Clinical Policy Title: Intravenous lidocaine infusion for neuropathic pain

Clinical Policy Number: 03.03.08

Effective Date: June 1, 2014
Initial Review Date: January 19, 2014
Most Recent Review Date: January 20, 2016
Next Review Date: January 2017

Policy contains:
- Lidocaine hydrochloride injection.
- Xylocaine® (APP Pharmaceuticals Inc., Schaumburg, IL).

Related policies:
- CP# 18.04.02 Hierarchy of chronic pain
- CP# 03.03.02 Intrathecal opioid therapy for chronic nonmalignant pain
- CP# 03.03.06 Biofeedback
- CP# 03.03.04 Spine pain — epidural injection
- CP# 03.02.07 Spine pain — facet joint injection
- CP# 03.02.01 Spine pain — trigger point injection

ABOUT THIS POLICY: AmeriHealth Caritas Northeast has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Northeast’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by AmeriHealth Caritas Northeast when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Northeast’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Northeast’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Northeast will update its clinical policies as necessary. AmeriHealth Caritas Northeast’s clinical policies are not guarantees of payment.

Coverage policy

AmeriHealth Caritas Northeast considers the use of intravenous lidocaine hydrochloride for treatment of neuropathic pain to be investigational and, therefore, not medically necessary.

Limitations:
- All other uses of intravenous lidocaine hydrochloride are not medically necessary, except for treatment of cardiac arrhythmia.

Note: The following CPT/HCPCS code is not listed in the Pennsylvania Medicaid fee schedule:

J2001 - Injection lidocaine HCL for intravenous infusion, 10 mg
Alternative covered services:
- Tricyclic antidepressants.
- Anticonvulsants (e.g., gabapentin and pregabalin).
- Carbamazepine for tic douloureux (idiopathic trigeminal neuralgia).
- Serotonin and norepinephrine reuptake inhibitors.
- Topical lidocaine.
- Tramadol.
- Opioids.
- Other anticonvulsants, such as lamotrigine.
- Topical capsaicin.
- Mexiletine.
- N-methyl-d-aspartate receptor antagonists.

Background

Neuropathic pain is pathologic or maladaptive pain from damage to the peripheral or central nervous systems, producing pain in the absence of stimulation of nociceptors or inappropriate response to stimulation of nociceptors. Neuropathic pain disorders are related to dysfunction or disease of the peripheral nervous system, central nervous system, or both. Peripheral neuropathies include damage to the motor, sensory and autonomic fibers that feed into the central nervous system. Central nervous system disorders occur from injury, stroke, disease or congenital conditions involving the brain and/or spinal cord. Patients with neuropathic pain typically describe burning, lancinating, stabbing, cramping, numbness, aching and sometimes “vice-like” pain. It can be paroxysmal or constant (Lema, 2013).

There are numerous causes of neuropathic pain in adults. In the United States more than 30 percent of all neuropathies are a result of diabetes. Trauma can result in phantom limb syndromes and/or complex regional pain syndromes (CRPS). Infectious conditions, such as postherpetic neuralgia and human immunodeficiency virus, are known to result in long-standing neuropathic pain. Other causes include nerve compression, autoimmune disorders, and congenital or hereditary diseases (Lema, 2013).

Neuropathic pain is relatively uncommon in pediatric populations. However, many of the neuropathic conditions found in adults are increasingly recognized in children and adolescents. Some rare neuropathic pain syndromes are fairly unique to the pediatric population, including toxic and metabolic neuropathies, hereditary neurodegenerative disorders (e.g., Fabry disease), mitochondrial disorders and primary erythromelalgia (Walco, 2010).

Neuropathic pain can be very difficult to treat, with only 40 percent to 60 percent of patients achieving partial relief. Courses of intravenous (IV) anesthetic agents may be given in the inpatient or outpatient setting as part of a pain management program (Walco, 2010). Lidocaine hydrochloride (lidocaine) is an anesthetic of the amide type and a class IB antiarrhythmic drug (U.S. Food and Drug Administration [FDA], 2014). Several American companies manufacture lidocaine in various concentrations for local and
parenteral administration, one example being Xylocaine (APP Pharmaceuticals Inc., Schaumburg, IL). Its mechanism of action as a sodium channel blocker also produces analgesia when administered intravenously by direct injection or continuous infusion. FDA approved lidocaine hydrochloride injection for systemic use in acute treatment of cardiac arrhythmias; its use for treatment of neuropathic pain is considered off-label (FDA, 2014).

Approximately 90 percent of lidocaine is metabolized in the liver. Following an IV bolus injection, lidocaine has an elimination half-life of approximately one-and-a-half hours to two hours, but may be three hours or longer following infusions lasting more than 24 hours. Because of the rapid rate at which lidocaine metabolizes, any condition that alters liver function, including changes in liver blood flow, may alter lidocaine kinetics. The half-life may be two-fold or greater in patients with liver dysfunction. Renal dysfunction does not affect lidocaine kinetics but may increase the accumulation of metabolites. Lidocaine readily crosses the placental and blood-brain barriers (Hayes, 2012).

While the drug is relatively safe, adverse effects of lidocaine may occur. Mild to moderate adverse effects 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. Clinical alternatives include tricyclic antidepressants, dual reuptake inhibitors of serotonin and norepinephrine, calcium channel alpha-2-delta ligands and topical lidocaine. Opioid analgesics, tramadol, other antidepressant and antiepileptic medications, topical capsaicin, mexiletine (an orally active local anesthetic, antiarrhythmic agent, structurally similar to lidocaine), and N-methyl-d-aspartate receptor antagonists may be indicated in some circumstances (Dworkin, 2010).

**Searches**

AmeriHealth Caritas Northeast searched PubMed and the databases of:
- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on December 16, 2013, December 30, 2014 and December 3, 2015. Search terms were: "pain"[MeSH], "pain management"[MeSH], "neuralgia"[MeSH] and the free-text term “lidocaine.”

We included:
- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews**.
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.
Findings

Five systematic reviews, five evidence-based guidelines and no economic analyses were identified for this policy. The overall quality of the evidence was poor to moderate, consisting of mostly small controlled studies of patients with neuropathic pain of varying etiologies, study designs, dosing regimens and outcome measures. Reporting of adverse effects was incomplete and inconsistent across studies. Follow up was of short duration. Finally, multidrug combinations in current practice require more study. Its long-term efficacy and safety, including outcome measures of patient satisfaction, have not been studied adequately. Therefore, the net health benefits of IV lidocaine for treating neuropathic pain are unclear.

Limited evidence suggests some patients with peripheral neuropathic pain from trauma or diabetes and central pain from spinal cord injury experienced a reduction in pain intensity, but relief was temporary, often terminating within hours of discontinuation of the infusion. There was insufficient evidence of its efficacy for treatment of chronic postoperative pain, procedural burn pain or postherpetic neuropathic pain. The analgesic effects of lidocaine were similar to those of other analgesics for treating neuropathic pain. Adverse events were reported inconsistently across studies. Where reported, they were common, mostly mild to moderate, and transient. Drowsiness, fatigue, nausea and dizziness were most frequently reported. Since lidocaine is not selective for pain-specific sodium channel subtypes, its use may result in a higher risk of adverse effects.

Many of the published studies on interventions for neuropathic pain in children are case reports or clinical series with few or no systematic controls and limited follow up. Evidence from systematic reviews is lacking. Extrapolating the results of interventions used for neuropathic pain in adults to children may not be appropriate. Since the FDA review process did not include studies of neuropathic pain in children or for pediatric problems, data are lacking on the safety and efficacy of these drugs in children (Walco, 2010).

Several evidence-based guidelines have been developed for pharmacological treatment of neuropathic pain:

- The Special Interest Group of the Canadian Pain Society stated patients with neuropathic pain who have not derived sufficient benefit from pharmacological treatment, clinicians may consider a trial of IV lidocaine at doses of 5 mg/kg to 7.5 mg/kg body weight for pain relief (Mailis, 2012). They gave a Grade B recommendation based on “high certainty with moderate effect or moderate certainty with moderate to substantial effect” that some patients with treatment-resistant neuropathic pain may experience pain relief for up to several weeks. However, the authors stressed there was no literature pertaining to the effectiveness of repeated IV lidocaine infusions.

- The Dutch Society of Rehabilitation Specialists and the Dutch Society of Anaesthesiologists found IV lidocaine had no added value in pain reduction compared to placebo in patients with CRPS type I based on the results of one small trial; they recommended further research into each of the therapeutic modalities discussed in the guideline (Perez, 2010).

- The Canadian Pain Society found that an IV infusion of lidocaine 5 mg/kg over 30 minutes to 60 minutes was generally safe and provided significant pain relief for two to three weeks at a time.
based on one small study (Moulin, 2007). However, they recommended neither for nor against its use in chronic neuropathic pain.

- The American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine and the American Academy of Physical Medicine and Rehabilitation found insufficient evidence of effectiveness to recommend IV lidocaine for painful diabetic neuropathy (Bril, 2011).
- A multinational group found insufficient evidence to recommend IV lidocaine as a treatment for short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) syndrome (Evers, 2011).

Policy updates:

Updates of two previously included systematic reviews were included in this policy (Hayes, 2014; Wasiak, 2014). These systematic review updates added no new data and made no changes to their conclusions. There is insufficient evidence to support its long-term safety or efficacy in persons with CRPS or other types of chronic pain. Therefore, there are no changes to the policy.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chaparro (2013)</td>
<td>Key points:</td>
</tr>
<tr>
<td>Cochrane review</td>
<td></td>
</tr>
<tr>
<td>Chronic postoperative pain</td>
<td>Identified one randomized controlled trial (RCT) evaluating chronic postoperative pain, measured at least three months postoperatively.</td>
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<tr>
<td></td>
<td>Insufficient evidence to support efficacy of IV lidocaine for prevention of chronic postoperative pain.</td>
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<tr>
<td>Wasiak (2012, updated 2014)</td>
<td>Key points:</td>
</tr>
<tr>
<td>Cochrane review</td>
<td></td>
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<tr>
<td>Procedural burn pain</td>
<td>Identified one randomized, double-blind, placebo-controlled, cross-over trial (n = 45).</td>
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<td></td>
<td>Subjective pain ratings as measured by the verbal rating scale improved during procedures in both treatment arms; however, the increase was less for the lidocaine arm. No significant clinical or statistical differences between arms regarding opioid requests and consumption, anxiety or level of satisfaction during a wound care procedure.</td>
</tr>
<tr>
<td></td>
<td>Insufficient evidence of efficacy in burn care.</td>
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<tr>
<td>Hayes (2012, updated 2014)</td>
<td>Key points:</td>
</tr>
<tr>
<td>Overall neuropathic pain</td>
<td></td>
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<tr>
<td></td>
<td>Identified 10 randomized, double-blind, placebo-controlled studies from published systematic reviews and meta-analyses, plus four additional RCTs and two cohort studies.</td>
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<tr>
<td></td>
<td>Overall quality of evidence = moderate; mostly small studies with short follow up, heterogeneous designs, patient populations, quality, dosing regimens and outcome measures.</td>
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<td></td>
<td>Findings suggest lidocaine infusion was superior to placebo in reducing pain intensity, and similar to other analgesics, but not sustained; long-term efficacy unclear.</td>
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<td></td>
<td>Therapeutic benefit was more consistent for peripheral pain (trauma, diabetes) and central pain.</td>
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<td></td>
<td>High frequency of side effects; most were mild to moderate and transient, with drowsiness, fatigue, nausea and dizziness being the most common.</td>
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<tr>
<td></td>
<td>Additional larger studies are needed to elucidate its long-term effectiveness and safety, and to evaluate the efficacy and practicality of repeated infusions.</td>
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<tr>
<td>Teasell (2010)</td>
<td>Key points:</td>
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<tr>
<td>Citation</td>
<td>Content, Methods, Recommendations</td>
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<td>--------------------------------------------</td>
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<tr>
<td>Spinal cord injury (SCI)</td>
<td>• Identified one small controlled clinical trials (CCTs) and two small RCTs.</td>
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<td></td>
<td>• Lidocaine was effective in treating post-SCI pain, but short-lived.</td>
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<td></td>
<td>• Lidocaine is not selective for pain-specific sodium channel subtypes, which may result in a higher risk of adverse effects.</td>
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<tr>
<td></td>
<td>• IV administration is not a practical long-term pain management solution.</td>
</tr>
<tr>
<td>Hempenstall (2005)</td>
<td><strong>Key points:</strong></td>
</tr>
<tr>
<td>Postherpetic neuralgia</td>
<td>• Identified two small RCTs.</td>
</tr>
<tr>
<td></td>
<td>• IV lidocaine not associated with efficacy for treatment of post-herpetic neuralgia.</td>
</tr>
</tbody>
</table>

**Glossary**

**Allodynia** — Pain from a stimulus that normally does not elicit a painful response (e.g., light touch, warmth).

**Dysesthesia** — A constant or ongoing unpleasant or electrical sensation of pain.

**Complex regional pain syndrome** — A type of neuropathic pain disorder that worsens over time, for poorly understood reasons, as a result of reorganization within the nervous system. One outcome of this reorganization is a lowered threshold to nociceptive processing, as well as distorted pain perceptions. Patients with neuropathic pain of the CRPS type may experience pain even in the absence of stimuli. CRPS may be classified as either type 1 or type 2:

- **Type 1 CRPS:**
  - Continuing pain, allodynia or hyperalgesia in which the pain is out of proportion to the initiating event.
  - Evidence of edema, changes in skin blood flow, or abnormal sudomotor activity in the painful region (this criterion is satisfied by either a sign or a symptom).
  - No other condition that would account for the degree of pain and dysfunction.

- **Type 2 CRPS:**
  - Diagnosed when, in addition to the above three criteria for CRPS 1, there is also an initiating noxious event or a cause of immobilization.

**Hyperalgesia** — An exaggerated response to normally painful stimuli that may continue for a period of time that is longer (e.g., six months or more) than clinically expected after an illness or injury.

**Neuropathic pain** — Pain caused by damage to the nervous system and often disproportionate to the extent of the primary triggering injury. It may consist of thermal or mechanical allodynia, dysesthesia, and/or hyperalgesia.

**Nociceptor** — A nerve cell that responds to potentially damaging stimuli by sending nerve signals to the spinal cord and brain; pain receptor.
Nociceptive pain — Pain caused by stimulation of peripheral nerve fibers that respond only to stimuli approaching or exceeding harmful intensity. Examples are temporary pain from a burn, twisted ankle or stubbed toe, or chronic pain from cancer or arthritis. It may be dull or sharp aching pain, and it can be mild to severe. Nociceptive pain usually responds well to pain medications, anti-inflammatory agents or other drug therapies. It usually does not respond well to neurostimulation.

References

Professional society guidelines/other:


Peer-reviewed references:


**Clinical trials:**

Searched clinicaltrials.gov on December 3, 2015, using terms | open studies | “intravenous lidocaine NOT surgery”. Forty-four studies were found, three were relevant.


**CMS National Coverage Determinations (NCDs):**

None identified.

**Local Coverage Determinations (LCDs):**

L35033 Pain Management. CMS website : [www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDid=35033&ContrId=325&ver=6&ContrVer=1&SearchType=Advanced&CoverageSelection=Local&ArticleType=SAD%7cEd&PolicyType=Final&s=All&KeyWord=lidocaine&KeyWordLookUp=Doc&KeyWordSearchType=Exact&kq=true&bc=IAAAABAAAAA%3d%3d&](http://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDid=35033&ContrId=325&ver=6&ContrVer=1&SearchType=Advanced&CoverageSelection=Local&ArticleType=SAD%7cEd&PolicyType=Final&s=All&KeyWord=lidocaine&KeyWordLookUp=Doc&KeyWordSearchType=Exact&kq=true&bc=IAAAABAAAAA%3d%3d&). Accessed December 3, 2015.
**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Codes</td>
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</table>

<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>I49.x</td>
<td>Other cardiac arrhythmias</td>
<td>Covered</td>
</tr>
<tr>
<td>I47.x</td>
<td>Paroxysmal tachycardia</td>
<td>Covered</td>
</tr>
<tr>
<td></td>
<td>All other diagnoses</td>
<td>Not covered</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HCPCS Level II</th>
<th>Description</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>J2001</td>
<td>Injection lidocaine HCL for intravenous infusion, 10 mg</td>
<td>Covered for cardiac arrhythmias only – Not covered for Neuropathic pain.</td>
</tr>
</tbody>
</table>