LIDOCAINE PATCH 5%

DESCRIPTION
LIDOCAINE PATCH 5% is comprised of an adhesive material containing 5% lidocaine, which is 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. The size of the patch is 10 cm x 14 cm.

Lidocaine is chemically designated as acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl), has an octanol:water partition ratio of 43 at pH 7.4, and has the following structure:

Each adhesive patch contains 700 mg of lidocaine (50 mg per gram adhesive) in an aqueous base. It also contains the following inactive ingredients: dihydroxyaluminum aminoacetate, disodium edetate, gelatin, glycerin, kaolin, methylparaben, polyacrylic acid, propyl alcohol, propylene glycol, propylparaben, sodium carboxymethylcellulose, sodium polycarbophylate, D-sorbitol, tartaric acid, and urea.

CLINICAL PHARMACOLOGY
Pharmacodynamics
Lidocaine is an amide-type local anesthetic agent and is suggested to stabilize neuronal membranes by inhibiting the ionic fluxes required for the initiation and conduction of impulses. The penetration of lidocaine into intact skin after application of LIDOCAINE PATCH 5% is sufficient to produce an analgesic effect, but less than the amount necessary to produce a complete sensory block.

Pharmacokinetics
Absorption
The amount of lidocaine systemically absorbed from LIDOCAINE PATCH 5% is directly related to both the duration of application and the surface area over which it is applied. In a pharmacokinetic study, three LIDOCAINE PATCH 5% patches were applied over an area of 420 cm² of intact skin on the back of normal volunteers for 12 hours. Blood samples were withdrawn for determination of lidocaine concentration during the application and for 12 hours after removal of patches. The results are summarized in Table 1.

Table 1
Absorption of lidocaine from LIDOCAINE PATCH 5%

<table>
<thead>
<tr>
<th>LIDOCAINE PATCH 5% Patch</th>
<th>Application Site</th>
<th>Area (cm²)</th>
<th>Dose Absorbed (mg)</th>
<th>C_max (µg/mL)</th>
<th>T_max (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 patches (3/100 mg)</td>
<td>Back</td>
<td>420</td>
<td>64 ± 32</td>
<td>0.13 ± 0.06</td>
<td>11 hr</td>
</tr>
</tbody>
</table>

When LIDOCAINE PATCH 5% is used according to the recommended dosing instructions, only 3% ± 2% of the dose applied is expected to be absorbed. At least 95% (665 mg) of lidocaine will remain in a used patch. Mean peak blood concentration of lidocaine is about 0.13 µg/mL (about 1/10 of the therapeutic concentration required to treat cardiac arrhythmias). Repeated application of three patches simultaneously for 12 hours (recommended maximum daily dose), once per day for three days, indicated that the lidocaine concentration does not increase with daily use. The mean plasma pharmacokinetic profile for the 15 healthy volunteers is shown in Figure 1.

Figure 1
Mean lidocaine blood concentrations after three consecutive daily applications of three LIDOCAINE PATCH 5% patches simultaneously for 12 hours per day in healthy volunteers (n = 15).

Pharmacokinetics
Distribution
When lidocaine is administered intravenously to healthy volunteers, the volume of distribution is 0.7 to 2.7 L/kg (mean 1.5 ± 0.6 SD, n = 15). At concentrations produced by application of LIDOCAINE PATCH 5%, lidocaine is approximately 70% bound to plasma proteins, primarily alpha-1-acid glycoprotein. At much higher plasma concentrations (1 to 4 µg/mL of free base), the plasma protein binding of lidocaine is concentration dependent. Lidocaine crosses the placental and blood brain barriers, presumably by passive diffusion.

Metabolism
It is not known if lidocaine is metabolized in the skin. Lidocaine is metabolized rapidly by the liver to a number of metabolites, including monoethyloxycarbonyl (MEGX) and glycinexylyde (GX), both of which have pharmacologic activity similar to, but less potent than that of lidocaine. A minor metabolite, 2,6-xylidine, has unknown pharmacologic activity but is carcinogenic in rats. The blood concentration of this metabolite is negligible following application of LIDOCAINE PATCH 5%. Following intravenous administration, MEGX and GX concentrations in serum range from 11 to 36% and from 5 to 11% of lidocaine concentrations, respectively.

Excretion
Lidocaine and its metabolites are excreted by the kidneys. Less than 10% of lidocaine is excreted unchanged. The half-life of lidocaine elimination from the plasma following IV administration is 81 to 149 minutes (mean 107 ± 22 SD, n = 15). The systemic clearance is 0.33 to 0.90 L/min (mean 0.64 ± 0.18 SD, n = 15).

CLINICAL STUDIES
Single-dose treatment with LIDOCAINE PATCH 5% was compared to treatment with vehicle patch (without lidocaine), and to no treatment (observation only) in a double-blind, crossover clinical trial with 35 post-herpetic neuralgia patients. Pain intensity and pain relief scores were evaluated periodically for 12 hours. LIDOCAINE PATCH 5% performed statistically better than vehicle patch in terms of pain intensity from 4 to 12 hours. Multiple-dose, two-week treatment with LIDOCAINE PATCH 5% was compared to vehicle patch (without lidocaine) in a double-blind, crossover clinical trial of withdrawal-type design conducted in 32 patients, who were considered as responders to the open-label use of LIDOCAINE PATCH 5% prior to the study. The constant type of pain was evaluated but not the pain induced by sensory stimuli (dysesthesia). Statistically significant differences favoring LIDOCAINE PATCH 5% were observed in terms of time to exit from the trial (14 versus 3.8 days at p-value <0.001), daily average pain relief, and patient’s preference of treatment. About half of the patients also took oral medication commonly used in the treatment of post-herpetic neuralgia. The extent of use of concomitant medication was similar in the two treatment groups.

INDICATION AND USAGE
LIDOCAINE PATCH 5% is indicated for relief of pain associated with post-herpetic neuralgia. It should be applied only to intact skin.

CONTRAINdications
LIDOCAINE 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
Accidental Exposure in Children
Even a used LIDOCAINE PATCH 5% patch contains a large amount of lidocaine (at least 665 mg). The potential exists for a small child or a pet to suffer serious adverse effects from chewing or ingesting a new or used LIDOCAINE PATCH 5% patch, although the risk with this formulation has not been evaluated. It is important for patients to store and dispose of LIDOCAINE PATCH 5% out of the reach of children, pets and others. (See HANDLING AND DISPOSAL)

Excessive Dosing
Excessive dosing by applying LIDOCAINE PATCH 5% to larger areas or for longer than the recommended wearing time could result in increased absorption of lidocaine and high blood concentrations, leading to serious adverse effects (see ADVERSE REACTIONS, Systemic Reactions). Lidocaine toxicity could be expected at lidocaine blood concentrations above 5 µg/mL. The blood concentration of lidocaine is determined by the rate of systemic absorption and elimination. Longer duration of application, application of more than the recommended number of patches, smaller patients, or impaired elimination may all contribute to increasing the blood concentration of lidocaine. With recommended dosing of LIDOCAINE PATCH 5%, the average peak blood concentration is about 0.13 µg/mL, but concentrations higher than 0.25 µg/mL have been observed in some individuals.

PRECAUTIONS
General
Hepatic Disease
Patients with severe hepatic disease are at greater risk of developing toxic blood concentrations of lidocaine, because of their inability to metabolize lidocaine normally.

Allergic Reactions
Patients allergic to para-aminobenzoic acid derivatives (procarb, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine. However, LIDOCAINE PATCH 5% should be used with caution in patients with a history of drug sensitivities, especially if the etiologic agent is uncertain.

Non-intact Skin
Application to broken or inflamed skin, although not tested, may result in higher blood concentrations of lidocaine from increased absorption. LIDOCAINE PATCH 5% is only recommended for use on intact skin.

External Heat Sources
Placement of external heat sources, such as heating pads or electric blankets, over LIDOCAINE PATCH 5% patches is not recommended as this has not been evaluated and may increase plasma lidocaine levels.

Eye Exposure
The contact of LIDOCAINE PATCH 5% with eyes, although not studied, should be avoided based on the findings of severe eye irritation with the use of similar products in animals. If eye contact occurs, immediately wash out the eye with water or saline and protect the eye until sensation returns.

Drug Interactions
Antiarrhythmic Drugs
LIDOCAINE PATCH 5% should be used with caution in patients receiving Class I antiarrhythmic drugs (such as tocainide and mexiletine) since the toxic effects are additive and potentially synergistic.

Local Anesthetics
When LIDOCAINE PATCH 5% is used concomitantly with other products containing local anesthetic agents, the amount absorbed from all formulations must be considered.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis
A minor metabolite, 2,6-xylidine, has been found to be carcinogenic in rats. The blood concentration of this metabolite is negligible following application of LIDOCAINE PATCH 5%.

Dosage and Administration

Distribution
When lidocaine is administered intravenously to healthy volunteers, the volume of distribution is 0.7 to 2.7 L/kg (mean 1.5 ± 0.6 SD, n = 15). At concentrations produced by application of LIDOCAINE PATCH 5%, lidocaine is approximately 70% bound to plasma proteins, primarily alpha-1-acid glycoprotein. At much higher plasma concentrations (1 to 4 µg/mL of free base), the plasma protein binding of lidocaine is concentration dependent. Lidocaine crosses the placental and blood brain barriers, presumably by passive diffusion.
**Side Effects**

LIDOCAINE PATCH 5% is generally well tolerated. However, side effects can occur, including:

- **Skin Reactions:** Numbness, tingling, or burning at the application site.
- **Symptoms of Absorption:** Nausea, vomiting, dizziness, headache, or tremors.
- **Systemic Effects:** Difficulty breathing, rapid or irregular heartbeat, or unusual weakness.

**Precautions for Use:**

- **Pediatric Use:** Safety and effectiveness in children have not been established.
- **Pregnancy:** Use during pregnancy only if clearly needed.
- **Lactation:** Lidocaine may be excreted in breast milk; use with caution.
- **Geriatric Use:** Increased sensitivity to lidocaine may occur in older adults.

**Hand Hygiene:**

Hands should be washed after handling LIDOCAINE PATCH 5% or any other/local anesthetics.

**Handling and Disposal:**

- Fold used patches into pieces to avoid accidental contact.
- Discard used patches in a closed container.
- Keep children and pets away from used patches.

**Adverse Reactions:**

Adverse reactions are rare and can include:

- **Skin Reactions:** Rash, hives, itching, or swelling.
- **Systemic Reactions:** Nausea, vomiting, or dizziness.
- **Other Reactions:** Fatigue, confusion, or difficulty breathing.

**Overdose:**

Lidocaine is primarily eliminated by the liver. In case of overdose, supportive care and dialysis may be necessary.

**Dosage and Administration:**

LIDOCAINE PATCH 5% is applied to intact skin and removed after 12 hours. DOI of application may vary based on pain severity.

**How Supplied:**

Carton of 30 patches, packaged in individual child-resistant envelopes. NDC 0603-1880-16

Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F). [See USP Controlled Room Temperature].

**Manufactured for:**

QUALITEST PHARMACEUTICALS

Huntsville, AL 35811

Printed in U.S.A.

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