttraumatic Stress Disorder. *Am J Psychiatry*. Feb 01 2021; 178(2): 193-202. PMID 33397139
18. Ionescu DF, Bentley KH, Eikermann M, et al. Repeat-dose ketamine augmentation for treatment-resistant depression with chronic suicidal ideation: A randomized, double blind, placebo-controlled trial. *J Affect Disord*. Jan 15 2019; 243: 516-524. PMID 30286416
19. Sharma LP, Thamby A, Balachander S, et al. Clinical utility of repeated intravenous ketamine treatment for resistant obsessive-compulsive disorder. *Asian J Psychiatry*. Aug 2020; 52: 102183. PMID 32554207
20. Cohen SP, Bhatia A, Buvanendran A, et al. Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Chronic Pain from the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists. *Reg Anesth Pain Med*. Jul 2018; 43(5): 521-546. PMID 29870458
21. Sanacora G, Frye MA, McDonald W, et al. A Consensus Statement on the Use of Ketamine in the Treatment of Mood Disorders. *JAMA Psychiatry*. Apr 01 2017; 74(4): 399-405. PMID 28249076
22. Peyrovian B, McIntyre RS, Phan L, et al. Registered clinical trials investigating ketamine for psychiatric disorders. *J Psychiatr Res*. Aug 2020; 127: 1-12. PMID 32315806

CLICK THE ENVELOPE ICON BELOW TO SUBMIT COMMENTS

This medical policy is made available to you for informational purposes only. It is not a guarantee of payment or a substitute for your medical judgment in the treatment of your patients. Benefits and eligibility are determined by the member's subscriber agreement or member certificate and/or the employer agreement, and those documents will supersede the provisions of this medical policy. For information on member-specific benefits, call the provider call center. If you provide services to a member which are determined to not be medically necessary (or in some cases medically necessary services which are non-covered benefits), you may not charge the member for the services unless you have informed the member and they have agreed in writing in advance to continue with the treatment at their own expense. Please refer to your participation agreement(s) for the applicable provisions. This policy is current at the time of publication; however, medical practices, technology, and knowledge are constantly changing. BCBSRI reserves the right to review and revise this policy for any reason and at any time, with or without notice. Blue Cross & Blue Shield of Rhode Island is an independent licensee of the Blue Cross and Blue Shield Association.

