



MASSACHUSETTS

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Medical Policy

Anesthetics for the Treatment of Chronic Pain and Major Depressive Disorder (MDD)

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Policy Number: 291

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NCD/LCD: N/A

Related Policies

- Repetitive transcranial magnetic stimulation (rTMS), ([#297](#))
- Outpatient Electroconvulsive Therapy (ECT), ([#319](#))

Policy¹

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

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, and fibromyalgia, is [INVESTIGATIONAL](#).

Inhaled, oral or intravenous ketamine for the treatment of major depressive disorder (MDD) including treatment resistant depression (TRD) is [INVESTIGATIONAL](#).

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	This is not a covered service.
Commercial PPO and Indemnity	This is not a covered service.
Medicare HMO Blue SM	This is not a covered service.

Medicare PPO Blue SM	This is not a covered service.
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CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

According to the policy statement above, the following HCPCS code considered investigational for the conditions listed for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

HCPCS Codes

HCPCS codes:	Code Description
J2001	Injection, lidocaine hydrochloride for intravenous infusion, 10 mg

Description

INTRAVENOUS ANESTHETIC AGENTS

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.

Lidocaine

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 intravenously to patients with normal conduction on electrocardiography and normal serum electrolyte concentrations to minimize the risk of cardiac arrhythmias.

Ketamine

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 do not require skeletal muscle relaxation. Respiratory depression may occur with overdosage or too rapid a rate of administration of ketamine; it should be used by or under the direction of physicians experienced in administering general anesthetics. 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 of pain control must be carefully weighed against the potential for serious, harmful adverse events.

Indications

IV administration of anesthetic 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 to be 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.

Inhaled, oral and intravenous infusion of Ketamine has been studied as a rapid release antidepressant for individuals with major depressive disorder (MDD). Conservative forms of treatment for MDD include antidepressant use which can take weeks or months to produce changes in symptoms. Ketamine differs from antidepressant medications in that it targets neuronal activity by blocking the biochemical receptor glutamate, producing an immediate reduction in depressive symptoms.

Summary

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 the treatment of depression and obsessive-compulsive disorder. For these applications, one or more courses of IV infusion would be administered over several hours or several days.

For individuals who have chronic pain syndromes (eg, complex regional pain syndrome, fibromyalgia, headache, neuropathic pain, spinal cord injury) who receive a course of IV anesthetics (eg, lidocaine, ketamine), the evidence includes several randomized controlled trials. Relevant outcomes are symptoms,

change in disease status, morbid events, functional outcomes, quality of life, medication use, and treatment-related morbidity. Evidence, primarily from outside of the United States, has suggested that courses of IV lidocaine and ketamine may provide—at least temporary—relief to some chronic pain patients. However, the intense treatment protocols, the severity of adverse events, and the limited treatment durability raise questions about the overall health benefit of this procedure. Additional clinical trials are needed to evaluate the long-term safety of repeat courses of IV anesthetics. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for ketamine use in MDD includes randomized controlled trials and multiple case series evaluating depression rating scores before and after treatment, quality of life measures, administration guidelines and appropriate dosing recommendations. Different methods of administration have been studied for ketamine treatment in MDD including inhaled, oral and intravenous infusion (IV). In most cases, patients were given a dose of IV ketamine in an office setting under the care of a licensed psychiatrist every 3 to 4 weeks. Patients reported reduction in symptoms lasting a period of 3 or 4 weeks when given intravenous infusion. A percentage of patients experienced side effects including mania, confusion, hallucinations, excitement, and aggressive behavior. Study limitations include small sample sizes, inconsistent study design, lack of placebo comparator and lack of randomization. Results were inconsistent across studies.

While studies have shown that ketamine can produce immediate changes in depressive symptoms for patients with MDD, longer term data documenting safety and efficacy is needed to permit conclusions about the medical necessity of this treatment. Appropriate dosing guidelines, patient selection criteria and appropriate administration of this drug are also needed to prove safety and efficacy. Therefore, this treatment is considered investigational.

Policy History

Date	Action
1/2019	BCBSA National medical policy review. Description, summary and references updated. Policy statements unchanged.
7/2018	New investigational indications described. Title changed. Effective 7/1/2018.
1/2016	New references added from BCBSA National medical policy. Clarified coding information.
3/2015	BCBSA National medical policy review. New investigational indications described. Clarified coding information. Effective 3/1/2015.
6/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
12/2013	New references from BCBSA National medical policy.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
12/3/2010	New policy effective 12/02/1020 describing ongoing non-coverage.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

[Medical Policy Terms of Use](#)

[Managed Care Guidelines](#)

[Indemnity/PPO Guidelines](#)

[Clinical Exception Process](#)

[Medical Technology Assessment Guidelines](#)

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Treatment of Chronic Pain

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Treatment of Depression

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Endnotes

¹ Based on expert opinion