PALLIATIVE PEARLS
BY ENCLARA PHARMACIA

Comparing Rx and OTC Lidocaine Patches
April 2022

This month, we compare prescription (Rx) and over-the-counter (OTC) lidocaine patches in response to the frequently asked question, "*Do OTC lidocaine patches require the same "off time" as Rx Lidoderm® 5% patches?"*

LOCALIZED PAIN

Acute and chronic pain are significant sources of suffering in advanced illness. Adverse effects from systemic analgesics (e.g., via oral or parenteral routes) contribute to and often exacerbate suffering and limit dose titration, thus hindering effectiveness. Topical analgesics, like lidocaine, offer a solution to limit systemic adverse effects and should be considered whenever pain is localized, and the severity allows for achievable pain relief with topical application.[1]

Acute ailments include strains, sprains, tendonitis, acute back pain, and muscle aches. Chronic conditions however are more common in the hospice and palliative population and may respond to local lidocaine application. These include arthralgia (e.g., osteoarthritis, rheumatoid arthritis), low back pain, and neuropathic pain (e.g., diabetic neuropathy, localized peripheral neuropathic pain, post-herpetic neuralgia).[2-4]

Lidocaine is available in creams, ointments, gels, lotions, and patches.[4]

PRESCRIPTION (RX) TRANSDERMAL PATCHES (E.G., LIDODERM® 5%, ZTLIDO® 1.8%)

The transdermal route is defined as "administration through the dermal layer of the skin to the systemic circulation by diffusion".[5] Although many literature sources and drug information databases categorize prescription lidocaine patches as transdermal, they are technically FDA-approved as topical, [6-7] delivering medication to the outer surface of the body. Perhaps the truth lies somewhere in between. Dose and application limitations in the product prescribing information exist to prevent systemic lidocaine toxicity, however Lidoderm systemic absorption when used according to package instructions is low and several pharmacokinetic studies have shown that systemic lidocaine levels remain safe, even with extended dosing (18-24 hours) and up to 4 patches per application. [8-10]

Lidoderm 5% and ZTlido 1.8% patches are FDA approved for postherpetic neuralgia, however, are used off-label for general topical anesthesia of skin.[4] These products have a drug-in-adhesive (DIA) system with two layers, a backing layer (furthest from the skin) and the drug-in-adhesive layer. A release liner covers the DIA layer and is removed before application.[11] Prescribing instructions include:

- Apply patch to most painful area. Up to 3 patches may be applied in a single application. Patch(es) may remain in place for up to 12 hours in any 24-hour period, leaving a patch-free period of at least 12 hours.[4,12]
- Patches may be cut into smaller sizes with scissors prior to removal of the release liner.[13]

A single 5% Lidoderm patch contains 700 mg lidocaine. When used according to the recommended dosing instructions, approximately 3 % of the dose applied is expected to be absorbed. At least 95% (665 mg) of lidocaine will remain in a used patch.[13] In comparison, a single 1.8% ZTlido patch contains 36 mg lidocaine yet provides equivalent lidocaine absorption.[14] ZTlido is designed with a more efficient delivery of lidocaine with less residual left in the patch after normal use[15] – it is also promoted as having improved adhesion to skin compared to Lidoderm.[16]

OVER-THE-COUNTER (OTC) TOPICAL PATCHES (E.G., LIDOCARE® 4%, ASPERCREME® 4%)

OTC products are not regulated by the FDA and usually have not been subject to the same clinical trials required for prescription products. As such, they lack individual pharmacokinetic and efficacy data as well as comparative trial data with prescription products. The FDA revisited the underlying regulations that allow external analgesics to be marketed over the counter without a new drug application (NDA) approval in 2003, and formally designated topical patches as Category III (safety and efficacy unknown).[11,17]

Nevertheless, OTC products are used widely by patients, and may be recommended by clinicians for less severe symptoms as a less costly and easier to access alternative. Instructions for use vary, making it important to refer to the manufacturer's labeling for product-specific recommendations. General guidance includes: [12,16]

- Apply 1 patch to painful area
- Frequency varies from 1 to 4 times daily in a 24-hour period
- Duration of application varies from 8 to 24 hours
- Absence of guidance on necessity of leaving a patch-free period

Recognize that several OTC lidocaine patches contain additional ingredients, like menthol, camphor, and methyl salicylate, which may limit patient tolerance and application frequency. Be mindful of the manufacturer's labeling and monitor for safety (e.g., application site irritation/lesions) and pain relief.

TAKE AWAY POINTS

- Efficacy and safety data exists for the Rx patches only
- Scarcity of literature comparing Rx and OTC patches
- OTC patches are usually less costly
- OTC patches are more accessible to patients potentially making them useful alternatives for mild symptoms
- Rx and OTC patches have different dosing frequencies, application durations, and patch-free requirements[16]

REFERENCES:

1. Portenoy RK, Krotova E, Lussier D. Chapter 45: Adjuvant analgesic drugs. In: Textbook of palliative medicine and supportive care. Boca Raton: Taylor & Francis Group, LLC; 2015.
2. Derry S, Wiffen PJ, Kalso EA, et al. Topical analgesics for acute and chronic pain in adults - an overview of Cochrane Reviews. *Cochrane Database Syst Rev*. 2017 May; 2017(5): CD008609.
3. Rosenquist EWK. Overview of the treatment of chronic non-cancer pain. In: UpToDate, Aronson ME, Crowley M, eds. UpToDate, Watham, MA. Updated February 5, 2019. Accessed 2019 Aug.
4. Clinical Pharmacology [database online]. Tampa, FL: Elsevier/Gold Standard, Inc.; 2022. Accessed 2022 April.
5. Food & Drug Administration (FDA). Routes of administration. 11/14/2017. Site link
6. Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. Lidoderm 5% NDA. Site link
7. Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations. ZTLido 1.8% NDA. Site link
8. Rosielle DA. Palliative Care Network of Wisconsin (PCNOW) Fast Facts #148: The Lidocaine Patch. 2015. Article link
9. Gammaitoni AR, Davis MW. Pharmacokinetics and tolerability of lidocaine patch 5% with extended dosing. *Ann Pharm*. 2002; 36:236-240.
10. Gammaitoni AR, Alvarez NA, Galer BS. Safety and tolerability of the lidocaine patch 5%, a targeted peripheral analgesic: A review of the literature. *J Clin Pharmacol*. 2003;43:111-117.
11. Nalamachu S, Gudin J. Characteristics of Analgesic Patch Formulations. *Journal of Pain Research.* 2020:13. Article link
12. Lexicomp [database online]. 2022. Accessed 2022 April.
13. Lidoderm (lidocaine patch 5%). Malvern, PA: Endo Pharmaceuticals Inc.; 2014. Resource link
14. ZTLido (lidocaine topical system 1.8%). Palo Alto, CA: Scilex Pharmaceuticals Inc.; 2021. Resource link
15. Hoffman M. ZTlido Lowers Doses While Raising Efficacy. *MD Magazine Neurology.* March 2018;8(2). Article link
16. Clinical Resource, Characteristics of Transdermal Patches. Pharmacist's Letter/Prescriber's Letter. August 2021.
17. Food & Drug Administration. Marketed Unapproved Drugs – Compliance Policy Guide. Sec. 440.100 Marketed New Drugs Without Approved NDAs or ANDAs. September 19, 2011. Article link