Corporate Medical Policy

Intravenous Anesthetics for the Treatment of Chronic Pain and Psychiatric Disorders

File Name: intravenous_anesthetics_for_the_treatment_of_chronic_pain

Origination: 8/2010

Last CAP Review: 4/2020

Next CAP Review: 4/2021

Last Review: 4/2020

Description of Procedure or Service

Courses of 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.

Ketamine is an antagonist of the N-methyl-D-aspartate (NMDA) 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 and can be accompanied by confusion, excitement, aggression, or irrational behavior. The occurrence of adverse effects 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 effects.

Lidocaine, which prevents neural depolarization through effects on voltage-dependent sodium channels, is also used systemically for the treatment of arrhythmias. Adverse effects 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 effects 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.

Intravenous (IV) administration of anesthetic has been reported for a variety of conditions, including chronic pain of neuropathy origin, chronic headache, fibromyalgia, depression, and obsessive compulsive disorders. Chronic daily headaches are defined as a headache disorder that occurs more than 15 days a month for at least 3 months. Chronic daily headaches include 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 (e.g., 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 for a period of time that is longer (e.g., 6 months or more) 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...
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sensitization and functional reorganization of the somatosensory, motor, and autonomic circuits in the central nervous system (CNS). Therefore, treatments focus on reducing activity and desensitizing pain pathways, thought to be mediated through N-methyl-d-aspartate (NMDA) receptors in the peripheral and CNS. Sympathetic ganglion blocks with lidocaine have been used for a number of years to treat sympathetically maintained chronic pain conditions, such as complex regional pain syndrome (CRPS, 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 intravenous (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 the management of chronic pain conditions, such as terminal cancer pain, which are not discussed in this policy.

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 that have been associated with fibromyalgia include alterations in NMDA 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.

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
Intravenous (IV) lidocaine is approved by the U.S. Food and Drug Administration (FDA) for systemic use in the acute treatment of arrhythmias and locally as an anesthetic. IV lidocaine for the treatment of chronic pain is an off-label use.

Ketamine hydrochloride injection is FDA-indicated for diagnostic and surgical procedures that do not require skeletal muscle relaxation, for the induction of anesthesia prior to 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.

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

Intravenous anesthetics for the treatment of chronic pain and psychiatric disorders are considered investigational for all applications. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.
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**When Intravenous Anesthetics for the Treatment of Chronic Pain and Psychiatric Disorders are covered**

Not applicable.

**When Intravenous Anesthetics for the Treatment of Chronic Pain and Psychiatric Disorders are not covered**

Intravenous infusion of anesthetics (e.g., ketamine or lidocaine) for the treatment of chronic pain, including, but not limited to chronic neuropathic pain, chronic daily headaches, fibromyalgia and psychiatric disorders, including but not limited to depression and obsessive-compulsive disorder is considered investigational.

**Policy Guidelines**

For individuals who have chronic pain syndromes (CRPS, fibromyalgia, headache, neuropathic pain, spinal cord injury) who receive IV anesthetics (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. Several RCTs have been performed using intravenous lidocaine for postherpetic neuralgia, complex regional pain syndrome, 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. Overall, the intense treatment protocols, severity of side effects, and limited durability raises 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.

For individuals who have psychiatric disorders (treatment-resistant depression, obsessive compulsive disorder) who receive IV anesthetics, the evidence consists of RCTs. 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. There is a possibility of publication bias due to the lack of publication of many other small trials. 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 active control, raising the possibility of placebo effects and unblinding of patients and investigators. Common side effects of ketamine infusion include headache, anxiety, dissociation, nausea, and dizziness. The intense treatment protocols, the severity of adverse events, and the limited treatment durability raise questions about the net health benefit of this procedure. High-quality clinical trials, several of which are in progress, are needed to evaluate the long-term safety and efficacy of IV ketamine for psychiatric disorders. The evidence is insufficient to determine the effects of the technology on health outcomes.

The American Psychiatric Association (2017) published an evidence review and consensus opinion of the use of ketamine in treatment-resistant depression. The Association noted that "while ketamine may be beneficial to some patients with mood disorders, it is important to consider the limitations of the available data and the potential risk associated with the drug when considering the treatment option."
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Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: J2001, 96365, 96366, 96374

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Senior Medical Director – 7/2010
Medical Director review – 1/2015
Medical Director review 1/2016
Specialty Matched Consultant Advisory Panel 04/2020
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Policy Implementation/Update Information

8/3/10 New Evidence Based Guideline. Intravenous infusion of anesthetics (e.g., ketamine or lidocaine) for the management of chronic neuropathic pain is not recommended.
Reviewed by Senior Medical Director 7/6/2010. (btw)

1/10/12 Removed the word “neuropathic” from policy title and throughout as appropriate. Specialty Matched Consultant Advisory Panel review 11/30/11. No changes to guideline intent. (btw)

9/18/12 Evidence based guideline converted to corporate medical policy. Intravenous infusion of anesthetics (e.g., ketamine or lidocaine) for the treatment of chronic pain, including, but not limited to chronic neuropathic pain and fibromyalgia, is considered investigational. Medical Director review 8/21/12. Notification given 9/18/2012 Policy effective 12/28/2012. (btw)

1/29/13 Specialty Matched Consultant Advisory Panel 1/16/2013. No change to policy. Reference added. (btw)

10/29/13 Reference added. (btw)

2/11/14 Specialty Matched Consultant Advisory Panel review 1/28/2014. No change to policy statement. (btw)

11/11/14 References updated. Description section updated. “When Not Covered” section updated to include chronic daily headaches. No change to Policy Statements. (td)


12/30/16 Specialty Matched Consultant Advisory Panel review 11/30/2016. No change to policy statement. (an)

2/24/17 Last paragraph of Description section regarding IV Ketamine revised for clarity to read: IV ketamine for the treatment of chronic pain or psychiatric disorders is an off-label use. (an)

5/26/17 Specialty Matched Consultant Advisory Panel review 4/26/2017. No change to policy statement. (an)


4/30/19 Added “psychiatric disorders” to list of non-covered indications. Reference added. Specialty Matched Consultant Advisory Panel review 4/17/2019. No change to policy statement. (an)
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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.