**CAPSAICIN 8% TOPICAL PATCH**

<table>
<thead>
<tr>
<th>THERAPEUTICS</th>
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<tr>
<td><strong>Brands</strong></td>
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<tr>
<td>Qutenza</td>
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<td><strong>Generic?</strong></td>
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<tr>
<td>Numerous over-the-counter topical products that contain low concentrations (up to 0.15% w/w)</td>
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<td><strong>Class</strong></td>
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<td>Transient receptor potential vanilloid (TRPV)-1 channel agonist</td>
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<td><strong>Commonly Prescribed For</strong> (FDA approved in bold)</td>
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<tr>
<td>Postherpetic neuralgia (PHN)</td>
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<td>Peripheral neuropathic pain, excluding painful diabetic neuropathy (in EU)</td>
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**How the Drug Works**

Capsaicin, 8-methyl-N-vanillyl-6-nonenamide, is an active ingredient in chili peppers that provokes a typical hot burning sensation. Capsaicin is insoluble in water but freely soluble in ethanol, ether, benzene, and chloroform. Capsaicin has a long history of use in pain treatment. The first detailed description of the effects of topical capsaicin on the sensory nervous system was published in 1949. Capsaicin is a highly selective agonist for TRPV1, a ligand-gated, nonselective cation channel preferentially expressed on small-diameter sensory neurons, especially on the nociceptors. TRPV1 is a heat-activated calcium channel that normally opens at approximately 43 °C, but with capsaicin bound, the threshold decreases below 37 °C or even to skin temperature.

The exposure of small-diameter neurons to short exposures of high doses of capsaicin result in a fast “desensitization” or “defunctionalization” of the pain fibers. Capsaicin-induced defunctionalization of cutaneous nociceptors is mediated by an increase in intracellular calcium, followed by mitochondrial dysfunction and peripheral nerve terminals death. The functionality of the peripheral endings, as measured by the ability to detect painful sensations, returns a few months after treatment. A recent study evaluated the effects of a single 60-minute application of Qutenza on the density of epidermal nerve fibers (ENFs) in healthy volunteers. After 1 week, there was an 80% reduction of ENF density compared with unexposed sites. However, at 12 weeks after exposure to capsaicin, ENF regeneration was evident, but not complete, and at week 24, nearly complete ENF recovery was observed.

**How Long until It Works**

- Up to 3 months

**If It Works**

- Treatment may be repeated in cycles

**If It Doesn’t Work**

- Alternative topical or oral therapies for neuropathic pain

**Best Augmenting Combos for Partial Response or Treatment Resistance**

- For PHN and other peripheral neuropathic pain conditions, topical and oral treatments include Lidoderm 5% patch, gabapentin, pregabalin, duloxetine, tricyclic antidepressants, and opioids

**Tests**

- None

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<tr>
<th>ADVERSE EFFECTS (AEs)</th>
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<td><strong>How Drug Causes AEs</strong></td>
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<td>When capsaicin binds to the receptor, the TRPV1 calcium channel opens and calcium enters the intracellular space of the nerve resulting in action potential generation leading to a burning sensation, hyperalgesia, allodynia, and erythema. The erythema results primarily from the release of the vasoactive neuropeptides, substance P and CGRP, from the sensory axons. In addition, there may be stimulation of mast cell degranulation with release of histamine. This phenomenon is known as neurogenic inflammation</td>
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**Notable AEs**

- The safety and tolerability of Qutenza in patients with PHN has been demonstrated in over 1400 subjects enrolled in clinical trials. The main adverse event associated with Qutenza is the pain with application

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<th>Life-Threatening or Dangerous AEs</th>
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<tbody>
<tr>
<td>None</td>
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<tr>
<td>If inhaled, capsaicin can cause cough and/or bronchoconstriction</td>
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51
Weight Gain
- No

Sedation
- No

What to Do about AEs
- Rescue pain medication use (e.g. short-acting opioid) and application of ice-packs

Best Augmenting Agents for AEs
- Preapplication of a topical local anesthetic

DOSING AND USE

Usual Dosage Range
- The recommended dose of the capsaicin 8% patch is a single, 60-minute application of up to 4 patches

Dosage Forms
- The Qutenza (capsaicin) 8% patch (640 μg/cm²) is a single-use patch stored in a sealed pouch

How to Dose
- The recommended dose of the capsaicin 8% patch is a single, 60-minute application of up to 4 patches
- Treatment with the capsaicin 8% patch may be repeated every 3 months or as warranted by the return of pain

Dosing Tips
- The capsaicin 8% patch may not be effective for neuropathic pain states in which the presumed “pain generators” are thought to be within or anatomically very close to the CNS, for example in the case of PHN complicated by spinal cord or nerve roots lesions

Overdose
- No

Long-Term Use
- Yes, by repeating the application every 3 months

Habit Forming
- No

How to Stop
- No relevant concerns

Pharmacokinetics
Capsaicin is poorly metabolized by human skin. Pharmacokinetic data in humans showed transient, low (<5 ng/mL) systemic exposure to capsaicin in about one-third of PHN patients following 60-minute applications of Qutenza. The highest plasma concentration of capsaicin detected was 4.6 ng/mL and occurred immediately after Qutenza removal. No detectable levels of metabolites were observed in any subject. There was a definite trend toward nondetectable levels 3–6 hours after patch removal. Data from in vitro cytochrome P450 inhibition and induction studies show that capsaicin does not inhibit or induce liver cytochrome P450 enzymes at concentrations which far exceed those measured in blood samples. Therefore, interactions with other drugs are unlikely

Drug Interactions
- None

Other Warnings/Precautions
- If inhaled, capsaicin can cause cough and/or bronchoconstriction
- Capsaicin may aggravate cough due to angiotensin-converting enzyme (ACE) inhibitor drugs according to studies using rats and humans
- Only physicians or healthcare professionals under the close supervision of a physician are to administer Qutenza (capsaicin 8% patch)
- Use only nitrile gloves when handling Qutenza, and when cleaning capsaicin residue from the skin. Do not use latex gloves as they do not provide adequate protection
- Immediately after use, dispose of used and unused cleansing gel and other treatment materials in accordance with the local biomedical waste procedures
- Use Qutenza (capsaicin 8% patch) only on dry, intact (unbroken) skin
- Apply the Qutenza (capsaicin 8% patch) within 2 hours of opening the pouch

Do Not Use
There are conflicting data from animal and in vitro models of wound healing, with some preclinical
data on corneal wounds in adult rabbits and in vitro observations on the effects of capsaicin on keratinocytes and fibroblasts suggesting that capsaicin may impair wound healing while other data suggest possible improvement. More research is needed to study the safety of capsaicin on the human skin-healing process. Until then, Qutenza should not be applied on any blisters, wounds, or skin lesions from a burn injury.

SPECIAL POPULATIONS

Renal Impairment
- No known effects

Hepatic Impairment
- No known effects

Cardiac Impairment
- Patients with unstable or poorly controlled hypertension, a recent history of cardiovascular or cerebrovascular events may be at an increased risk of adverse cardiovascular effects. Consider these factors prior to initiating Qutenza (capsaicin 8% patch) treatment

Elderly
- No known effects

Children and Adolescents
- The safety and effectiveness of the capsaicin 8% patch in patients younger than 18 years of age have not been studied

Pregnancy
- Category B. There are no adequate and well-controlled studies evaluating Qutenza (capsaicin 8% patch) in pregnant women

Breast-Feeding
- There are no adequate and well-controlled studies in nursing women. Studies in rats have demonstrated that capsaicin is excreted into breast milk of this species. It is unknown whether capsaicin is excreted in human breast milk

THE ART OF PAIN PHARMACOLOGY

Potential Advantages
- Used safely along with other pain medications
- Well tolerated and has minimal systemic AEs

Potential Disadvantages
- Qutenza requires skilled medical personnel to handle the application and the initial pain increase that patients experience during the procedure and immediately after. However, clinical trials have demonstrated that use of short-acting oral opioids, pretreatment with local anesthetics and cooling of the site following patch removal are usually sufficient in managing the temporary increase in pain
- Qutenza can be of problematic use when very large skin areas are affected, or when, in the treatment of peripheral neuropathic pain in nondiabetic adults (as per European label), multiple patches are required to cover bilateral distal limbs, including hands or feet, since only up to 4 patches have been recommended per application
- There is no experience with Qutenza when applied to the face. Therefore, at present, its application is not recommended for trigeminal PHN, due to the proximity of eyes, as well as oral and nasal mucosa proximity to the patch

Primary Target Symptoms
- Neuropathic pain

Pearls
- The mechanisms underlying capsaicin-induced defunctionalization are concentration-dependent. Higher doses of capsaicin can produce faster and more prolonged defunctionalization of pain fibers, this being the rationale behind the use of Qutenza, the high-concentration 8% capsaicin patch, which when applied over 1 hour can achieve up to 3 months of pain relief
- Qutenza has probably the highest potential for patient compliance with treatment when compared with all the other FDA-approved products for PHN. It requires a single-application treatment over 1 hour to generate several months’ duration of pain relief. This reduces the risk of noncompliance, which is often encountered with oral agents
- The lidocaine 5% patch is the only other topical product with an FDA-approved indication for PHN. The lidocaine patch has an excellent safety profile. Nevertheless, the lidocaine patch has to be applied on a daily basis to the affected skin in order to provide sustained benefit
Suggested Reading


