

Topical Lidocaine Criteria for Use in Peripheral Neuropathic Pain January, 2016

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information. For further information, see the VA National PBM-MAP-VPE supporting literature review for these criteria at www.pbm.va.gov or <http://vawww.pbm.va.gov>.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive topical lidocaine:*

- Indication is trigeminal or glossopharyngeal neuralgia, atypical facial pain, central neuropathy (post-stroke, multiple sclerosis, or spinal cord injury related), HIV-related neuropathy, or fibromyalgia
- Planned area of application includes non-intact skin
- Sensitivity to amide-type local anesthetics or any other component of the product.
- Concomitant use of oral Class I antiarrhythmic drugs (e.g., mexiletine)

Inclusion Criterion *The following criterion must be fulfilled for provision of topical lidocaine:*

- Indication is localized postherpetic neuralgia (PHN) **OR** other localized peripheral neuropathy with an inadequate response despite appropriate trials, intolerance, contraindication or risk factor for potentially serious adverse effects to **two** of the following agents from different drug classes (see definitions in *Issues for Consideration*):
- **Tricyclic antidepressant** (amitriptyline, desipramine, or nortriptyline)
 - **Gabapentinoid** (gabapentin or pregabalin)
 - **Serotonin-norepinephrine reuptake inhibitor** (venlafaxine or duloxetine)

Dosage and Administration

- Lidocaine 5% patch should be applied to intact skin to cover the most painful area once daily for up to 12 hours (12 hours on, 12 hours off). Patches measure 10 cm x 14 cm, each containing 700mg lidocaine; patches should be cut in half (before removing the release liner) when intended area of application is $\leq 35\text{cm}^2$. Maximum daily area of application is 3 patches (30cm x 42 cm, containing 2100mg lidocaine).
- Dosing and application of lidocaine cream or ointment formulations is empirical (see *Issues for Consideration*).

Efficacy Monitoring and Renewal Criteria

- Topical lidocaine prescription renewals require documentation of benefit and tolerability approximately 2 weeks after initiation of treatment and every 3 months thereafter. Discontinue topical lidocaine in patients who have no beneficial response within 2 weeks of initiation, spontaneous resolution of PHN or other peripheral neuropathic pain, or apparent loss of benefit in the course of long term use.

Safety

- Systemic uptake of lidocaine is low ($3 \pm 2\%$, or $21 \pm 14\text{mg/patch}$) when patches are applied as recommended; lidocaine C_{MAX} achieved with patch application is $\sim 0.13 \text{ mcg/mL}$ (about 1/10 of the concentration required to treat cardiac arrhythmias and approximately 2.5% of that associated with toxicity).
- Lidocaine toxicity resulting from transcutaneous absorption is theoretically possible. Signs and symptoms of systemic lidocaine toxicity include CNS excitation and/or depression, nervousness, confusion, dizziness, tinnitus, blurred or double vision, vomiting, twitching, tremors, seizures, unconsciousness, respiratory depression, bradycardia, hypotension, and cardiopulmonary arrest. If there is suspicion of lidocaine-related systemic toxicity, check lidocaine blood concentrations.
- Dose adjustments are not required in patients with mild or moderate hepatic impairment; however, topical lidocaine should be used with caution in patients with severe hepatic dysfunction due to the possibility of impaired clearance.
- The most frequently reported adverse events in clinical studies of lidocaine 5% patch were mainly mild to moderate application site skin reactions, including erythema, pruritus, rash, burning, dermatitis, and edema. Skin reactions are typically transient and resolve spontaneously after removal of the patch.
- Serious adverse effects may occur if a used or unused lidocaine patch is chewed or ingested (used patches contain up to 665mg lidocaine); patches should be stored and disposed of in a manner where they will be inaccessible to children and pets.

Issues for Consideration

1. **Localized peripheral neuropathies** include: diabetic and non-diabetic painful neuropathy, post-amputation pain, post-traumatic or post-surgical neuropathic pain, radicular pain from the neck or back and neuropathic cancer-related pain/radiculopathy.
2. **Inadequate response despite appropriate trials** is defined as inability to achieve acceptable pain management after at least 6 weeks of continuous therapy at the following minimum daily dosages: amitriptyline 75mg, desipramine 70mg, nortriptyline 70mg, gabapentin 1800mg (600mg in renal impairment), pregabalin 300mg, duloxetine 60mg, venlafaxine 150mg. Sodium valproate \geq 500mg daily and topical capsaicin 0.0075% QID are additional therapeutic options for painful diabetic neuropathy and should be considered prior to a trial of lidocaine patch.
3. **Risk factors for potentially serious adverse events (SAE)** may be identified by review of the Warnings and Precautions contained in the FDA-approved labeling for each agent in the 3 drug categories. In this circumstance, risk factors for SAE are typically encountered with greater frequency in elderly patients (>65 years of age), patients on multiple CNS-active medications, patients with h/o previous fall(s), and patients with cardiac arrhythmia, heart failure, renal impairment or cerebrovascular disease.
4. **Guideline summaries:**

Postherpetic neuropathy:
American Academy of Neurology (AAN 2004): **1st line:** Gabapentinoids, tricyclic antidepressants (TCAs); lidocaine patch, opioids; **2nd line:** topical capsaicin

European Federation of Neurological Societies (EFNS 2010): **1st line:** Gabapentinoids, TCAs, lidocaine patch; **2nd/3rd line:** topical capsaicin, opioids

Canadian Pain Society (2014): **1st line:** Gabapentinoids, TCAs, serotonin-norepinephrine reuptake inhibitors (SNRIs); **2nd line:** lidocaine patch, tramadol, opioids

Painful Diabetic Neuropathy (PDN):
American Academy of Neurology (AAN 2011): **Level A:** pregabalin; **Level B:** gabapentin, sodium valproate, amitriptyline, SNRIs, topical capsaicin, opioids; **Level C:** lidocaine patch

EFNS (2010): **1st line:** Gabapentinoids, TCAs, SNRIs; **2nd line:** tramadol with/without acetaminophen, opioids; **3rd line:** cannabinoids; **4th line:** lidocaine patch + others

Mixed Peripheral Neuropathies:
Canadian Pain Society (2014): **1st line:** Gabapentinoids, TCAs, SNRIs; **2nd/3rd line:** tramadol, opioids

International Association for the Study of Pain (IASP 2015): **1st line:** Gabapentinoids, TCAs, SNRIs; **2nd line:** capsaicin 8% patch, lidocaine patch (can be considered 1st line in elderly), tramadol; **3rd line:** botulinum toxin A, opioids
5. A Cochran review determined that there were 3 positive single dose trials that utilized lidocaine 8% spray or 5% gel in patients with PHN or post-traumatic peripheral neuropathy, and reported additional results from a fourth trial where lidocaine 5% cream (in a specialized PLO vehicle) had been applied twice daily for 1 week in 30 patients who had PHN, PDN, or post-traumatic neuropathy. Due to the relative absence of data, none of the non-patch lidocaine alternatives received consideration as therapeutic options in consensus recommendations for treatment of peripheral neuropathic pain.
6. Despite the lack of controlled studies, there is widespread utilization of non-patch topical lidocaine formulations in pain management and some of this use has resulted in anecdotal reports of benefit. When such use occurs it is a reasonable expectation that there be observation of the same exclusionary, inclusionary, monitoring and discontinuation criteria as recommended for lidocaine 5% patch. Lidocaine cream/ointment is most commonly dosed two to three times daily per review of VA prescription database.

7. There have been no comparative trials of lidocaine cream or ointment formulations with lidocaine 5% patch; for this reason, these non-patch topical formulations of lidocaine should not be considered therapeutically equivalent to the patch. In addition, it is unknown whether an individual's response (or lack of response) to one topical lidocaine formulation is predictive of response (or lack of response) to another formulation.
8. It is recommended that the use of Schedule II–IV opioids for peripheral neuropathies be avoided or minimized due to the potential risks of harm to the patient and the public.

Prepared: January, 2016 Contact: Michael Chaffman, PharmD, National Clinical Pharmacy Program Manager, VA Pharmacy Benefits Management Services

References:

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5. Bril V, England J, Granklin GM, et al. Evidence-based Guideline: Treatment of Painful Diabetic Neuropathy: Report of the American Academy of Neurology, the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation. *Neurology* 2011; 76: 1758-65.
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