Lidocaine Topical Patch 5%
Literature Review Addendum
October 2015
VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The purpose of VA PBM Services drug monographs is to provide a comprehensive drug review for making formulary decisions. Updates will be made when new clinical data warrant additional formulary discussion. Documents will be placed in the Archive section when the information is deemed to be no longer current.

FDA Approval Information [1,2]	
Description / Mechanism of Action	Each patch is comprised of an adhesive material containing lidocaine 5% applied to a non-woven polyester felt backing and covered with a polyethylene terephthalate (PET) film release liner. The release liner is removed prior to application to the skin. Lidocaine applied topically is believed to act as a local analgesic by selective partial inhibition of voltage-regulated sodium channels of damaged or dysfunctional unmyelinated C fibers and small myelinated Aδ fibers. This action stabilizes the neuronal membrane potential on these fibers resulting in a reduction of ectopic discharges. Lidocaine topical patch 5% has been shown to reduce the painful surface area and positively affect allodynia and hyperalgesia, but does not cause local anesthesia.
Indication(s) Under Review in this Document	FDA-approved Indication(s): Lidocaine topical patch 5% is indicated for relief of pain associated with postherpetic neuralgia (PHN).
Dosing and Administration	Refer to the Prescribing Information for complete and up-to-date dosing and administration information. Lidocaine topical patch 5% should only be applied to intact skin. The most painful area should be covered with up to 3 patches only once for up to 12 hours within a 24 hour period (12 hours on, 12 hours off). Patches may be cut to smaller sizes prior to removal of the PET film release liner; cutting does not affect absorption of the drug.
Dosage Form(s) Under Review	Topical patches measuring 10 cm x 14 cm, each containing 700 mg lidocaine (5%)
REMS	☐ REMS ☒ No REMS *See Other Considerations for additional REMS Information.*
Pregnancy Rating	Category B *See Special Populations for additional information*

Executive Summary	
Efficacy	• Lidocaine 5% patches have been shown to be effective in the treatment of postherpetic neuropathic (PHN) pain in placebo- and active-controlled comparisons. Lidocaine patches appear less effective in the treatment of non-PHN peripheral neuropathies. • Evidence-based consensus recommendations for PHN and non-PHN peripheral neuropathies are consistent with these findings.
Safety	• Systemic adverse reactions following appropriate use of lidocaine patch 5% are unlikely due to the small amount of drug absorbed • The most frequently reported adverse events in clinical studies were mainly mild to moderate application site skin reactions; skin reactions are typically transient and resolve spontaneously after removal of the patch.
Other Considerations	• Clinically relevant pharmacokinetic or pharmacodynamic interactions between lidocaine 5% patches and other medications are unlikely.
Potential Impact	• **Projected Place in Therapy:** Evidence-based consensus guidelines indicate that lidocaine topical patch 5% can be considered a first or second line therapeutic option for management of PHN. Lidocaine patch has several characteristics which may make it an optimal choice in PHN, particularly in the elderly: no need for dose titration, appropriate in patients with renal or hepatic impairment, rapid onset of analgesic effect, and no systemic adverse effects. There is a lesser role for lidocaine 5% patch in the treatment of non-PHN peripheral neuropathies.

Background [3, 4]

Purposes for review

Lidocaine topical patch 5% (Lidoderm) was approved by the FDA in March, 1999; a generic equivalent was approved in August, 2012.

A 56-page VA PBM-MAP-VPE document titled "Lidocaine Patch 5% Literature Review" was published to the PBM intranet and internet pages in October, 2011. **The purposes of this literature review addendum** are to (1) update and evaluate the available evidence of safety, tolerability, efficacy, cost, and other pharmaceutical issues that would be relevant to considering lidocaine topical patch 5% for addition to the VA National Formulary; (2) define its role in therapy; and (3) identify parameters for its rational use in the VA.

Also to be determined: Does lidocaine topical patch 5% have clinical advantages over existing alternatives? What safety issues need to be considered?

Other therapeutic options [5- 9]

Formulary Alternatives	Other Considerations
Gabapentin	1st line
Duloxetine	1st line
Venlafaxine ER	1st line; duloxetine is preferred SNRI
Tricyclic antidepressants (Amitriptylene, Desipramine Nortriptyline)	1st line; not recommended at doses >75mg/day in adults > 65 years due to anticholinergic and sedative effects, risk of falls, and sudden cardiac death (at doses >100mg/day)
Tramadol	2nd line
Opioid analgesics	3rd line; long term use associated with abuse, cognitive impairment, endocrine and immunological changes

Nonformulary Alternatives	Other Considerations
Gabapentin extended release or enacarbil	1st line
Pregabalin	1st line
Capsaicin 8% patches	2nd line; long term safety not clearly established
Botulinium toxin A	3rd line; specialist use only

Primary source for table: Finnerup et al. (2015), which makes treatment recommendations for mixed peripheral neuropathies and lists lidocaine patch as a 2nd line agent.

AAN 2004 Treatment Categories for postherpetic neuralgia give lidocaine patch a Level A recommendation (strong evidence to support). EFNS 2010 Guidelines (Attal et al., 2010) list lidocaine patch as having level A evidence in postherpetic neuropathic pain. Canadian Pain Society (2014)) guidelines (Moulin et al., 2014) lists lidocaine patch as 2nd line for postherpetic neuralgia and 4th line for other neuropathic pain syndromes.AAN 2011 Treatment Guidelines for painful diabetic neuropathy (Bril et al., 2011) list lidocaine patch as having weak evidence/level C recommendation for that indication.

Efficacy

Literature Search Summary

For this addendum, a literature search was performed on PubMed/Medline (2011 to October 2015) using multiple search terms and combinations of terms including lidocaine patch, lidocaine 5%, and lidocaine plaster – each alone and in combination with 'postherpetic neuralgia' or 'neuropathic pain'. The search was limited to studies performed in adult humans and published in the English language. Reference lists of review articles were searched for relevant clinical trials.

Review of Efficacy [3, 4, 6- 8, 10, 11]

FDA-approved indication - Postherpetic Neuralgia

Literature review

Initial FDA approval of lidocaine 5% patches for the treatment of postherpetic neuralgia (PHN) was based upon two RCT performed by Rowbotham et al.; these trials are described in the VA PBM-MAP-VPE document "Lidocaine Patch 5% Literature Review, October 2011" (pages 27-30, and elsewhere).[4] There have been additional placebo- or active-controlled and open efficacy trials of lidocaine patches in the treatment of PHN since FDA approval; however, all but one were previously described in the 2011 PBM-MAP-VPE Literature Review.

Sabatowski et al. (2012) reported 4 year efficacy and safety outcomes from a phase III open-label study of patients given lidocaine 5% patches for postherpetic neuralgia [a 2 year follow up, Hans et al. (2009), was included in the 2011 PBM-MAP-VPE Literature Review].[10] For initial enrollment, patients were required to have neuropathic pain persisting for ≥ 3 months after healing of a herpes zoster rash and a baseline pain intensity of ≥ 4 on an 11-point numerical rating scale. Patients could apply up to three 5% lidocaine patches on the painful skin area for up to 12 hours per day, with a patch-free interval of at least 12 hours per day. Efficacy measures included patients' recall of pain relief (6-point verbal rating scale), clinical global impression of change (CGIC), patients' global impression of change (PGIC), and the global evaluations of study medication. Safety parameters were assessed at regular visits. Of 102 patients who continued participation in a study extension (following the first year), 85 and 27 patients remained after 3 and 4 years, respectively. Throughout the study, on average, patients applied 1.8 ± 0.6 (SD) patches per day, resulting in an average pain relief of at least 4.3 units. At all visits the CGIC and the PGIC were much/very much improved in about 80% of patients. At the final visit, study medication was rated at least to be good by 91% of physicians and 89% of patients. Drug-related adverse events were reported in 19 of 102 patients, mainly mild to moderate localized skin reactions. Among the 102 patients, lack of efficacy and adverse events respectively accounted for 9.8 and 8.8% of drug discontinuation.

A 2014 Cochran review included studies of lidocaine 5% patches in postherpetic neuralgia (see discussion in *Potential Off-Label Use*). Practice guideline recommendations for lidocaine patch in postherpetic neuralgia are listed in Table 1.

Table 1: Practice guideline recommendations – Postherpetic neuralgia place in therapy

	1st line	2nd line	3rd line	4th line
American Academy of Neurology (AAN 2004)[6]	Gabapentinoids[a] Tricyclic antidepressants[b] ***Lidocaine patch*** Opioids[c]	Topical aspirin Topical capsaicin	-	-
European Federation of Neurological Societies (EFNS 2010)[7]	Gabapentinoids[a] Tricyclic antidepressants[b] ***Lidocaine patch***	Topical capsaicin Opioids[d]		-
Canadian Pain Society (2014)[8]	Gabapentinoids[a] Tricyclic antidepressants[b] SNRIs[e]	Tramadol Opioids[f] ***Lidocaine patch***	Cannabinoids	SSRIs[g] Lamotrigine Lacosamide Topiramate Valproic acid Methadone

[a]Gabapentinoids = gabapentin or pregabalin; [b]tricyclic antidepressants = amitriptyline, nortriptyline, desipramine, and maprotiline; [c]opioids = controlled-release oxycodone or morphine; [d]opioids = oxycodone, morphine, methadone; [e]SNRIs = duloxetine and venlafaxine; [f]opioids = controlled-release oxycodone or morphine, or fentanyl patch or hydromorphone; [g] SSRIs = citalopram, escitalopram, paroxetine

EFNS Guidelines combine 2nd and 3rd line categories.

Potential Off-Label Uses [4, 5, 7-9, 11-24]

This section is not intended to promote any off-label uses. Off-label use should be evidence-based. See VA PBM-MAP and Center for Medication Safety's Guidance on "Off-label" Prescribing (available on the VA PBM intranet site only).

See the VA PBM-MAP-VPE document titled "Lidocaine Patch 5% Literature Review, October 2011"; since that review, additional positive and negative study and case report series results have been published regarding the efficacy of lidocaine topical patch 5% in the treatment of the following off-label indications *(underlining denotes study was of randomized, double-blind, placebo-controlled design):*

Positive results: Neuropathic cancer pain accompanied by allodynia (resulting from painful scar or chest wall tumor) [12], rib fractures [13], neuropathic pain related to cancer (resulting from tumor, surgery, other oncology treatment, or mixed syndromes) or unrelated to cancer [14], post-operative port site wound pain after laparoscopic gynecologic surgery [15], myofascial pain syndrome of the upper trapezius [16], localized neuropathic pain after disc herniation [17], chronic trigeminal neuropathic pain (various causes) [18], localized neuropathic pain secondary to traumatic peripheral nerve injury [19].

Negative results: Post-operative pain after total knee arthroplasty [20], acute pain after robotic cardiac surgery/prevention of persistent incisional pain [21], persistent inguinal postherniorrhaphy pain [22], chronic back pain [23], persistent cancer-related postsurgical incisional pain[24].

A 2104 Cochrane Review assessed the analgesic efficacy of topical lidocaine for chronic neuropathic pain syndromes.[11] Twelve studies (508 participants) were included where topical lidocaine had been compared with placebo or an active control. Half of the studies enrolled participants with moderate or severe postherpetic neuralgia, while the remaining studies enrolled different or mixed neuropathic pain conditions, including trigeminal neuralgia and postsurgical or post-traumatic neuralgia. Five of the 12 studies used a topical lidocaine formulation other than a 5% patch (5% gel or cream, 8% spray). Four studies were single-dose evaluations. Pooling of data for assessment was not possible. While all but one study concluded that topical lidocaine was beneficial, the reviewers cautioned that evidence was of very low quality due to the small size/short duration of the trials and the potential for major bias.

Table 2: Practice guideline recommendations – Painful diabetic neuropathy and mixed neuropathies

	Level of evidence[a]			
	Level A	**Level B**	**Level C**	**Level U**
American Academy of Neurology (AAN 2011)[9] **Painful diabetic neuropathy**	Pregabalin	Gabapentin Sodium valproate Amitriptyline SNRIs Topical capsaicin Opioids[b] Isosorbide dinitrate spray	***Lidocaine patch***	Topiramate Desipramine Imipramine Fluoxetine Nortriptyline + Fluphenazine Vitamins α-lipoic acid
	1st line	**2nd line**	**3rd line**	**4th line**
European Federation of Neurological Societies (EFNS 2010)[7] **Painful diabetic neuropathy**	Gabapentinoids SNRIs Tricyclic antidepressants	Oxycodone Tramadol Tramadol/acetaminophen		-
Canadian Pain Society (2014)[8] **Mixed neuropathies[c]**	Gabapentinoids Tricyclic antidepressants SNRIs	Tramadol Opioids[d]	Cannabinoids	SSRIs Lamotrigine Lacosamide Topiramate Valproic acid Methadone ***Lidocaine patch***[f] Botulinium toxin A[f]
International Association for the Study of Pain (IASP 2015)[5] **Mixed neuropathies[e]**	Gabapentinoids Tricyclic antidepressants SNRIs	Capsaicin 8% patch[f] ***Lidocaine patch***[f] Tramadol	Botulinium toxin A[f] Strong opioids (morphine and oxycodone)	

[a] ***AAN (2011):*** *Level A evidence = strong, level B = moderate, level C = weak, level U = insufficient.*
[b] *Opioids = dextromethorphan, morphine, tramadol, oxycodone.*
[c] ***Canadian Pain Society*** *guidelines mixed neuropathies included: painful diabetic neuropathy, post-surgical and chemotherapy-induced neuropathies, and central neuropathies (post-stroke, multiple sclerosis, spinal cord injury related).*
[d] *Opioids = controlled-release oxycodone or morphine, or fentanyl patch or hydromorphone*
[e] ***IASP*** *guidelines mixed neuropathies included: postherpetic neuralgia, diabetic and non-diabetic painful polyneuropathy, post-amputation pain, post-traumatic or post-surgical neuropathic pain, neuropathic cancer-related pain, and central neuropathies.*
[f] *Recommendations apply to peripheral neuropathic pain syndromes only*

- The Canadian Pain Society 2014 Guidelines considered 87 systematic reviews/meta-analyses and 21 consensus staements/guidelines published since that organization's previous review in 2007.[8] All neuropathic pain syndromes were considered with the exceptions of some cancer-related neuropathic pain syndromes and trigeminal or glossopharyngeal neuralgias. Consensus recommendations were based upon quality of evidence of analgesic efficacy [decided by number needed to treat (NNT) or effect size], grading of tolerability and ease of use (the latter two based solely on consensus opinion of the authors). *First line* recommendations required high-quality evidence of efficacy (at least one class I study or two consistent class II studies – level of recommendation grade B or better), positive results in at least 2 neuropathic pain models, and the drug had to be considered straightforward to use and of sufficient tolerability to prescribe and monitor. *Second or third line* recommendations were made when there was high-quality evidence of efficacy, but the medication required more specialized follow-up and monitoring. *Fourth-line* recommendations had to have at least one positive RCT but also a requirement for additional study. A second line recommendation was given to lidocaine 5% patch for PHN; a fourth line recommendation was given for non-PHN peripheral neuropathies.

- The International Association for Study of Pain (IASP) 2015 reviewers performed a systematic review and meta-analysis of randomized, double-blind studies of both oral and topical therapies for neuropathic pain.[5] The review included 196 trials published in peer-reviewed journals since 1966 and 33 unpublished trials sourced from www.ClinicalTrials.gov or pharmaceutical manufacturer's websites.The primary measure was NNT for 50% pain relief; methodological quality and publication bias were also assessed. The GRADE approach was used to judge quality of evidence and strength of recommendations. Studies included various neuropathic pain syndomes: postherpetic neuropathy, diabetic and non-diabetic painful neuropathy, post-amputation pain, post-traumatic or post-surgical neuropathic pain, central post-stroke, SCI- and MS-associated pain, and neuropathic CA-related pain. Studies of trigeminal neuralgia were excluded. Of the 229 reports reviewed, NNT for 50% pain relief could be calculated in 176. NNT for 1st and 2nd line therapies ranged from 3.6 to 10.6; NNT could not be calculated for lidocaine 5% patch. The authors concluded that the quality of evidence for lidocaine 5% patch was low for peripheral neuropathies but a weak second line recommendation was given due to the drug's favorable tolerability and safety profile.

Safety [1]

(For more detailed information refer to the Prescribing Information.)

Boxed Warning	• None
Contraindications	• Lidocaine topical patch 5% is contraindicated in patients with a known history of sensitivity to local anesthetics of the amide type or to any other component of the product
Warnings/Precautions (*also see Boxed Warnings*)	• Serious adverse effects may occur if a child or pet were to chew or ingest a used or unused lidocaine patch. Lidocaine patches should be stored and disposed of in a safe manner, inaccessible to children and pets. • Excessive dosing by applying lidocaine patches to larger areas or for longer than the recommended wearing time could result in increased absorption of lidocame and high blood concentrations, leading to serious systemic adverse effects. • Patients with severe hepatic disease have a greater risk of developing toxic blood concentrations of lidocaine • While patients allergic to para-aminobenzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine. Lidocaine patches should be used with caution in patients with a history of drug sensitivities, especially if the etiologic agent is uncertain • Application of patches to broken or inflamed skin may result in higher blood concentrations of lidocaine from increased absorption; lidocaine patches are only recommended for application to intact skin. • Lidocaine patch contact with eyes, should be avoided due to the possibility of severe eye irritation; if eye contact occurs, immediately wash out the eye with water or saline and protect the eye until sensation returns.

Safety Considerations [1, 3, 4, 10]

See the VA PBM-MAP-VPE document titled "Lidocaine Patch 5% Literature Review, October 2011" (pages 5-6 and associated tables) in addition to the following information.

Lidocaine patch 5% is generally well tolerated; the very low systemic exposure after application results in a minimal risk of either systemic adverse events or pharmacokinetic interactions with concomitant medications (see *Drug Interactions*).

Adverse Events[1, 3, 10]

Common Adverse Events	The most frequently reported adverse events in clinical studies 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.

Deaths/Serious Adverse Reactions	Systemic adverse reactions following appropriate use of lidocaine patch 5% are unlikely, due to the small dose absorbed (see *Other Considerations*). Allergic and anaphylactoid reactions associated with topical lidocaine are rare but have occurred.[3] Systemic effects of lidocaine are similar to those observed with other amide local anesthetic agents, including CNS excitation and/or depression (light-headedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred or double vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest). Cardiovascular manifestations may include bradycardia, hypotension and cardiovascular collapse leading to arrest.
Discontinuations Due to Adverse Events	Early placebo-controlled studies of patients given lidocaine 5% patches to treat postherpetic neuralgia revealed very low treatment discontinuation rates due to adverse events. In a long term open label follow up of patients given lidocaine 5% patches for postherpetic neuralgia; of 102 patients, only 9 (9.8%) discontinued treatment due to adverse events during years 2 through 4.[10]

Drug Interactions [1]

As systemic absorption is only approximately 3%, clinically relevant pharmacokinetic or pharmacodynamic interactions with other medications are unlikely.

Antiarrhythmic Drugs: Lidocaine patches should be used with caution in patients receiving Class 1 antiarrhythmic drugs (such as tocainide and mexiletine) since the toxic effects are additive and potentially synergistic.

Local Anesthetics: When lidocaine patches are used concomitantly with other products containing local anesthetic agents, the amount absorbed from all formulations must be considered.

Risk Evaluation

As of October 16, 2015

Sentinel event advisories

- None
- Sources: ISMP, FDA, TJC

Look-alike / sound-alike error potential

NME Drug Name	Lexi-Comp	First DataBank	ISMP	Clinical Judgment
Lidocaine 5% patch	None	None	None	Lidocaine-tetracaine patch Topical lidocaine - various strengths/forms Lodine Lindane
Lidoderm	None	None	None	Lubriderm

- Sources: Based on clinical judgment and an evaluation of LASA information from three data sources (Lexi-Comp, First Databank, and ISMP Confused Drug Name List)

Other Considerations[1]

Lidocaine Patch Absorption: The amount of lidocaine systemically absorbed from the patch is directly related to area and duration of application. Only 3 ± 2% of the applied lidocaine enters systemic circulation when patches are applied according to label instructions; i.e. a minimum of 665mg (95%) will remain in a used patch. Although the absorption of lidocaine from the skin is generally low, patches must be used with caution in patients receiving Class I antiarrhythmic drugs (e.g., tocainide, mexiletine) and other local anesthetics, because the risk of additive systemic effects cannot be excluded.

Mean peak blood concentration of lidocaine achieved with patch application is about 0.13 pg/mL (about 1/10 of the therapeutic concentration required to treat cardiac arrhythmias and well below the toxic range for lidocaine); repeat application of three patches simultaneously for 12 hours was not observed to result in drug accumulation.

Special Populations [1-4]

Elderly ≥ 65 years	• The incidence of postherpetic neuralgia (PHN) increases with age and the majority of patients in efficacy trials of lidocaine 5% patches for PHN were elderly; thus, study efficacy and safety results generally apply to elderly patients. • Lidocaine absorption through intact skin appears to decrease as age increases; this would reduce the amount of lidocaine reaching systemic circulation.
Pregnancy	• Lidocaine topical patch 5% is Pregnancy Category B • There are no adequate and well-controlled studies in pregnant women.
Lactation	• Lidocaine topical patch 5% has not been studied in nursing mothers. • Lidocaine is excreted in human milk; caution should be exercised when lidocaine patches are administered to a nursing woman.
Renal Impairment	• Lidocaine topical patches 5% may be used without dose adjustments in patients with mild or moderate renal impairment. Caution is recommended in patients with severe renal dysfunction.
Hepatic Impairment	• Dose adjustments are not required for lidocaine patches with mild to moderate hepatic impairment; caution is recommended in patients with severe hepatic dysfunction as these patients have a greater risk of developing toxic blood concentrations of lidocaine
Pharmacogenetics/genomics	• There are no data identified in the FDA approved labeling or at this site: http://www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm (accessed October 16, 2015).

Place in Therapy [1, 2, 4-8]

- Herpes zoster (HZ) is a common, painful and debilitating condition caused by a reactivation of the varicella-zoster virus (VZV) from a latent infection of sensory ganglia; its incidence is 3-5 cases per 100 person-years but there is a steep increase in incidence > 50 years of age due to an age-related decline in VZV-specific cell immunity.
- Postherpetic neuralgia (PHN) is the most common complication of HZ; it may be defined as pain that persists for ≥ 90 days following onset of a HZ rash. The incidence of PHN increases rapidly in individuals after the age of 60 years and, among patients with HZ who are ≥ 50 years old, as many as 10-20% will develop PHN.
- The pain of PHN is highly intense, often disproportionate to the initial injury, and characterized by a high chronicity (approximately 50% of patients developing PHN are moderately symptomatic 1 year after onset).
- Treatment options for PHN remain limited and the disease can have devastating effects on patients' quality of life. Physical and psychological health can be affected as well as ability to continue normal daily and social activities.
- Lidocaine topical patch 5% was FDA-approved in 1999 as treatment for PHN; evidence-based consensus guidelines indicate it can be considered a first or second line therapeutic option for management of that condition. In addition, it has been used as an 'add-on' medication with other effective therapies.
- Lidocaine patch has several characteristics which may make it an optimal choice in PHN, particularly in the elderly:
  - no need for dose titration
  - appropriate in patients with renal or hepatic impairment, even if severe
  - rapid onset of analgesic effect
  - no systemic adverse effects (i.e.sedation or anticholinergic effects)
- Lidocaine 5% patch may be effective for non-PHN peripheral neuropathies; however, the literature concerning use in these off-label conditions is not consistently favorable. Consensus recommendations for lidocaine use in non-PHN neuropathies are not as strong as those for PHN.

References

1. Lidocaine Patch 5% [package insert]. Watson Laboratories, Inc., Salt lake City, UT 84108; December, 2013.
2. Navez ML, Monella C, Bösl et al. 5% Lidocaine Medicated Plaster for the Treatment of Postherpetic Neuralgia: A Review of the Clinical Safety and Tolerability. Pain Ther 2015: 4: 1-15.
3. Department of Health and Human Services, Lidocaine 5% Derma Delivery System (patch) Lidoderm™, NDA 20-612, Medical Officer Review, December 1, 1998, accessed October 18, 2015 at http://www.accessdata.fda.gov/drugsatfda_docs/nda/99/20612.cfm
4. Lidocaine Patch 5% Literature Review, VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives, October 2011. Accessed October 18, 2015 at https://vaww.cmopnational.va.gov/cmop/PBM/default.aspx
5. Finnerup NB, Attal N, Haroutounian S et al. Pharmacotherapy for Neuropathic Pain in Adults: A Systematic Review and Meta-Analysis. Lancet Neurol 2015; 162-73, published online, January 7, 2015 at http://dx.doi.org/10.1016/S1474-4422(14)70251-0
6. Dubinsky RM, Kabbani H, El-Chami Z et al. Practice Parameter: treatment of Postherpetic Neuralgia. An Evidence-Based Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2004: 63: 959-65.

7. Attal N, Cruccu G, Baron R et al. EFNS Guidelines on the Pharmacological Treatment of Neuropathic Pain: 2010 Revision. Eur J Neuro 2010; 17: 1113-23.
8. Moulin DE, Boulanger A, Clark AJ et al. Consensus Statement: Pharmacological Management of Chronic Neuropathic Pain: Revised Consensus Statement from the Canadian Pain Society. Pain Res Manag 2014; 18: 328-35.
9. 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.
10. Sabatowski R, Hans G, Tacken I, et al. Safety and Efficacy Outcomes of Long-Term Treatment up to 4 Years with 5% Lidocaine Medicated Plaster in Patients with Post-Herpetic Neuralgia. Curr Med Res Opin 2012; 28: 1337-46.
11. Derry S, Wiffen PJ, Moore RA et al. Topical Lidocaine for Neuropathic Pain in Adults (Review). Cochrane Database of Systemic Reviews 2014: 7: 1-41.
12. Garzón-Rodríguez C, Merchan MC, Calsina-Berna A et al. Lidocaine 5% Patches as an Effective Short-Term Co-Analgesic in Cancer Pain. Preliminary Results. Support care Cancer 2013; 21: 3153-8.
13. Zink KA, Mayberry J, Peck E et al. Lidocaine Patches Reduce Pain in Trauma Patients with Rib Fractures. Am Surg 2011; 77: 438-42.
14. Ramírez EL. Treatment of Acute and Chronic Focal Neuropathic Pain in Cancer Patients with Lidocaine 5% Patches; A Radiation and Oncology Department Experience. Support Care Cancer 2013; 21: 1329-34.
15. Kwon Y-S, Kim JB, Jung HJ et al. Treatment for Postoperative Wound Pain in Gynecologic Laparoscopic Surgery: Topical Lidocaine Patches. J Laparoendosc Adv Surg Tech 2012; 22: 668-73.
16. Lin Y-C, Kuan T-S, Hsieh P-C et al. Therapeutic Effects of Lidocaine Patch on Myofascial Pain Syndrome of the Upper Trapezius: A Randomized, Double-Blind, Placebo-Controlled Study. Am J Phys Med Rehab 2012; 91: 871-82.
17. Likar R, Kager I, Obmann M et al. Treatment of Localized Neuropathic Pain After Disk Herniation with 5% Lidocaine Medicated Plaster. Int J Gen Med 2012; 5: 689-92.
18. Khawaja N, Yilmaz Z, Renton T. Case Studies Illustrating the Management of Trigeminal Neuropathic Pain Using Topical 5% Lidocaine Plasters. Brit J Pain 2013; 7: 107-13.
19. Correa-Illanes G, Roa R, Piñeros JL et al. Use of 5% Lidocaine Medicated Plaster to Treat Localized Neuropathic Pain Secondary to Traumatic Injury of Peripheral Nerves. Local Reg Anesth 2012; 5: 47-53.
20. Khanna M, Peters C, Singh JR. Treating Pain With the Lidocaine Patch 5% After Total Knee Arthroplasty. PM&R 2012; 4: 642-6.
21. Vrooman B, Kapural L, Sarwar S, et al. Lidocaine 5% Patch for Treatment of Acute Pain After Robotic Cardiac Surgery and Prevention of Persistent Incisional Pain: A Randomized, Placebo-Controlled, Double-Blind Trial. Pain Med 2015; 16: 1610-21.
22. Bischoff JM, Petersen M, Üçeyler N et al. Lidocaine Patch (5%) in Treatment of Persistent Inguinal Postherniorrhaphy Pain: A Randomized, Double-Blind, Placebo-Controlled, Crossover Trial. Anesthesiology 2013; 119: 1444-52.
23. Hashmi JA, Baliki MN, Huang L et al. Lidocaine Patch (5%) Is No More Potent Than Placebo in Treating Chronic Back Pain When Tested in a Randomized Double Blind Placebo Controlled Brain Imaging Study. Molecular Pain 2012; 8: 29-38.
24. Cheville AL, Sloan JA, Northfelt DW et al. Use of a Lidocaine Patch in the Management of Postsurgical Neuropathic Pain in Patients with Cancer: A Phase III Double-Blind Crossover Study (N01CB). Support Care Cancer 2009; 17: 451-60.
25. Johnson RW, Bouhassira D, Kassianos G et al. The Impact of Herpes Zoster and Post-Herpetic Neuralgia on Quality-of-Life. BMC Med 2010; 8: 37-50.

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