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 18, 2017
Next Review Date: January 2018

About this policy: AmeriHealth Caritas Pennsylvania has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Pennsylvania’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 Pennsylvania 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 Pennsylvania’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 Pennsylvania’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Pennsylvania will update its clinical policies as necessary. AmeriHealth Caritas Pennsylvania’s clinical policies are not guarantees of payment.

Coverage Policy:

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

Limitations:

All other uses of IV 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 (Lema, 2013). Neuropathic pain disorders are related to dysfunction or disease of the peripheral nervous system, central nervous system, or both (Foundation for Peripheral Neuropathy, 2016). 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 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. The 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 Pennsylvania 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 November 17, 2016. 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 that for 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>
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<tr>
<td>Cochrane review</td>
<td></td>
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<tr>
<td>Chronic postoperative pain</td>
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<tr>
<td></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>Hayes (2012, updated 2014)</td>
<td>Key points:</td>
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<tr>
<td>Overall neuropathic pain</td>
<td></td>
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<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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<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>- 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>- Therapeutic benefit was more consistent for peripheral pain (trauma, diabetes) and central pain.</td>
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<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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<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>Wasiak (2012, Key points:</td>
<td></td>
</tr>
<tr>
<td>Citation</td>
<td>Content, Methods, Recommendations</td>
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| updated 2014)                    | • Identified one randomized, double-blind, placebo-controlled, crossover trial (n = 45).  
                                   | • 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.  
                                   | • Insufficient evidence of efficacy in burn care.                                                                                                                                                                                  |
| Cochrane review                  |                                                                                                                                                                                                                                  |
| Procedural burn pain             |                                                                                                                                                                                                                                  |
| Teasell (2010)                   | **Key points:**                                                                                                                                                                                                                  |
| Spinal cord injury (SCI)         | • Identified one small controlled clinical trials (CCTs) and two small RCTs.  
                                   | • Lidocaine was effective in treating post-SCI pain, but short-lived.  
                                   | • Lidocaine is not selective for pain-specific sodium channel subtypes, which may result in a higher risk of adverse effects.  
                                   | • IV lidocaine administration is not a practical long-term pain management solution.                                                                                      |
| Hempenstall (2005)               | **Key points:**                                                                                                                                                                                                                  |
| Postherpetic neuralgia           | • Identified two small RCTs.  
                                   | • IV lidocaine not associated with efficacy for treatment of post-herpetic neuralgia.                                                                                     |

References

**Professional society guidelines/other:**


Peer-reviewed references:

Drugs@FDA. FDA-approved drug products. Lidocaine Hydrochloride. FDA website. 


What is peripheral neuropathy? The Foundation for Peripheral Neuropathy website.  

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

No NCDs identified as of the writing of this policy.


**Local Coverage Determinations (LCDs):**


**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.

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<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
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</thead>
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<table>
<thead>
<tr>
<th>ICD-10 Code</th>
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<tbody>
<tr>
<td>G62.9</td>
<td>Neuropathic pain</td>
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<table>
<thead>
<tr>
<th>HCPCS Level II</th>
<th>Description</th>
<th>Comments</th>
</tr>
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<tbody>
<tr>
<td>J2001</td>
<td>Injection lidocaine HCL for intravenous infusion, 10 mg</td>
<td>Not covered for Neuropathic pain.</td>
</tr>
</tbody>
</table>