Introduction

Anesthetics are drugs to control pain. Anesthesia can be used to aid relaxation, block pain, or make a person unconscious during surgery. A local anesthetic is used to block pain in a small part of the body. Regional anesthesia is used to block pain in larger areas of the body, like the arms or legs. General anesthesia affects the whole body and makes a person unconscious. Different types of anesthetics have been well studied and are approved by the Food and Drug Administration for specific uses. Other uses of anesthetics have not been as well studied. One area of current inquiry is the use of certain anesthetics given intravenously (through a vein) to try to treat pain from conditions like complex regional pain syndrome, fibromyalgia, or chronic headache. Using intravenous anesthetic in this way is investigational (unproven). More and larger studies are needed to determine if using intravenous anesthetics in this way is safe and effective.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
### Service

<table>
<thead>
<tr>
<th>Service</th>
<th>Investigational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous infusion of anesthetics</td>
<td>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 headache, and fibromyalgia, is considered investigational.</td>
</tr>
</tbody>
</table>

### Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>CPT</strong></td>
<td></td>
</tr>
<tr>
<td>96365</td>
<td>Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour</td>
</tr>
<tr>
<td>96366</td>
<td>Each additional hour (list separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>96374</td>
<td>Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); intravenous push, single or initial substance/drug</td>
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<tr>
<td><strong>HCPCS</strong></td>
<td></td>
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<tr>
<td>J2001</td>
<td>Injection, lidocaine hydrochloride for intravenous infusion, 10 mg</td>
</tr>
<tr>
<td>J3490</td>
<td>Unclassified drugs</td>
</tr>
</tbody>
</table>

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### Related Information

- **N/A**

### Evidence Review
Description

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, 1 or more courses of IV infusion would be administered over a period of several hours or several days.

Background

Intravenous Anesthetic Agents

Courses of IV anesthetic agents are either given in the inpatient or outpatient setting as part of a pain management program.

Lidocaine

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.

Ketamine

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; 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 a variety of conditions, including chronic pain of neuropathic origin, chronic headache, fibromyalgia, depression, and obsessive-compulsive disorders. 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 (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) 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 NMDA receptors in the peripheral and central nervous system. 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 (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 the management of chronic pain conditions, such as terminal cancer pain, which are 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 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.

Summary of Evidence

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 effects, and the 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 (eg, depression, obsessive-compulsive disorder) who receive a course of IV anesthetics (eg, lidocaine, ketamine), the evidence is limited. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, quality of life, medication use, and treatment-related morbidity. Several trials on the IV infusion of ketamine for the treatment of suicidal ideation in patients with depression are ongoing. The evidence is insufficient to determine the effects of the technology on health outcomes.

Ongoing and Unpublished Clinical Trials

Some trials that might influence this policy are listed in Table 1.
Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
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<tr>
<td><strong>Ongoing</strong></td>
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<td></td>
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<tr>
<td>NCT02299440</td>
<td>Evaluation of the Effects of Ketamine in the Acute Phase of Suicidal Ideation: a Multicenter Randomized Double-blind Trial</td>
<td>156</td>
<td>Dec 2017</td>
</tr>
<tr>
<td><strong>Unpublished</strong></td>
<td></td>
<td></td>
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<tr>
<td>NCT01371110</td>
<td>Intravenous Ketamine in the Treatment of Obsessive-Compulsive Disorder</td>
<td>12</td>
<td>Jun 2015 (terminated)</td>
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<tr>
<td>NCT01920555</td>
<td>Double-Blind, Placebo-Controlled Trial of Ketamine Therapy in Treatment-Resistant Depression (TRD)</td>
<td>99</td>
<td>Feb 2017 (completed)</td>
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<tr>
<td>NCT02106325</td>
<td>A Randomized, Double-Blinded Controlled Trial of an N-Methyl D-Aspartate Antagonist as a Rapidly-Acting Antidepressant in Depressed Emergency Department Patients</td>
<td>28</td>
<td>Mar 2017 (completed)</td>
</tr>
</tbody>
</table>

NCT: national clinical trial

Practice Guidelines and Position Statements

The 2010 practice guidelines for chronic pain management from the American Society of Anesthesiologists and the American Society of Regional Anesthesia and Pain Medicine discuss a variety of treatment options for chronic pain. Use of ionotropic N-methyl-D-aspartate receptor antagonists and topical agents for neuropathic pain is addressed; IV infusion of lidocaine or ketamine is not mentioned.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.
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 is an 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 is an off-label use.

References


**History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/08/14</td>
<td>Policy reinstated; previously in archive status. Intravenous infusion of anesthetics (eg, ketamine or lidocaine) for the treatment of chronic pain is considered investigational.</td>
</tr>
<tr>
<td>01/01/18</td>
<td>Annual Review, approved December 6, 2017. Policy updated with literature review through September 2017; no references added. Policy statement unchanged.</td>
</tr>
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</table>

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  - Qualified interpreters
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Toll free 855-332-4535, Fax 425-918-5592. TTY 800-844-5357
Email AppealsDepartmentInquiries@Premera.com

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U.S. Department of Health and Human Services
200 Independence Avenue SW, Room S09F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)

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Kreyòl ayisyen (Creole):

Avi sila a gen Enfòmasyon Enpòtan ladan. Avi sila a kapab genyen enfòmasyon enpòtan konsènan aplikasyon w lan oswa konseinan kouvèti asirans lan atrave Premera Blue Cross. Kapab genyen dat ki enpòtan nan av si a. Ou ka gen pou pran kék aksyon av anv tèn dat limit pou ka tenbe kouvèti asirans sante w la oswa pou yo ka ede w avèk dépans yo. Se dwa w pou resewa enfòmasyon sa a ak asistans nan lang ou pa pale a, san ou pa gen pou peye pou sa. Rate nan 800-722-1471 (TTY: 800-844-5357).

Deutsche (German):


Hmoob (Hmong):


Iloko (Ilocano):

Daytoy a pakdaar ket naglaon itu Napateg nga Impormasion. Daytoy a pakdaar mabalin nga adda ket naglaon itu napateg nga impormasion maipanggep iti aplikasyonen weno coverage babaen iti Premera Blue Cross. Daytoy ket mabalin dagiti importante a pelta iti daytoy a pakdaar. Mabalin nga adda rumbeng nga aramidenyo nga addang sakbay dagiti partikular a naituding nga aldaw tapno maipanggep nga badjesa a kasay kana a naadANG daytoy nga naituding nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno naituding nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga badjesa a kasay nga tajjilay nga aldaw tapno maipanggep nga ba...
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