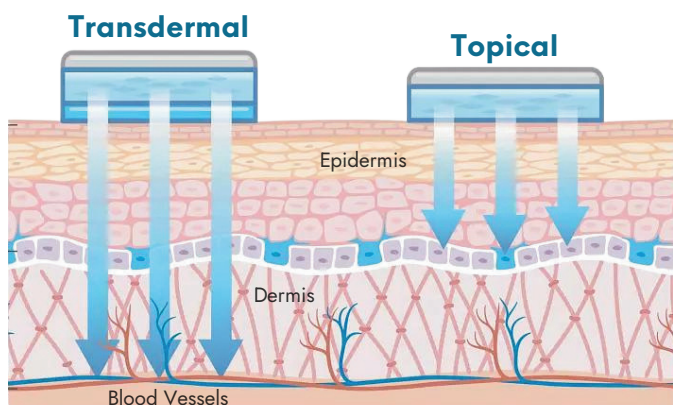


Transdermal vs. Topical

While both Topical and Transdermal patch systems are applied directly to the skin, only Transdermal route applications are able to penetrate deep into tissues and exert their effects beyond the epidermis.¹ Transdermal formulations are designed to deliver active and inactive ingredients through the dermal layer and into systemic circulation, targeting pain beyond the local application site. This unique, adhesive-matrix design allows for an extended time release dose of medication² - an important feature when treating pain.

Advantages

- + Deeper Penetrating than Topical Patches
- + Controlled & Constant Dose Administration
- + Improved Therapeutic Drug Bioavailability³
- + Contains 35% Less Water Composition Than Topicals for Advanced Drug Absorption



Transdermal Delivery System

Next-generation patch technology for superior medication route administration



Extended Time Release

Steady release of ingredients for a long, continuous dose of medication



Durable Hydrogel Adhesive

Reusable patch (up to 2x) that is able to withstand water exposure and long-wear



DSCSA Compliant

Transaction Reporting, and Unit & Case Tracing with 2D GTIN Serialized Barcodes

Common Uses

- ✓ Chronic Pain
- ✓ Acute Pain
- ✓ Work Injuries
- ✓ Neuropathic Pain
- ✓ Musculoskeletal Pain
- ✓ Osteoarthritic Pain

1. Leppert W, Malec-Milewska M, Zajaczkowska R, Wordliczek J. Transdermal and Topical Drug Administration in the Treatment of Pain. *Molecules*. 2018;23(3):681. Published 2018 Mar 17. doi:10.3390/molecules23030681
2. Gupta H, Babu RJ. Transdermal delivery: product and patent update. *Recent Pat Drug Deliv Formul*. 2013;7(3):184-205. doi:10.2174/187221130703131128121747
3. Jeong WY, Kwon M, Choi HE, Kim KS. Recent advances in transdermal drug delivery systems: a review. *Biomater Res*. 2021;25(1):24. Published 2021 Jul 28. doi:10.1186/s40824-021-00226-6

NDC 83295-4000-01 (30-Day Supply)

NDC 83295-4000-04 (4-Day Supply)

Apply 1 patch per day for up to 12 hours at a time (12 on, 12 off)

Medicated transdermal patch can be worn up to twice per day.

Active Ingredients: Lidocaine 4.75%
Capsaicin 0.025%

Inactive Ingredients: Magnesium, Arnica, Vegan Glycerol, Polyacrylate, and Water.

Rx Trubrexal Transdermal Extended-Time Release Patch contains Lidocaine 4.75%, Capsaicin 0.025%, Magnesium, and Arnica. This combination of ingredients is recommended for the treatment of acute pain, chronic pain, musculoskeletal pain, neuropathic pain, osteoarthritis pain, fibromyalgia pain, and more. Rx Trubrexal Transdermal Extended-Time Release Patch was designed and formulated using **ODG, MTUS, and ACOEM Evidence-Based Treatment Guidelines** to improve return-to-work outcomes and help patients recover from injury.

Lidocaine 4.75%

Lidocaine transdermal patch is recommended as first-line or second-line treatment option for patients with postherpetic neuralgia. – *ODG*

Lidocaine is a local anesthetic that blocks the initiation and conduction of neuronal impulses, including impulses responsible for the perception of pain. (1) (2) (EG 2). – *ODG*

For postherpetic neuralgia, a systematic review and network meta-analysis evaluating the efficacy of topical treatments for postherpetic neuralgia included 3 randomized trials comparing lidocaine with placebo and found that lidocaine was associated with improved pain control compared with placebo. (3) (EG 1). – *ODG*

For postherpetic neuralgia, a systematic review and network meta-analysis evaluating the efficacy of treatment for postherpetic neuralgia included 3 studies comparing transdermal lidocaine with either placebo or pregabalin and found that lidocaine was associated with a longer time to discontinuation due to loss of pain relief. – *ODG*

Capsaicin 0.025%

Capsaicin activates the transient receptor potential vanilloid 1 receptor on nociceptive nerve fibers in the skin. With continued application, the density and sensitivity of nerve fibers decreases, resulting in analgesia. – *ODG*

Capsaicin is recommended as a treatment option for neuropathic pain and osteoarthritis pain. For neuropathic pain, a systematic review of studies evaluated the efficacy of low-concentration capsaicin for the treatment of chronic neuropathic pain found that more patients treated with capsaicin experienced pain relief compared to patients treated with placebo. For osteoarthritis pain, a systematic review and network meta-analysis evaluating topical medications for the management of osteoarthritis pain found that topical capsaicin was associated with a greater effect size compared to placebo. – *ODG*

Capsaicin patches are recommended for improved pain control with neuropathic pain that includes superficial pain generation (e.g., postherpetic neuralgia), peripheral nerve injury, and possibly some toxic neuropathies with superficial pain generation. [1175, 1176] – *ACOEM*

Magnesium – Inactive Ingredient

Magnesium has been used for the treatment of fibromyalgia. – *ACOEM*

Transdermal magnesium applied on upper and lower limbs may be beneficial to patients with fibromyalgia. – <https://www.sciencedirect.com/science/article/abs/pii/S2095496415601959>

Magnesium plays an important role in the prevention of central sensitization and in the attenuation of established pain hypersensitivity, and its main mode of action appears to involve its voltage-gated antagonist action at N-methyl-D-aspartate (NMDA) receptors. Given the putative function of the NMDA receptor in pain transduction, magnesium has been investigated in various clinical conditions associated with acute or chronic pain. The parenteral administration of magnesium may reduce pain, and anesthetic and analgesic requirements during post-operative periods. The beneficial effects of magnesium treatment have also been demonstrated in patients suffering from neuropathic pain, such as in those with malignancy-related neurologic symptoms, postherpetic neuralgia, diabetic neuropathy, and chemotherapy-induced peripheral neuropathy. Numerous clinical studies have found that magnesium has beneficial effects in patients suffering from neuropathic pain, dysmenorrhea, tension headache, acute migraine attack, and others. These effects are considered to be due to blockage of the NMDA receptor, attenuation of central sensitization, and muscle relaxing effects. The postoperative analgesic adjuvant role of magnesium and its use as an analgesic therapy for the treatment of acute or chronic pain have been suggested for decades. Its antinociceptive effect has been suggested to be due to the blocking of NMDA receptors, and thus, the prevention of central sensitization. – *Na HS, Ryu JH, Do SH. The role of magnesium in pain. In: Vink R, Nechifor M, editors. Magnesium in the Central Nervous System [Internet]. Adelaide (AU): University of Adelaide Press; 2011. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK507245/>*

The research interest in NMDA receptors has led to an examination of the interactions between NMDA receptors and the induction and maintenance of central sensitization after nociceptive stimuli ([Woolf and Thompson, 1991](#)). Ketamine and magnesium are representative NMDA receptor antagonists, and in particular, magnesium can regulate calcium access into cells by antagonizing the NMDA receptor ([Paoletti and Neyton, 2007](#)), which has encouraged investigations on the use of magnesium as an analgesic adjuvant. Recent studies have proposed a role for NMDA receptor antagonists in the management of postoperative pain and in other acute and chronic pain conditions. Central sensitization is the result of the enhancement of neuronal properties in nociceptive pathways of the central nervous system, and is triggered by repetitive nociceptive afferent inputs, which manifests as a prolonged reduction in the pain threshold. Central sensitization produces pain hypersensitivity, such as wind-up or long-term potentiation of pain, that is, it causes pain even when peripheral stimuli are not intense and continues to cause pain after the initiating stimuli have disappeared ([Latremoliere and Woolf, 2009](#); [Woolf, 1983](#); [Woolf and Salter, 2000](#)).

Many authors have investigated the adjuvant role of magnesium in the context of intra- and post-operative analgesia. Magnesium has been shown to be effective for treating intra- and post-operative pain and for blunting autonomic, somatic, and endocrine reflexes to noxious stimuli ([Kara et al., 2002](#); [Koinig et al., 1998](#); [Levaux et al., 2003](#)).