**Intravenous Anesthetics for the Treatment of Chronic Pain**

**POLICY**

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, fibromyalgia, and psychiatric disorders, is considered investigational.

**POLICY GUIDELINES**

See the Codes table for details.

**BENEFIT APPLICATION**

**BLUECARD/NATIONAL ACCOUNT ISSUES**

Intravenous lidocaine or ketamine may be best addressed contractually as a component of a pain management program.

Some facilities may negotiate global fees for pain management; however, charges for pain management may be subject to individual contractual limitations.
BACKGROUND

INTRAVENTOUS 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, dyesthesia, and/or hyperalgesia. Allodynia is pain that occurs from a stimulus that normally does not elicit a painful response (eg, light touch, warmth). Dyesthesia 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.

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.

RATIONALE
This evidence review was created in April 2004 and has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed through September 6, 2018.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances,
nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

**INTRAVENOUS ANESTHETICS FOR INDIVIDUALS WITH CHRONIC PAIN**

**Clinical Context and Test Purpose**
The purpose of a course of intravenous (IV) anesthetics (eg, lidocaine, ketamine) is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with chronic pain syndromes (eg, complex regional pain syndrome [CRPS], fibromyalgia, headache, neuropathic pain, spinal cord injury).

The question addressed in this evidence review is: Does a course of IV anesthetics improve the net health outcome in individuals with chronic pain syndromes (eg, CRPS, fibromyalgia, chronic headache, chronic neuropathic pain, spinal cord injury)?

The following PICOTS were used to select literature to inform this review.

**Patients**
The relevant populations of interest are individuals with chronic pain syndromes (eg, CRPS, fibromyalgia, headache, neuropathic pain, spinal cord injury).

**Interventions**
The therapy being considered is a course of IV anesthetics (eg, lidocaine, ketamine).

**Comparators**
The following therapy is currently being used to treat chronic pain syndromes: oral pain medication.

**Outcomes**
The general outcomes of interest are symptoms, change in disease status, morbid events, functional outcomes, quality of life, medication use, and treatment-related morbidity.

**Timing**
Follow-up at 4 weeks is of interest to monitor for outcomes.

**Setting**
Patients with chronic pain syndromes are actively managed by physical therapists, neurologists, and primary care providers in an outpatient setting.

**Study Selection Criteria**
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.
Lidocaine
A search of literature for the period of 1994 through February 2004, when this evidence review was created, revealed that the degree and duration of pain relief with IV lidocaine did not appear to be clinically significant in most patients.\(^1\) While some patients have reported diminished pain concurrent with IV administration of lidocaine that may continue for an extended duration beyond the infusion period, overall, responses to IV lidocaine in relief of allodynia, dysesthesia, and hyperalgesia were mixed. These studies and a review of the evidence available in 2004 indicated a need for additional double-blinded RCTs to determine the incremental effects of lidocaine over active placebo and to compare IV lidocaine with other standard treatments for chronic pain, such as the use of antidepressants for fibromyalgia. The studies concluded that a placebo response, due to the significant adverse events with IV lidocaine, warrants the use of active placebos to increase the probability of determining the true analgesic effect of lidocaine in clinical trials. Additionally, further studies are needed to determine appropriate patient selection criteria, predictive values, effective dosage ranges, frequencies, and duration of treatment. Key studies, focusing on RCTs by pain syndrome, are described next.

**Complex Regional Pain Syndrome**
Tables 1 and 2 summarize the characteristics and results of selected RCTs.

### Table 1. Summary of Key Randomized Controlled Trial Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al (2018)(^8)</td>
<td>South Korea</td>
<td>1</td>
<td>2015-2016</td>
<td>Patients had PHN or CRPS type II with an 11-point NRS score of 4 or ≥3 mo</td>
<td>21 patients received IV lidocaine 3 mg/kg for 4 weekly treatments of 1 h each</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>without pain relief from conservative treatment</td>
<td>21 patients received IV saline for 4 weekly treatments of 1 h each</td>
</tr>
<tr>
<td>Wallace et al (2000)(^6)</td>
<td>U.S.</td>
<td>1</td>
<td>NR</td>
<td>Patients had CRPS type I or II with allodynia</td>
<td>Patients received IV infusion of lidocaine and diphenhydramine separated by 1 wk</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Treatment order reversed</td>
</tr>
</tbody>
</table>

CRPS: complex regional pain syndrome; IV: intravenous; NRS: numeric rating scale; NR: not reported; PHN: postherpetic neuralgia.

### Table 2. Summary of Key Randomized Controlled Trial Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Lidocaine Dose, mg</th>
<th>Plasma Level</th>
<th>Effect of Lidocaine on Allodynia and Pain Scores</th>
<th>Reduction in NRS Pain Score (SD), %(^a)</th>
<th>AEs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Measured</td>
<td>Targeted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kim et al (2018)(^8)</td>
<td></td>
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<td></td>
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<tr>
<td>N</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>42</td>
</tr>
<tr>
<td>LIT group</td>
<td></td>
<td></td>
<td></td>
<td>48.71 (40.59)</td>
<td>3</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>mild</td>
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</tr>
</tbody>
</table>
Kim et al (2018) published a prospective, randomized, double-blind, placebo-controlled trial evaluating 43 patients with postherpetic neuralgia (PHN) or CRPS who were randomized to lidocaine or placebo (saline) in 4 weekly infusions. The groups did not differ significantly at weeks 1 and 2 in a reduction in pain; however, there were between-group differences after weeks 3 and 4 (respectively, p=0.001 and p=0.009). In the lidocaine-treated group, there was a significantly greater reduction in pain following the final infusion compared with the placebo group (p=0.011). However, this difference in the percentage of pain reduction was not reported at follow-up assessments in 1 and 4 weeks after the final infusion, suggesting only a temporary analgesic effect.

Wallace et al (2000) reported on a randomized, double-blind, placebo-controlled study of 16 patients with CRPS types I and II. While IV lidocaine significantly reduced the pain response to cool stimuli, mechanical pain relief was not significantly improved. Limitations were not reported.

The purpose of the gaps tables (see Tables 3 and 4) is to display notable gaps identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of evidence supporting the position statement.

### Table 3. Relevance Gaps

<table>
<thead>
<tr>
<th>Study</th>
<th>Population&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Intervention&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Comparator&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Outcomes&lt;sup&gt;d&lt;/sup&gt;</th>
<th>Follow-Up&lt;sup&gt;e&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al (2018)&lt;sup&gt;8&lt;/sup&gt;</td>
<td>4. Patients with PHN and CRPS were included</td>
<td>2. Did not use active placebo (diphenhydramine)</td>
<td>4. Did not measure plasma concentration of lidocaine during infusions</td>
<td></td>
<td></td>
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<tr>
<td>Wallace et al (2010)&lt;sup&gt;6&lt;/sup&gt;</td>
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</table>

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

CRPS: complex regional pain syndrome; PHN: postherpetic neuralgia.

<sup>a</sup>Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
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b Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

 Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

d Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 4. Study Design and Conduct Gaps

<table>
<thead>
<tr>
<th>Study</th>
<th>Allocationa</th>
<th>Blindingb</th>
<th>Selective Reportingd</th>
<th>Data Completenesse</th>
<th>Powerd</th>
<th>Statisticalf</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al (2018)</td>
<td></td>
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<tr>
<td>Wallace et al (2010)</td>
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</tbody>
</table>

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.


Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Fibromyalgia

Vlainich et al (2011) reported on a randomized, double-blind trial of IV lidocaine plus amitriptyline vs amitriptyline monotherapy in 30 patients with fibromyalgia.9 Infusion of lidocaine or saline was given once a week for 4 weeks. Pain intensity decreased in both groups during treatment; however, there was no significant difference between the treatment groups (visual analog scale [VAS], 4.1 for combined treatment vs 4.0 for monotherapy).

In a randomized, double-blind, crossover study of 18 patients with fibromyalgia, Sorensen et al (1997) found mixed responses with IV lidocaine plus ketamine, morphine, or both, suggesting that pain-processing mechanisms must differ in fibromyalgia.9 None of these patients responded to IV lidocaine alone.

Chronic Headache

A small RCT by Reutens et al (1991) found no significant difference between IV lidocaine and placebo for the treatment of acute migraine.10 No RCTs were identified that evaluate the long-term relief of chronic
daily headache following IV infusion of lidocaine. Uncontrolled studies were identified,\textsuperscript{11,12} but they do not provide sufficient evidence on the efficacy of IV lidocaine treatment for this condition.

\textbf{Chronic Neuropathic Pain}

\textit{Systematic Reviews}

A Cochrane review by Challapalli et al (2005) examined controlled trials of lidocaine and its oral analogues (ie, mexiletine, tocainide, flecainide) for neuropathic pain treatment and found the drugs safely provided more pain relief than placebo and with similar effectiveness as other analgesics.\textsuperscript{13} Reviewers noted that further investigation is needed to determine the clinical meaning of statistically significant pain relief and to test for less toxic analogues. A separate publication by the same authors estimated an 11-point (of 100) improvement in pain scales with IV lidocaine or oral analogues compared with placebo.\textsuperscript{14} Although adverse events were reported as not significantly different from other active controls (amitriptyline, carbamazepine, gabapentin, morphine), the severity and nature of the adverse events could not be assessed. As indicated in an accompanying editorial by Rathmell and Ballantyne (2005), “the limitations of the contributing studies preclude drawing useful conclusions about the adverse effect profiles of these drugs.”\textsuperscript{15} In addition, the editorialists noted that (1) lidocaine’s short serum half-life (120 minutes) precludes its use for chronic pain and (2) all trials measured pain relief within 24 hours because, in most patients, the effect disappears a few hours after treatment. Given the high frequency of adverse events and the short duration of action, the health benefits of IV lidocaine remain unclear for chronic pain.

\textit{Randomized Controlled Trials}

Tremont-Lukats et al (2006) reported the results of a randomized, double-blinded, placebo-controlled pilot trial in 32 subjects with ongoing neuropathic pain.\textsuperscript{16} Infusion of 5 mg/kg/h (but not 1 or 3 mg/kg/h) over 6 hours was observed to decrease pain by approximately 30%. This effect lasted for the next 4 hours of observation. Adverse events were frequent; in 2 subjects, the infusion was terminated early due to adverse events.

In a randomized, double-blind, placebo-controlled, crossover trial, Kvarnstrom et al (2003) evaluated the effects of lidocaine in 12 patients with long-term peripheral neuropathic pain of traumatic origin.\textsuperscript{3} The authors reported no significant differences in pain reduction over placebo on a VAS.

Wu et al (2002) evaluated the effects of IV lidocaine on 31 patients with postamputation pain in a randomized, double-blind, active placebo-controlled, crossover trial.\textsuperscript{7} They found stump pain was significantly reduced with IV lidocaine, yet the phantom pain was not, and the stump pain relief was short-lived.

In a study of 24 patients with PHN, Baranowski et al (1999) reported that IV lidocaine provided significant pain reduction over placebo; however, the pain was not eliminated.\textsuperscript{2} Medrik-Goldberg et al (1999) evaluated 30 patients with sciatica in a randomized, double-blind, 3-arm crossover trial.\textsuperscript{4} They found that lidocaine significantly reduced spontaneous pain as reported by VAS and pain evoked by straight leg raises. The pain reduction continued during saline infusion for 1 hour after the 2-hour lidocaine infusion. However, the evaluation did not extend beyond the 3-hour treatment period.

\textit{Retrospective Studies}

A retrospective analysis by Przeklasa-Muszynska et al (2016) examined the use of 3 to 25 IV infusions of lidocaine (5 mg/kg of body weight over 30 min) in 85 patients (57% women; mean age 63 years) with neuropathic pain.\textsuperscript{17} These disorders included: trigeminal neuralgia (n=18), chemo-induced peripheral neuropathy (n=6), PHN (n=16), diabetic neuropathy (n=7), persistent postoperative pain (n=21), and
other pain syndromes, including phantom pains, mononeuropathies, compression neuropathies, central pain syndrome, CRPS, and facial neuropathy (n=17). A total of 814 infusions were delivered to 85 patients; however, treatment was discontinued in 4 patients after the first infusion due to the lack of efficacy. Assessment of pain using a numeric rating scale (NRS) ranged from 0 to 10. Efficacy increased significantly with age (71-90 years, p<0.05). There was a correlation between treatment efficacy and the number of infusions (6-10 infusions, p<0.01) and the severity of pain (NRS range, 9-10; p<0.001). There was no correlation between treatment efficacy and the number of years patients had experienced pain symptoms (range, 19-30 years; p<0.05). Reviewers reported that infusions were not interrupted due to adverse events; however, they did not report whether adverse events occurred. Additionally, the authors reported no study limitations. It should be noted that use of single pain assessment tools may not be useful in measuring pain over time because patients may develop coping strategies for pain, acceptance, and tolerance of chronic pain; moreover, patients may have anxiety about reporting pain.

In a retrospective analysis by Carroll et al (2007), 104 patients with suspected neuropathic pain who had undergone diagnostic IV lidocaine were found from screening 635 sequential charts; of these 104 patients, 5 patients had requested discontinuation mid-infusion, resulting in a cohort of 99 patients with baseline and posttreatment NRS score for pain (range, 0-10). Mean pain reduction, measured on the NRS, during infusion was 2.34 (95% CI, 2.83 to 1.85, p<0.001).

**Spinal Cord Injury**

Finnerup et al (2005) reported on a randomized, double-blind crossover trial of IV lidocaine in 24 patients with spinal cord injury–related neuropathic pain.\(^{19}\) In this trial, spontaneous and evoked pain were significantly reduced as measured on a VAS, as administered before infusion and 25 to 35 minutes after infusion initiation. Mostly mild adverse events (experienced by 19 patients) and relief of pain formed the basis of 21 patients identifying the lidocaine treatment period correctly. Identification of the correct treatment group draws into question whether successful blinding was achieved, thus limiting interpretation of results. This concern about successful blinding also suggests the need for an active placebo in future trials, as noted. The trialists concluded that IV lidocaine (and similar agents) may be a treatment option for spinal cord injury pain—although, they also noted that long-term treatment with lidocaine is usually not suitable.

In a double-blind, placebo-controlled, crossover study of 16 patients either poststroke or spinal cord injury, Attal et al (2000) reported IV lidocaine significantly reduced pain over placebo.\(^{4}\) However, the duration of the effect lasted only 45 minutes.

Tables 5 and 6 summarize the characteristics and results of selected RCTs on spinal cord injury.

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
<th>Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finnerup et al (2005)(^{19})</td>
<td>Denmark</td>
<td>2002-2003</td>
<td>24 adults with neuropathic pain from trauma, spinal cord disease, or cauda equina with median pain intensity of 3 on 10-point NRS</td>
<td>Active: 23 patients received lidocaine 5 mg/kg over 30 min; 1 patient had adverse events and received only 4.75 mL/kg in 28.5 min</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>Attal et al</td>
<td>France</td>
<td>NR</td>
<td>NR</td>
<td>16 patients with</td>
<td>Patients received 3 wk after</td>
<td></td>
</tr>
</tbody>
</table>
poststroke or SCI pain

<table>
<thead>
<tr>
<th>Study</th>
<th>Effect on Spontaneous Pain (VAS)</th>
<th>Proportion With VAS Score Decrease ≥50%, n/N</th>
<th>Median Difference in Pain Reduction (95% CI)</th>
<th>Responders to Treatment, n</th>
<th>Patient-Reported Pain Relief During Treatment, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finnerup et al (2005)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>24</td>
<td>24</td>
<td>24</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>NR</td>
<td>11</td>
<td>2</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>NR</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Between-group comparison</td>
<td>Significantly greater reduction in pain for lidocaine vs placebo (p&lt;0.01)</td>
<td>Overall: 36% (18% to 50%)</td>
<td>p=0.008</td>
<td>p&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>16</td>
<td>16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lidocaine, mean (SD)</td>
<td>Preinjection: 61 (18)</td>
<td>• End of injection: 10/16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Postinjection 31 (28)</td>
<td>• 30 min&lt;sup&gt;a&lt;/sup&gt;: 7/16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 60 min&lt;sup&gt;a&lt;/sup&gt;: 4/16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo, mean (SD)</td>
<td>Preinjection: 61 (17)</td>
<td>• End of injection: 6/16</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Postinjection 46 (24)</td>
<td>• 30 min&lt;sup&gt;a&lt;/sup&gt;: 4/16</td>
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<td></td>
<td></td>
<td>• 60 min&lt;sup&gt;a&lt;/sup&gt;: 3/16</td>
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</tbody>
</table>

CI: confidence interval; NR: not reported; VAS: visual analog scale.
<sup>a</sup> Length of time after end of injection.

NR: not reported; NRS: numeric rating scale; SCI: spinal cord injury.
<sup>1</sup> Two treatments were performed in separate sessions 3 weeks apart.

Table 6. Summary of Key Randomized Controlled Trial Results

NR: not reported; NRS: numeric rating scale; SCI: spinal cord injury.
<sup>2</sup> Second infusion, patients received mexiletine 200 mg/d

<sup>2</sup> Length of time after end of injection.
**Section Summary: Lidocaine for Chronic Pain**
The evidence for IV anesthetics in patients with CRPS, fibromyalgia, chronic headache, chronic neuropathic pain, or spinal cord injury includes several RCTs, systematic reviews, and a retrospective analysis of a range of neuropathic conditions. The evidence would suggest that courses of IV lidocaine may provide temporary pain relief, particularly in elderly patients at a low dose (5 mg/kg of body weight over 30 min). However, there are few data on long-term usage. Additionally, there are limitations to measuring pain over time in retrospective studies, particularly without the use of multiple assessment tools (this is because patients may develop coping strategies for pain, acceptance, and tolerance of chronic pain; moreover, patients might have anxiety about reporting pain). Intense treatment protocols, the presence of severe adverse events, and limited durability raise questions about the net health benefit.

**Ketamine**

**Systematic Reviews**
A systematic review by Hocking and Cousins (2003) on the treatment of chronic neuropathic pain with IV ketamine assessed the quality of evidence for ketamine’s effectiveness in central pain, CRPS, fibromyalgia, ischemic pain, nonspecific pain of neuropathic origin, acute pain in patients with chronic neuropathic pain, orofacial pain, phantom/stump pain, and PHN. Some small RCTs were available for review, and meta-analysis was considered inappropriate. Reviewers concluded that, despite extensive use of ketamine, there was insufficient evidence to advocate its routine use for patients with chronic pain. Of particular concern were the significant adverse events of this N-methyl-D-aspartate receptor antagonist in the central and peripheral nervous systems. Few data were available on appropriate dosing and long-term administration.

**Randomized Controlled Trials**
A prospective, randomized, double-blind, double-dummy trial published by Motov et al (2017) compared IV low-dose ketamine (as a push dose over 5 minutes) with short infusion (over 15 minutes) in a convenience sample of 48 patients in an emergency department setting (n=24 push group; n=24 drip group). There were similar pain scores at baseline (NRS score, 8). From baseline to 15 minutes, the NRS score decreased in the IV push group 5.17 (95% CI, 3.67 to 6.66) and in the short infusion group 5.75 (95% CI, 4.28 to 7.22; p=0.026). Adverse events were similar in both groups. However, the sample size was inadequate to evaluate safety variances between the 2 routes of drug administration.

**Complex Regional Pain Syndrome**

**Systematic Reviews**
A network meta-analysis by Wertli et al (2014) evaluated the efficacy of all agent classes investigated in RCTs and provided a rank order of various substances. Sixteen studies on bisphosphonates, calcitonin, N-methyl-D-aspartate analogues, analgesics, vasodilators, steroids, anticonvulsive agents, and radical scavengers were analyzed. Of these, only bisphosphonates, N-methyl-D-aspartate analogues (ketamine), and vasodilators showed better long-term pain reduction than placebo. The 2 RCTs on ketamine were reported by Schwartzman et al (2009) (N=19) and Sigtermans et al (2009) (N=60), the latter of which is described below.

The same 16 studies were selected by O'Connell et al (2013) in a Cochrane overview of interventions for CRPS, which found low-quality evidence that a course of IV ketamine may be effective for CRPS-related pain; however, the effects of such a course were not sustained beyond 4 to 11 weeks posttreatment.
Randomized Controlled Trials
Tables 7 and 8 summarize the characteristics and results of selected RCTs.

Table 7. Summary of Key Randomized Controlled Trial Characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sigtermans et al (2009)</td>
<td>NL</td>
<td>1</td>
<td>2006-2008</td>
<td>Patients were diagnosed with CRPS type I</td>
<td>30 patients randomized to ketamine infused over 4 d (titrated up to 30 mg/h for a 70-kg patient)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>30 patients randomized to saline infused over 4 d</td>
</tr>
</tbody>
</table>

CRPS: complex regional pain syndrome; NL: Netherlands.

Table 8. Summary of Key Randomized Controlled Trial Results

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean Change in NRS Pain Score, Baseline to End of Week 11 (SD)</th>
<th>Differences in Pain Reduction</th>
<th>Side Effects During Infusion, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sigtermans et al (2009)</td>
<td>7.20 (1.16) to 2.68 (0.51)</td>
<td>• Nausea: 63</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>60</td>
<td>• Vomiting: 47</td>
<td></td>
</tr>
<tr>
<td>Ketamine</td>
<td>60</td>
<td>• Psychomimetic effects: 93</td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>6.87 (1.43) to 5.45 (0.48)</td>
<td>• Headache: 37</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maintained until week 11; at week 12, ketamine’s treatment effect no longer significant (p=0.07)</td>
<td>• Nausea: p&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Vomiting: p=0.004</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Psychomimetic effects: p=0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Headache: p=0.78</td>
<td></td>
</tr>
</tbody>
</table>

NRS: numeric rating scale.

A large double-blind RCT of ketamine for CRPS is the aforementioned European report by Sigtermans et al (2009). Sixty patients were randomized to ketamine (titrated up to 30 mg/h for a 70-kg patient) or saline infused over 4 days. The mean ketamine infusion rate was 22 mg/h (normalized to a 70-kg patient) at the end of the treatment phase. Blood samples were collected to assess the plasma concentration of ketamine, and patients were monitored for adverse events. Two patients terminated ketamine infusion early due to psychomimetic effects (eg, delusions, hallucinations). At baseline, NRS scores for pain were 7.2 (maximum, 10) for ketamine and 6.9 for the placebo group. The lowest pain scores (ketamine, 2.7; placebo, 5.5) were observed at the end of the first week (no patients were lost to follow-up for the primary outcome measure). Although pain scores remained statistically lower through week 11, the clinically significant difference of 2 points was maintained until week 4. None of the secondary (functional) outcome measures were improved by treatment. Moreover, 60% of patients in the placebo group correctly deduced treatment assignment (slightly better than chance); 93% of
patients in the ketamine group correctly deduced treatment assignment due primarily to psychomimetic effects.

No relevance, study design, and conduct gaps were identified for this set of RCTs.

**Fibromyalgia**
Noppers et al (2011) also reported on a randomized, double-blind, active placebo-controlled trial conducted in Europe using a 30-minute infusion of ketamine (n=12) or midazolam (n=12). Baseline VAS pain scores were 5.4 in the ketamine group and 5.8 in the midazolam group. At 15 minutes after termination of infusion, significantly more patients in the ketamine group showed a reduction in VAS score for pain exceeding 50% than in the placebo group (8 vs 3). There were no significant differences between the groups at 180 minutes after infusion (6 vs 3), at the end of week 1 (2 vs 0), or at the end of week 8 (2 vs 2), all respectively. There was no difference between groups on the Fibromyalgia Impact Questionnaire scores measured weekly over 8 weeks. In this well-conducted study, a short infusion of ketamine (30 minutes) did not have a long-term analgesic effect on fibromyalgia pain.

**Other Chronic Pain**
A study by Eichenberger et al (2008) compared the efficacy of placebo, ketamine, calcitonin, and combined calcitonin plus ketamine to relieve phantom limb pain (N=20, within-subject design). One-hour infusion of ketamine or ketamine plus calcitonin resulted in a reduction of more than 40% in pain immediately after treatment. The mean and maximum pain scores remained significantly better than placebo for 48 hours after treatment.

Tables 9 and 10 summarize the characteristics and results of selected observational studies.

**Table 9. Summary of Key Observational Comparative Study Characteristics**

<table>
<thead>
<tr>
<th>Study</th>
<th>Study Type</th>
<th>Country</th>
<th>Dates</th>
<th>Participants</th>
<th>Treatment</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patil &amp; Anitescu</td>
<td>Retrospective chart review</td>
<td>U.S.</td>
<td>2004-2009</td>
<td>Patients with CRPS, refractory headaches, or severe back pain</td>
<td>Ketamine 0.5 mg/kg over 30-45 min</td>
<td>NR</td>
</tr>
<tr>
<td>(2012)²⁸</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Webster &amp; Walker</td>
<td>Retrospective</td>
<td>U.S.</td>
<td>2002-2004</td>
<td>Patients with severe neuropathic pain treated with prolonged IV ketamine</td>
<td>Ketamine 100 mg/mL; mean duration of infusion treatment, 16.4 d (range, 5-55 d)</td>
<td>NR</td>
</tr>
<tr>
<td>(2006)²⁹</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CRPS: complex regional pain syndrome; IV: intravenous; NR: not reported.

**Table 10. Summary of Key Observational Comparative Study Results**

<table>
<thead>
<tr>
<th>Study</th>
<th>Decrease in VAS From Start of Infusion to Discontinuation</th>
<th>Global Pain Relief From Baseline to EOT</th>
<th>Adverse Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patil &amp; Anitescu</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2012)²⁸</td>
<td>49</td>
<td>49</td>
<td>23 (46.9) reported; 35 nonserious</td>
</tr>
<tr>
<td>N</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient-reported, n</td>
<td>5.9 (0.35)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### VAS (SE)

Webster & Walker (2006)\(^{29}\)

<table>
<thead>
<tr>
<th>N</th>
<th>13</th>
<th>13</th>
<th>13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient-reported, n (%)</td>
<td>11 (85)</td>
<td>• Improvement: 8 (62)</td>
<td>• Irritation from delivery: 5 (38)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• No improvement: 3 (23)</td>
<td>• Fatigue: 4 (31)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Decrease in relief: 2 (15)</td>
<td>• Dizziness: 3 (23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Confusion: 2 (15)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Spinal pain: 2 (15)</td>
</tr>
</tbody>
</table>

**Mean VAS score**
- 7.7 at baseline
- 4.8 at EOT (p=0.003)

EOT: end of treatment; VAS: visual analog scale.

Patil and Anitescu (2012) retrospectively analyzed data from 49 patients with severe refractory pain who had undergone 369 outpatient ketamine infusions during a 5-year period at a U.S. academic medical center.\(^{28}\) Eighteen patients were diagnosed with CRPS, and 31 had other diagnoses including refractory headache (n=8) and severe back pain (n=7). All patients exhibited signs of central sensitization. Following pretreatment with midazolam and ondansetron, ketamine infusions were administered at the highest tolerated dose for a duration ranging from 30 minutes to 8 hours. The interval between infusions ranged from 12 to 680 days (median, 233.7 days). The immediate reduction in VAS score was 7.2 for patients with CRPS and 5.1 for non-CRPS pain. Query of available patients (59%) indicated that, for 38%, pain relief lasted more than 3 weeks. Adverse events, which included confusion and hallucination, were considered minimal.

Webster and Walker (2006) published retrospective analysis describing outpatient ketamine treatment in 13 patients with severe neuropathic pain; diagnoses included CRPS (n=8), migraine (n=1), neuropathy (n=3), and phantom limb (n=1).\(^{29}\) Low-dose ketamine (beginning at 0.12 mg/kg/h with slow upward titration) was delivered by a programmable pump. With an average infusion duration of 16 days, pain severity decreased by 38% (VAS score range, 7.7-4.8), with an 85% response rate. About half of the patients reported a perceived benefit 1 month after treatment. Adverse events included fatigue, dizziness, confusion, and spinal pain. No patients reported hallucinations.

**Spinal Cord Injury**

Amr (2010) published results from a double-blind, randomized, placebo-controlled study of 40 patients with neuropathic pain secondary to spinal cord injury that was conducted in Egypt.\(^{30}\) All patients received gabapentin (300 mg) 3 times daily. The experimental group also received ketamine infusion (80 mg) over a 5-hour period daily for 7 days. The control group received an infusion of isotonic saline over the same period. VAS scores for pain were similar in both groups at baseline (VAS of 84 of 100). During the week of infusion, VAS scores decreased more in the ketamine-infused group than in the gabapentin-only group (VAS score of 14 in the ketamine group vs 43 in the control group at day 7). In the control group, VAS pain scores remained about the same during the 4-week follow-up. Pain scores in the ketamine-infused group increased from 14 to 22 at 1-week follow-up and remained at that level for 2 weeks after infusion. By the third week after the ketamine infusion, VAS scores had increased to 43 and were the same as the placebo-control group. Three patients were reported to have had short-lasting delusions with ketamine infusion.

Kvarnstrom et al (2004) assessed the effect of subanesthetic levels of IV ketamine or lidocaine on pain after spinal cord injury.\(^{31}\) This randomized, double-blind, placebo-controlled crossover trial found a 38%
reduction in pain during ketamine infusion, with 5 of 10 subjects responding to treatment, compared with 1 of 10 in the lidocaine infusion group and 0 of 10 in the placebo group. Adverse events were common with both active treatments; ketamine produced 39 adverse events in 9 of 10 subjects. They included somnolence, dizziness, out-of-body sensation, changes in hearing and vision, paresthesia, and other “unpleasant experiences.”

Section Summary: Ketamine for Chronic Pain
Evidence, primarily from outside of the United States, has suggested that courses of IV ketamine both as a push dose or short infusion may provide temporary relief to some chronic pain patients in some settings. 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.

INTRAVENOUS ANESTHETICS FOR PATIENTS WITH PSYCHIATRIC DISORDERS

Clinical Context and Test Purpose
The purpose of a course of IV anesthetics (eg, lidocaine, ketamine) is to provide a treatment option that is an alternative to or an improvement on existing therapies in patients with psychiatric disorders (eg, depression, obsessive-compulsive disorder).

The question addressed in this evidence review is: Does a course of IV anesthetics improve the net health outcome in individuals with psychiatric disorders (eg, depression, obsessive-compulsive disorder)?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is individuals with psychiatric disorders (eg, depression, obsessive-compulsive disorder).

Interventions
The therapy being considered is a course of IV anesthetics (eg, lidocaine, ketamine).

Comparators
The following therapy is currently being used to treat psychiatric disorders: psychotropic medication.

Outcomes
The general outcomes of interest are symptoms, change in disease status, morbid events, functional outcomes, quality of life, medication use, and treatment-related morbidity.

Timing
Though not completely standardized, follow-up for psychiatric disorders symptoms would typically occur in the months to years after starting treatment.

Setting
Patients with psychiatric disorders are actively managed by psychiatrists and primary care providers in an outpatient clinical setting.

Study Selection Criteria
Methodologically credible studies were selected using the principles outlined for indication 1.
Clinical Studies
There is very limited evidence on the use of lidocaine or ketamine for treatment of a psychiatric disorder such as depression and obsessive-compulsive disorder.

Section Summary: Intravenous Anesthetics for Patients With Psychiatric Disorders
Current evidence does not support the utility of IV anesthetic injections for patients with psychiatric disorders.

SUMMARY OF EVIDENCE
For individuals who have chronic pain syndromes (eg, CRPS, 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.

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.

SUPPLEMENTAL INFORMATION

PRACTICE GUIDELINES AND POSITION STATEMENTS
The practice guidelines on managing chronic pain from the American Society of Anesthesiologists and the American Society of Regional Anesthesia and Pain Medicine (2010) discussed various treatments for chronic pain. Use of ionotropic N-methyl-D-aspartate receptor antagonists and topical agents for neuropathic pain was addressed; intravenous infusion of lidocaine or ketamine was not.

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS
Not applicable.

MEDICARE NATIONAL COVERAGE
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

ONGOING AND UNPUBLISHED CLINICAL TRIALS
Some currently unpublished trials that might influence this review are listed in Table 11.

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td>Evaluation of the Effects of Ketamine in the Acute</td>
<td>156</td>
<td>Oct 2018</td>
</tr>
</tbody>
</table>
Intravenous Anesthetics for the Treatment of Chronic Pain

Phase of Suicidal Ideation: a Multicenter Randomized Double-blind Trial

<table>
<thead>
<tr>
<th>Unpublished</th>
<th>Study Description</th>
<th>ID</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<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>
<tr>
<td>NCT01371110</td>
<td>Intravenous Ketamine in the Treatment of Obsessive-Compulsive Disorder</td>
<td>3</td>
<td>Jun 2015 (terminated)</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

ESSENTIAL HEALTH BENEFITS

The Affordable Care Act (ACA) requires fully insured non-grandfathered individual and small group benefit plans to provide coverage for ten categories of Essential Health Benefits (“EHBs”), whether the benefit plans are offered through an Exchange or not. States can define EHBs for their respective state.

States vary on how they define the term small group. In Idaho, a small group employer is defined as an employer with at least two but no more than fifty eligible employees on the first day of the plan or contract year, the majority of whom are employed in Idaho. Large group employers, whether they are self-funded or fully insured, are not required to offer EHBs, but may voluntarily offer them.

The Affordable Care Act requires any benefit plan offering EHBs to remove all dollar limits for EHBs.

REFERENCES


**CODES**

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

**ICD-10-CM**

Investigational for all diagnoses

**ICD-10-PCS**

ICD-10-PCS codes are only used for inpatient services.

**3E0T3CZ**

Introduction, peripheral nerves, percutaneous, regional anesthetic

**Type of service** Medicine

**Place of service** Inpatient/outpatient

**POLICY HISTORY**

<table>
<thead>
<tr>
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<th>Action</th>
<th>Description</th>
</tr>
</thead>
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<tr>
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<td>Replace policy</td>
<td>Policy updated with literature review through August 27, 2014; reference 28 added; chronic daily headache added to the investigational statement.</td>
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<td>Policy updated with literature review through August 27, 2015;</td>
</tr>
<tr>
<td>Date</td>
<td>Action</td>
<td>Details</td>
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<td>------------</td>
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<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>02/24/17</td>
<td>Replace policy</td>
<td>Blue Cross of Idaho annual review; no change to policy.</td>
</tr>
<tr>
<td>11/30/17</td>
<td>Replace policy</td>
<td>Blue Cross of Idaho adopted changes as noted. Policy updated with literature review through September 11, 2017; no references added. Policy statement unchanged.</td>
</tr>
<tr>
<td>11/15/18</td>
<td>Replace policy</td>
<td>Blue Cross of Idaho adopted changes as noted, effective 11/15/2018. Policy updated with literature review through September 6, 2018; reference 8 added. Psychiatric disorders added to investigational policy statement; statement otherwise unchanged.</td>
</tr>
</tbody>
</table>