



Kansas City

An Independent Licensee of the Blue Cross and Blue Shield Association

## The Treatment of Chronic Pain by Infusion of IV Anesthetic and the Prevention of Phantom Limb Pain

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**Last Review:** 4/2014

**Origination:** 4/2009

**Next Review:** 4/2015

### **Policy**

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Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for the treatment of chronic neuropathic pain by infusion of IV anesthetic or the prevention of phantom limb pain as described below. These are considered investigational.

### **When Policy Topic is covered**

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Not Applicable

### **When Policy Topic is not covered**

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Intravenous infusion of anesthetics (e.g., ketamine or lidocaine) for the management of chronic pain including, but not limited to chronic neuropathic pain and fibromyalgia, is considered **investigational**.

Pre-operative epidural or epineural analgesia to prevent phantom limb pain is considered **investigational**.

### **Considerations**

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

Ketamine hydrochloride injection is FDA-indicated for diagnostic and surgical procedures that do not require skeletal muscle relaxation, for the induction of anesthesia prior to the administration of other general anesthetic agents, and to supplement low-potency agents, such as nitrous oxide. IV ketamine for the treatment of chronic pain is an off-label use.

### **Description of Procedure or Service**

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Intravenous (IV) infusion of lidocaine or ketamine has been used for the treatment of chronic neuropathic pain. Chronic neuropathic pain disorders include phantom limb pain, postherpetic neuralgia, complex regional pain syndromes, diabetic neuropathy, and pain related to stroke or spinal cord injuries.

For this application, one or more courses of intravenous infusion would be administered over a period of several hours or several days.

Neuropathic pain is often disproportionate to the extent of the primary triggering injury and may consist of thermal or mechanical allodynia, dysesthesia, and/or hyperalgesia. Allodynia is pain that occurs from a stimulus that normally does not elicit a painful response (e.g., light touch, warmth). Dysesthesia is a constant or ongoing unpleasant or electrical sensation of pain. Hyperalgesia is an exaggerated response to normally painful stimuli. In the latter, symptoms may continue for a period of time that is longer (e.g., 6 months or more) than clinically expected after an illness or injury. It is proposed that

chronic neuropathic pain results from peripheral afferent sensitization, neurogenic inflammation, and sympathetic afferent coupling, along with sensitization and functional reorganization of the somatosensory, motor, and autonomic circuits in the central nervous system (CNS). Therefore, treatments focus on reducing activity and desensitizing pain pathways, thought to be mediated through N-methyl-d-aspartate (NMDA) receptors in the peripheral and CNS. Sympathetic ganglion blocks with lidocaine have been used for a number of years to treat sympathetically maintained chronic pain conditions, such as complex regional pain syndrome (CRPS, previously known as reflex sympathetic dystrophy). Test infusion of an anesthetic has also been used in treatment planning to assess patient responsiveness to determine whether medications, such as oral mexiletine or oral ketamine, may be effective. A course of intravenous (IV) lidocaine or ketamine, usually at subanesthetic doses, has also been examined. This approach for treating chronic neuropathic pain differs from continuous subcutaneous or IV infusion of anesthetics for the management of chronic pain conditions, such as terminal cancer pain, which are not discussed in this policy.

Courses of IV anesthetic agents may be given in the inpatient or outpatient setting as part of a pain management program, with the infusion of a subanesthetic dose preceded by a bolus infusion to achieve desired blood levels sooner. Lidocaine, which prevents neural depolarization through effects on voltage-dependent sodium channels, is also used systemically for the treatment of arrhythmias. Adverse effects for lidocaine are common, can be mild to moderate, and include general fatigue, somnolence, dizziness, headache, periorbital and extremity numbness and tingling, nausea, vomiting, tremors, and changes in blood pressure and pulse. Severe adverse effects may include arrhythmias, seizures, loss of consciousness, confusion, or even death. Lidocaine should only be given intravenously to patients with normal conduction on electrocardiography and normal serum electrolyte concentrations to minimize the risk of cardiac arrhythmias.

Ketamine is an antagonist of the NMDA receptor and a dissociative anesthetic. It is the sole anesthetic agent approved for diagnostic and surgical procedures that do not require skeletal muscle relaxation. Respiratory depression may occur with overdosage or too rapid a rate of administration of ketamine; it should be used by or under the direction of physicians experienced in administering general anesthetics. Ketamine is a schedule III controlled substance. Psychological manifestations vary in severity from pleasant dream-like states to hallucinations and delirium and can be accompanied by confusion, excitement, aggression, or irrational behavior. The occurrence of adverse effects with IV anesthetics may be reduced by the careful titration of subanesthetic doses. However, the potential benefits of pain control must be carefully weighed against the potential for serious, harmful adverse effects.

### **Regulatory Status**

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

Ketamine hydrochloride injection is FDA-indicated for diagnostic and surgical procedures that do not require skeletal muscle relaxation, for the induction of anesthesia prior to the administration of other general anesthetic agents, and to supplement low-potency agents, such as nitrous oxide. IV ketamine for the treatment of chronic pain is an off-label use.

### **Rationale**

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A review of the peer-reviewed literature on MEDLINE for the period of 1994 through February 2004, when this policy was created, revealed that the degree and duration of pain relief with intravenous (IV) lidocaine does not appear to be clinically significant in the majority of patients. (1-7) While some patients have reported diminished pain concurrent with IV administration of lidocaine that may continue beyond the infusion period for an extended duration, overall, responses to IV lidocaine in relief of allodynia, dysesthesia, and hyperalgesia have been mixed. These studies and a review of the evidence available in 2004 indicated a need for additional randomized, controlled, and double-blinded studies to determine the incremental effects of lidocaine over active placebo and compared to other standard

treatments for chronic pain, such as the use of antidepressants for fibromyalgia. It was concluded that a placebo response due to the significant adverse effects with IV lidocaine warrants the use of active placebos to increase the probability of determining the true analgesic effect of lidocaine in clinical trials. In addition, further studies were needed to determine appropriate patient selection criteria, predictive values, effective dosage ranges, frequencies, and duration of treatment. The literature has been periodically updated since 2004 using the MEDLINE database, and includes studies of IV ketamine for the treatment of chronic pain; the most recent update was performed for the period of June 2011 through June 2012. Key studies are described below.

## **Lidocaine**

### Spinal Cord Injury

In a double-blind, placebo-controlled, crossover study of 16 patients either post-stroke or spinal cord injury, Attal and colleagues reported IV lidocaine significantly reduced pain over placebo. (1) However, the duration of this significance lasted only 45 minutes. The 2006 literature review update identified a randomized, double-blind crossover trial of IV lidocaine in 24 patients with spinal cord injury neuropathic pain. (2) In this trial, spontaneous and evoked pain were significantly reduced on the visual analog scale (VAS), as measured before infusion and 25–35 minutes after the start of the infusion. Mostly mild adverse effects (experienced by 19 patients) and the 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 in this study, thus limiting interpretation of results. This also suggests the need for an active placebo in future trials, as noted. The authors concluded that intravenous lidocaine (and like agents) may be a treatment option for spinal cord injury pain. Although, the authors note, long-term treatment with lidocaine is usually not suitable.

### Complex Regional Pain Syndrome

Wallace et al. reported on a randomized, double-blind, placebo-controlled study of 16 patients with complex regional pain syndrome types I and II. (3) While IV lidocaine significantly reduced the pain response to cool stimuli, mechanical pain relief was not significantly improved.

### Fibromyalgia

In a randomized, double-blind, crossover study of 18 patients with fibromyalgia, Sorensen and colleagues found mixed responses with IV lidocaine with ketamine, morphine, or both, suggesting that pain-processing mechanisms must differ in fibromyalgia. (4) None of these patients responded to IV lidocaine alone. Vlavinich et al. reported a randomized double-blind trial of IV lidocaine plus amitriptyline versus amitriptyline monotherapy in 30 patients with fibromyalgia. (5) Infusion of lidocaine or saline was given once a week for 4 weeks. Pain intensity decreased in both groups over the course of treatment; but there was no significant difference between the treatment groups (VAS 4.1 for combined treatment vs. 4.0 for monotherapy).

### Other Neuropathic Pain

Tremont-Lukats and colleagues reported results of a randomized, double-blinded, placebo-controlled pilot trial in 32 subjects with ongoing neuropathic pain. (6) Infusion of 5 mg/kg/h, but not 1 or 3 mg/kg/h, over a period of 6 hours was observed to decrease pain by approximately 30%. This effect lasted for the next 4 hours of observation. Adverse effects were frequent; in 2 subjects, infusion was terminated early due to bothersome adverse effects. In a retrospective analysis, 104 patients with suspected neuropathic pain who had undergone diagnostic IV lidocaine were found from screening 635 sequential charts; of these, 5 patients had requested discontinuation mid-infusion, resulting in a cohort of 99 patients with baseline and post-treatment numerical pain ratings (score of 0-10). (7) Forty-two of the patients (42%) met the criteria of 30% or greater pain reduction; some of this subset was subsequently treated with mexiletine.

In a randomized, double-blind, placebo-controlled, crossover designed trial, Kvarnstrom and colleagues evaluated the effects of lidocaine in 12 patients with long-term peripheral neuropathic pain of traumatic origin. (8) The authors reported no significant differences in pain reduction over placebo on VAS. Wu et al. evaluated the effects of IV lidocaine on 31 patients with postamputation pain in a randomized,

double-blind, active placebo-controlled, crossover trial. (9) Wu and colleagues found stump pain was significantly reduced with IV lidocaine, yet phantom pain was not relieved, and the stump pain relief was short-lived. In a study of 24 patients with postherpetic neuralgia, Baranowski et al. reported IV lidocaine provided significant pain reduction over placebo (10); however, the pain was not eliminated. Medrik-Goldberg and colleagues evaluated 30 patients with sciatica in a randomized, double-blind, 3-arm crossover trial. (11) The authors 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.

A 2005 Cochrane review examined controlled clinical trials on lidocaine and its oral analogs (i.e., mexiletine, tocainide, and flecainide) for neuropathic pain treatment and found these drugs safely provided more pain relief than placebo and with similar effectiveness as other analgesics. (12) The Cochrane review noted that further investigation is needed to determine the clinical meaning of statistically significant pain relief and to test for less toxic analogs. 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. (13) Although adverse effects were reportedly 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, “the limitations of the contributing studies preclude drawing useful conclusions about the adverse effect profiles of these drugs.” (14) In addition, the authors noted that 1) lidocaine’s short serum half-life (120 min) precludes the use of this drug for chronic use, and 2) all of the 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 effects and the short duration of action, the health benefits of IV lidocaine remain unclear.

### **Ketamine**

A comprehensive systematic review of the treatment of chronic neuropathic pain with IV ketamine, published in 2003, assessed the quality of evidence for ketamine’s effectiveness in central pain, complex regional pain syndromes (CRPSs), fibromyalgia, ischemic pain, nonspecific pain of neuropathic origin, acute pain in patients with chronic neuropathic pain, orofacial pain, phantom/stump pain, and postherpetic neuralgia. (15) Some small randomized controlled trials (RCTs) were available for review, and meta-analysis was considered not appropriate. The report concluded that despite the use of ketamine for more than 30 years, there was insufficient evidence to advocate the routine use of this treatment for patients with chronic pain. Of particular concern were the significant adverse effects of this N-methyl-d-aspartate (NMDA) receptor antagonist in the central and peripheral nervous system. Few data were available concerning appropriate dosing and long-term administration.

### Spinal Cord Injury

In 2004, Kvarnstrom and colleagues assessed the effect of subanesthetic levels of IV ketamine or lidocaine on pain after spinal cord injury. (16) This randomized, double-blind, placebo-controlled crossover design 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. No significant pain reduction was observed following IV administration of lidocaine or saline. Adverse events were common with both treatments; ketamine produced 39 adverse effects in 9 of 10 subjects. These included somnolence, dizziness, out of body sensation, changes in hearing and vision, paresthesia, and other “unpleasant experiences.”

In 2010, Amr 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. (17) 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 infusion of isotonic saline over the same period. VAS scores for pain were similar in the 2 groups at baseline (VAS of 84 out of 100 for both groups). During the week of infusion, VAS scores decreased more in the ketamine-infused group than 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.

### Complex Regional Pain Syndrome (CRPS)

The largest double-blind RCT of ketamine for CRPS was a European report by Sigtermans et al. in 2009. (18) Sixty patients were randomly assigned 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 side effects. Two patients terminated the ketamine infusion early due to psychomimetic effects (e.g., delusions, hallucinations). At baseline, numerical pain scores were 7.2 (maximum of 10) for ketamine and 6.9 for the placebo group. The lowest pain scores (ketamine 2.7 and 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. Sixty percent of the patients in the placebo group correctly indicated treatment assignment (slightly better than chance); 93% of patients in the ketamine group correctly indicated treatment assignment due primarily to psychomimetic effects.

Multi-day courses of ketamine infusion in an inpatient setting have been reported for treatment of CRPS. A 2004 retrospective analysis described the effect of ketamine infusion in 33 patients with CRPS. (19) Inpatient infusion of a subanesthetic dose of ketamine over 2 to 20 days was found to provide relief for 9 months (median of 4 months). Twelve of the patients received a second infusion, with a reported mean relief duration of 25 months (median of 36 months). Dosing was titrated by the occurrence of adverse effects, which included a feeling of inebriation, dizziness, blurred vision, or nausea. Hallucinations occurred in 6 of the 33 patients.

In 2008, Kiefer et al. reported a multicenter (U.S. and Europe) prospective open-label Phase II study of anesthetic dosing of ketamine in 20 patients with refractory CRPS. (20) Symptoms were either long-standing (range: 6–68 months), spreading, or rapidly progressive, and refractory to conventional nonmedical (physical therapy, psychological approaches), or pharmacologic (mono- or combined therapy) and interventional treatments (at least 3) including selective nerve blocks, epidural analgesia, brachial plexus blocks, sympathetic ganglion blocks, intravenous regional sympathetic blocks, spinal cord stimulation, surgical sympathectomy, or intrathecal drug delivery systems. Following consent, patients were intubated and mechanically ventilated (except for the first 3 patients). Ketamine infusion was titrated up to a dose of 7 mg/kg/h with infusion over 5 days, then tapered downward until consciousness was attained. Midazolam was coadministered to a level of deep sedation to attenuate agitation and other adverse effects. All patients received IV low-dose heparin, the proton pump inhibitor pantoprazole, and clonidine to control cardiovascular and psychomimetic side effects of ketamine. Intubated patients received enteral nutrition with insulin as needed to maintain normoglycemia. Standard intensive care monitoring along with blood gas analysis, blood chemistry, and screening for infectious complications was performed regularly.

Outcomes were assessed at 1 week and 1, 3, and 6 months after treatment. Pain intensity decreased from a numerical rating scale of 9 at baseline to 0.5 at 1 week and remained low (2.0) at 6 months. Three patients relapsed but with lower pain (3.8) than at baseline. Pain relief was 94%, 89%, and 79% at 1, 3, and 6 months, respectively. Upper and lower extremity movement improved from 3.2 at baseline to 0.4 at 6 months for arm movement and from 2.3 at baseline to 0.6 at 6 months for walking. At 6 months, there was a significant difference in the ability to perform activities of daily living; 1 patient rated total impairment, 3 severe impairment, 6 moderate impairment, and 10 patients no impairment. Impairment in the ability to work was rated at baseline as complete by 11, severe by 5, and as moderate by 4 patients. At 6 months, 2 patients remained unable to work, 4 had moderate impairment, and 14 patients reported no impairment. Psychotropic adverse effects resolved in the first week in the

majority of patients, although 5 patients reported difficulties with sleeping and recurring nightmares for 1 month following treatment. Muscle weakness was reported in all patients for as long as 4–6 weeks following treatment. As indicated by the authors, a strong placebo response to this intensive intervention might be expected, and a large, multicenter RCT would be needed to definitively establish efficacy and safety. At this time, the beneficial effect of intravenous administration of ketamine is considered suggestive but not proven; additional trials are needed.

In 2011, Noppers et al. reported ketamine-induced hepatotoxicity in 3 of 6 patients during the second of 2 100-hour intravenous infusions. (21) The 3 patients developed elevated liver enzymes during the start of the second 100-hour infusion, which began 16 days after the first. One of the patients also developed an itching rash and fever. Infusions were terminated and the liver enzymes returned to reference values within 2 months. The study was stopped early due to the adverse events.

### Fibromyalgia

In 2011, Noppers et al. reported a randomized, double-blind, active placebo-controlled trial that was conducted in Europe using a 30-minute infusion of S(+)-ketamine (n=12) or midazolam (n=12). (22) 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 pain of greater than 50% compared to placebo (8 vs. 3). There was no significant difference between the groups at 180 minutes after infusion (6 vs. 3), at the end of week 1 (2 vs. 0) or end of week 8 (2 vs. 2, all respectively). There was no difference between groups on the fibromyalgia impact questionnaire 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 published in 2008 compared the efficacy of placebo, ketamine, calcitonin, and combined calcitonin and ketamine to relieve phantom limb pain (n=20, within subject design). (23) One-hour infusion of ketamine or ketamine plus calcitonin resulted in greater than 40% improvement in pain immediately after treatment. The mean and maximum pain scores remained significantly better than placebo for 48 hours after treatment.

A 2012 retrospective analysis from an academic medical center in the U.S. identified 49 patients with severe refractory pain who had undergone 369 outpatient ketamine infusions during a 5-year period. (24) 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 12-680 days (median of 233.7 days). The immediate reduction in VAS 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. A 2006 retrospective analysis described 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). (25) Low-dose ketamine (beginning at 0.12 mg/kg/h with slow upward titration) was delivered by a programmable pump through a peripherally inserted central catheter (PICC) line. With an average infusion duration of 16 days, pain severity decreased 38% (VAS of 7.7 to 4.8) with an 85% response rate. About half of the patients reported a perceived benefit 1 month after treatment. Adverse effects included fatigue, dizziness, confusion, and spinal pain. No patients reported hallucinations.

### **Summary**

Intractable pain presents a great challenge to patients and their healthcare providers. Recent evidence, primarily from outside of the U.S., suggests that IV courses of ketamine may provide at least temporary relief to some chronic pain patients. However, the intense treatment protocols, severity of side effects, and limited durability raises questions about the overall health benefit of this procedure. Additional clinical trials are needed to evaluate the long-term safety of repeat courses of IV anesthetics. Therefore, this treatment is considered investigational.

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### **Rationale for Pre-operative prevention of phantom limb pain**

In 1994, Jahangiri et. al. studied the effect of a preoperative epidural infusion of bupivacaine, clonidine and diamorphine in prevention of phantom limb pain among a group of 24 patients undergoing limb amputation (11 control, 13 study group). Results demonstrated that one-year following surgery, fewer patients in the treatment group had phantom pain than those in the control group who received standard therapy of on demand opioid analgesia ( $P < 0.002$ ).

In a randomized clinical trial of the effect of lumbar epidural blockade among 25 patients undergoing limb amputation, Bach et. al. found the incidence of phantom pain to be significantly reduced at 6 months, but not 1 year following surgery. In this study, the treatment group received epidural morphine, bupivacaine 0.25% or both in combination to achieve pre-operative pain control for three days and the control group received various analgesic drugs. Outcomes were assessed at 7 days, 6 months, and one year after surgery. All patients in the treatment group at 6 months were pain free while 5 patients (38%) had pain ( $p < 0.05$ ). While all the patients in the blockade group remained pain free at 1 year, this difference was not significant ( $p < 0.20$ ).

In a randomized-controlled double-blind trial conducted among 60 patients undergoing lower-limb amputation in 1997, Nikolajsen et. al. found no difference in treatment groups one year following surgery. Patients in the treatment group received epidural bupivacaine 0.25% and morphine 0.16 – 0.28 mg/hour for 18 hours before and during the procedure while those in the control group received epidural normal saline. Outcomes were assessed at 3, 6, and 12 months post surgery by independent examiners using a visual analog scale for phantom and stump pain. Three months post surgery, 82% in the treatment group and 50% in the control group experienced phantom pain. Among the 28 patients who completed a one-year follow-up examination, 75% in the treatment group and 69% in the control group experienced phantom pain.

Similarly, one year later, a randomized-controlled study to evaluate the effectiveness of preoperative extradural bupivacaine and morphine on post-operative stump sensation among a group of 31 lower limb amputees found no difference between groups at 1 week or 6 months following surgery. Patients in the treatment group had a catheter placed one day prior to surgery followed by a bolus of 2 mg. of extradural morphine, 5-10 ml. of bupivacaine 0.25%, an infusion of bupivacaine 0.25% at 4-7 ml./hour and morphine at 0.16-0.28 mg./hour infusion rate prior to surgery. Those in the control group had an extradural catheter placed and were given a bolus of normal saline followed by an infusion of saline over the next 24 hours. Additionally, the control group received oral or intra-muscular pain medications. Outcomes were assessed using a visual analog scale. After one week, the percentage of patients with phantom pain was 57.1% in the treatment group and 58.8% in the control group. After six months, more patients in the treatment group experienced phantom pain (78%) than those in the control group (58%).

Randomized clinical trials to study the effectiveness of new treatment modalities are few and difficult to compare due to the differences in treatments. Among three randomized clinical trials, only one

demonstrated a significant benefit of preoperative anesthesia. The limitations among these studies include an inadequate sample size to detect a difference between treatment groups combined with a high drop out rate. The randomized clinical trial that demonstrated a treatment difference suffered from the absence of a true placebo group, i.e. an epidural injection, and that lack of a standardized questionnaire for the assessment of phantom limb pain.

Epidural preoperative treatment of pain to reduce the incidence of phantom pain following amputation remains promising. Phantom limb pain is a debilitating condition that can lead to a decline in daily activities and overall health and well being. More is needed to investigate the causal pathway of phantom pain among amputees that may lead to new and effective treatments.

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#### **Billing Coding/Physician Documentation Information**

|              |   |
|--------------|---|
| <b>J2001</b> | Injection, lidocaine HCl for intravenous infusion, 10 mg  |
| <b>62318</b> | Injection, including catheter placement, continuous infusion or intermittent bolus, not including neurolytic substances, with or without contrast (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic, antispasmodic, opioid, steroid, other solution), epidural or subarachnoid; cervical or thoracic    |
| <b>62319</b> | Injection, including catheter placement, continuous infusion or intermittent bolus, not including neurolytic substances, with or without contrast (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic, antispasmodic, opioid, steroid, other solution), epidural or subarachnoid; lumbar, sacral (caudal) |
| <b>64999</b> | Unlisted procedure, nervous system  |
| <b>96365</b> | Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour   |
| <b>96366</b> | Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)  |
| <b>96374</b> | Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); intravenous push, single or initial substance/drug  |

#### **Additional Policy Key Words**

N/A

#### **Policy Implementation/Update Information**

|        |  |
|--------|--|
| 4/1/09 | New policy; considered investigational. Combined with previous policy that addressed only the prevention of phantom limb pain. |
| 4/1/10 | Policy title changed – “Management” replaced with “Treatment”, “Neuropathic” added.  |
| 4/1/11 | No policy statement changes.   |
| 4/1/12 | “Neuropathic” removed from title; fibromyalgia added to policy statement.  |
| 4/1/13 | No policy statement changes  |
| 4/1/14 | Reviewed – no changes made   |

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