

Annals of Long-Term Care®

P R O D U C T B U L L E T I N

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As a person ages their susceptibility to chronic conditions increases, and as the conditions increase, so do the treatments. Eighty percent of persons over age 65 have at least one chronic condition and half have more than one. This same group of people use between 2 to 6 prescribed medications and 1 to 3.4 nonprescribed medications on a regular basis.¹

As the amount of medications begins to add up, so does the possibility of adverse drug reactions.¹ For the 1.5 million Americans residing in nursing homes,² the responsibility for administering this potential toxic mix of treatments is largely in the hands of staff caregivers who are often stressed. Ease of administration and low incidence of adverse events (AEs) are, therefore important qualities to be considered when assigning treatment.

EXPERT COMMENTARY Christopher Gharibo, MD

Postherpetic neuralgia (PHN) and reactivation of the varicella zoster virus (VZV) occur more frequent in the elderly.³ It is, therefore, not surprising that this painful condition appears in long-term care facility residents. And, as the number of medications that are prescribed to treat the medical conditions of nursing home patients increases, the number of adverse reactions they develop also increases.¹

According to Dworkin et al in the Journal of the American Geriatrics Society, 2007, as many as 80% of PHN patients are misdiagnosed. PHN pain presents with multiple pain qualities, making it difficult to diagnose.⁴

In my opinion, an important consideration is the number of medications patients are taking, in particular in long-term care settings.¹

OVERVIEW OF POSTHERPETIC PAIN

PHN is pain extending beyond 3 months after the acute herpes zoster (shingles) rash has healed.^{5,6} Herpes zoster constitutes the reactivation of VZV, the same virus that causes chickenpox.⁷ After a VZV infection, the virus become latent in the dorsal root ganglia, cell-mediated

immunity (CMI) keeps the virus under control.⁶ When the CMI to VZV is insufficient to keep it under control, the virus reemerges from the dorsal root ganglia, usually resulting in acute herpes zoster rash and severe pain.⁶ PHN, the most common complication of herpes zoster, is a common cause of neuropathic pain.⁶

Chicken pox is the primary risk factor for shingles and subsequent PHN pain, and 95% of Americans have had chicken pox.^{3,6} An estimated 1 million new cases of herpes zoster occur each year in the United States.⁶ Although herpes zoster can occur at any age, incidence increase as a person gets older.⁷ The risk of developing PHN among patients 50 years and older who have had shingles is 50% and increases to 80% among patients 80 years and older.³ In addition with advanced age, the presence of a prodrome, severe acute pain, and severe rash are risk factors for PHN.⁶

Diagnosing PHN is a challenge for healthcare professionals because this neuropathic condition presents with multiple pain qualities.^{4,8} Data suggests that as many as 80% of patients with PHN are undiagnosed.⁹ The pain of PHN takes many forms, including dysesthesia, allodynia, and hyperalgesia. Patients describe the pain as tender, burning, stabbing, throbbing, shooting, and sharp.⁶ While the pain of PHN usually occurs in the area of the prior herpes rash, the size of the area may be smaller or larger. PHN can occur anywhere on the body, and sometimes in multiple places.^{10,11} The most common sites of occurrence are on the torso, waistline, upper arm, or face.

TREATING PHN TOPICALLY

A crucial factor in treatment is the individual variability of PHN. A treatment plan that is both effective and well-tolerated by the patient may present a challenge to long-term care clinicians because of the complex pathophysiology of PHN and differences in responses to therapy, particularly because the condition predominately affects the elderly population.¹¹ Therefore,

managing PHN often requires a customized plan. Several treatment options are available; each work differently to address PHN pain. The agents include topical lidocaine patch, capsaicin patch, tricyclic antidepressants, opioids, and anticonvulsants.¹² Only topical lidocaine patch, capsaicin patch, and some anticonvulsants (pregabalin and gabapentin) are specifically indicated for PHN pain.

Elderly patients tend to suffer from concomitant diseases, which require multiple medications. Persons over age 65 use between 2 to 6 prescribed medications and 1 to 3.4 non-prescribed medications on a regular basis.¹ This can restrict the use of particular systemic analgesics because of both contraindications due to increased safety risks and greater monitoring requirements.⁵

In managing PHN in the elderly, clinicians need to factor in the efficacy, tolerability, and safety of drug therapy. Studies have shown that the topical administration of lidocaine is effective and well-tolerated in the elderly population because it provides localized analgesia to the affected skin area.^{5,13}

Furthermore, requirements for the management of pain in the long-term care setting have been articulated by the Centers for Medicare & Medicaid Services through the Issuance of Revised Quality of Care Guidance at F309. Under the guidance nursing facilities must assess and address pain in all residents, recognize when residents are experiencing pain, evaluate the existing pain and its causes, and manage or prevent pain. This initiative is particularly applicable to the treatment of PHN.¹⁴

LIDODERM® (LIDOCAINE PATCH 5%) AS A TREATMENT OPTION

LIDODERM® is the first and only lidocaine-based topical medication FDA-approved for the treatment of PHN pain.¹¹ LIDODERM is recommended as a first-line treatment for PHN pain, alone or with oral analgesics, by the American Pain Society – Endorsed (US Chapter of International Association for the Study of Pain), council members of the International Association for the Study of Pain (in an independent analysis), and the American Academy of Neurology (subcommittee).^{12,15,16}

The customized fit and once-daily application of LIDODERM requires no dose titration or repeat dosing throughout the day, offering long-term care healthcare professionals an

INDICATION

- LIDODERM is indicated for relief of pain associated with postherpetic neuralgia. Apply only to **intact skin**.

IMPORTANT SAFETY INFORMATION

- LIDODERM is contraindicated in patients with a history of sensitivity to local anesthetics (amide type) or any product component.
- Even a used LIDODERM patch contains a large amount of lidocaine (at least 665 mg). The potential exists for a small child or pet to suffer serious adverse effects from chewing or ingesting a new or used LIDODERM patch, although the risk with this formulation has not been evaluated. It is important for patients to **store and**



LIDODERM® (lidocaine patch 5%) is indicated for relief of pain associated with postherpetic neuralgia. It should be applied only to **intact skin**.¹⁹

EXPERT COMMENTARY

Christopher Gharibo, MD

When treating PHN pain, an analgesic such as LIDODERM that targets the peripheral nervous system at the site of the pathophysiology offers an elegant opportunity to “wind down” the peripheral nervous system that is responsible for the spontaneous and provoked pain as well as tactile, thermal, and mechanical allodynia that patients with PHN experience on a daily basis.^{11,17}

The topical delivery technology of LIDODERM is thought to work primarily at the first order neurons that reach the skin from the spinal cord.¹¹ The plasma levels of lidocaine are low enough that systemic side effects are unlikely.⁴ Furthermore, the lidocaine absorption with LIDODERM is minimal and linear over time when it is used as directed over intact skin.¹⁸

Use of the topical analgesic LIDODERM as a first-line treatment of PHN pain, either as monotherapy or as part of a multimodal treatment approach, may decrease the medical risk to the patient of systemic adverse reactions.¹¹ In my opinion these are important considerations when treating elderly patients with PHN.

appropriate treatment option for elderly patients with PHN pain.^{8,11} These patients may have up to 3 patches applied only once for up to 12 hours within a 24-hour period. And, adding to the customizable quality of the patch, patches may be cut into smaller sizes with scissors prior to the removal of the release liner. The patch provides a physical barrier and clothing may be worn over the area of application.¹⁸

EFFICACY OF LIDODERM

The efficacy of LIDODERM has been demonstrated in 2 pivotal clinical trials. A randomized, double-blind, vehicle controlled, 4-way crossover study assessed the safety and efficacy of LIDODERM in 35 PHN patients over a 12-hour period.^{18,19} Patients were allodynic with a mean age of 75 years and mean PHN duration of 48 months. Patients were allowed to continue use of oral medications for control of PHN pain, including as needed analgesics.¹⁹ Pain intensity was assessed

dispose of LIDODERM out of reach of children, pets, and others.

- Excessive dosing, such as applying LIDODERM 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.
- Avoid contact of LIDODERM with the eye. If contact occurs, immediately wash the eye with water or saline and protect it until sensation returns. Avoid the use of external heat sources as this has not been evaluated and may increase plasma lidocaine levels.
- Patients with severe hepatic disease are at greater risk of developing

continued

using a horizontal 100-mm visual analog scale; 0=no pain and 100=worst pain imaginable. Measurements were recorded before patch application, at 30 minutes, and at 1, 2, 4, 6, 9, and 12 hours.¹⁹

The study results found LIDODERM® significantly reduced pain at all time points 30 minutes to 12 hours ($P=0.0001$ to $P=0.021$), compared with observation cohort. LIDODERM significantly reduced pain at 4 to 12 hours ($P<0.001$ to $P=0.038$), compared with vehicle.^{18,19}

Multiple-dose, 2-week treatment with LIDODERM was compared to vehicle patch (without lidocaine) in a double-blind, enriched enrollment, crossover trial of withdrawal-type design conducted in 32 patients, who were considered as responders to open-label use of LIDODERM prior to the study.^{13,18} Results of enriched-enrollment studies cannot be generalized to the entire population; subjects in such studies may be able to distinguish the active drug from placebo based on non-therapeutic features of treatments. All study patients had been using LIDODERM for ≥ 1 month before study enrollment with a mean age of 77.4 years and mean PHN duration of 7.3 years. About half of the patients used concomitant analgesic as needed, including opiates, acetaminophen, nonsteroidal anti-inflammatory drugs, and tricyclic antidepressants.^{13,18}

The study's primary endpoint was time to exit; patients were allowed to exit either treatment period if their pain relief score decreased by 2 or more items on a 6-item pain relief scale for any 2 consecutive days. Statistically significant differences favoring LIDODERM were observed in the median time to exit period (>14 days vs 3.8 days for the vehicle patch, $P<0.001$).^{12,16}

A third study conducted in 12 European countries reaffirmed the efficacy of lidocaine patch 5%. The double-blind, placebo plaster-controlled, parallel-group, multicenter study employing

EXPERT COMMENTARY
Christopher Gharibo, MD

I have found that a history and physical examination of the long-term care patient are sufficient to reveal the body area where that patient is experiencing PHN.²⁰ A history and physical exam that obtains the location, quality, and intensity of the pain forms the basis of how many patches will be needed to cover the area that is painful to the patient.²¹ I ask the patient to outline their area of pain, keeping in mind that dermatomes adjacent to the original dermatomes that experienced the acute herpes zoster may also be involved.^{20,21}

LIDODERM should be applied directly over the painful area that is outlined by the patient. The number patches of LIDODERM per day should be individualized to cover the area of pain as completely as possible, up to 3 patches per day, 12 hours on, 12 hours off.¹¹ LIDODERM patches can also be cut to improve the coverage of the painful area and its adherence.¹⁸

enriched enrollment with randomized withdrawal included 263 patients.⁵ Results of enriched-enrollment studies cannot be generalized to the entire population; subjects in such studies may be able to distinguish the active drug from placebo based on nontherapeutic features of treatments. The study comprised 2 phases: an 8-week, open-label, run-in phase in which patients were treated with lidocaine patch 5% only, followed by a randomized, placebo-controlled, double-blind phase of up to 2 weeks in which patients either continued with lidocaine patch 5% or switched to placebo. Patients were aged ≥ 50 years; had experienced neuropathic pain persisting for ≥ 3 months after rash healing; and had a mean pain intensity of ≥ 4 on a 11-point numerical scale.⁵

The study's primary endpoint was time to exit due to a ≥ 2 point reduction in pain relief on 2 consecutive days of plaster application using a 6-point verbal rating scale. The study results demonstrated PHN patients remained on lidocaine patch 5%

Start with LIDODERM® (lidocaine patch 5%): It's as easy as 1, 2, 3



A simple application in your office, or at home by your patients

- Can be custom cut to fit the area of PHN pain¹⁸
- Patients can wear up to 3 patches simultaneously¹⁸
- Patches can be worn for up to 12 hours, followed by 12 hours off¹⁸
- LIDODERM may take up to 2 weeks to achieve the best outcome¹⁸

IMPORTANT SAFETY INFORMATION

toxic blood concentrations of lidocaine because of their inability to metabolize lidocaine normally. LIDODERM 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. LIDODERM should also be used with caution in pregnant (including labor and delivery) or nursing mothers.

- Allergic reactions, although rare, can occur.
- During or immediately after LIDODERM treatment, the skin at the site of application may develop blisters, bruising, burning sensation, depigmentation, dermatitis, discoloration, edema, erythema, exfoliation, irritation, papules, petechia, pruritus, vesicles, or may be

the locus of abnormal sensation. These reactions are generally mild and transient, resolving spontaneously within a few minutes to hours. Other reactions may include dizziness, headache, and nausea.

- When LIDODERM is used concomitantly with local anesthetic products, the amount absorbed from all formulations must be considered.
- Immediately discard used patches or remaining unused portions of cut patches in household trash in a manner that prevents accidental application or ingestion by children, pets, or others.

Before prescribing LIDODERM, please refer to the enclosed full Prescribing Information.

more than twice as long as placebo in the 2-week phase. Per protocol population (n=34), median time to exit was 14 days, compared with 6 days for placebo ($P=0.0398$).⁵ Median times to exit in the 14 day placebo-controlled phase were 13.5 days with lidocaine patch 5% versus 9.0 days with placebo patch (intent-to-treat population, $P=0.1510$).⁵

In terms of administering treatment, healthcare professionals should explain to patients the importance of using LIDODERM® as directed. It may take up to 2 weeks to achieve the best outcome.^{13,18}

SAFETY AND TOLERABILITY

Studies have demonstrated that LIDODERM is well tolerated and has a favorable safety profile.^{5,11,13,18,19} Systemic adverse reactions have not been reported in clinical studies and are unlikely, since systemic absorption of lidocaine is not clinically significant with this delivery system.¹¹ When LIDODERM is used according to the recommended dosing instructions, only $3\pm 2\%$ of the dose applied is expected to be absorbed into the bloodstream, even with 3 patches daily.¹⁸ Applying LIDODERM 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 side effects. Factoring in use of concomitant analgesics among patients in clinical trials, LIDODERM has a low risk of drug–drug interactions.^{11,19} In 2 pivotal trials, no serious AEs and no withdrawals due to AEs were reported among the 67 patients in the studies and there were no significant differences between LIDODERM and placebo.^{13,19} LIDODERM may be used in patients who have comorbidities or who are taking concomitant medications. LIDODERM is nonnarcotic, nonsedating, nonscheduled, and does not produce a complete sensory block.¹⁸ During or immediately after LIDODERM treatment, the skin at the site of application may develop blisters, bruising, burning, burning sensation, depigmentation, dermatitis, discoloration, edema, erythema, exfoliation, irritation, papules, petechia, pruritis, vesicles, or may be the locus of abnormal sensation. These reactions are generally mild and transient, resolving spontaneously within a few minutes to hours.¹⁸

LIDODERM has demonstrated long-term use in treating PHN pain. After 7 years, patients continued to use LIDODERM in a compassionate-use program (N=20).²²

IMPORTANT SAFETY INFORMATION

- LIDODERM is contraindicated in patients with a history of sensitivity to local anesthetics (amide type) or any product component.
- Even a used LIDODERM patch contains a large amount of lidocaine (at least 665 mg). The potential exists for a small child or pet to suffer serious adverse effects from chewing or ingesting a new or used LIDODERM patch,

although the risk with this formulation has not been evaluated. It is important for patients to **store and dispose of LIDODERM out of reach of children, pets, and others.**

- Excessive dosing, such as applying LIDODERM 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.
- Avoid contact of LIDODERM with the eye. If contact occurs, immediately wash the eye with water or saline and protect it until sensation returns. Avoid the use of external heat sources as this has not been evaluated and may increase plasma lidocaine levels.
- Patients with severe hepatic disease are at greater risk of developing toxic blood concentrations of lidocaine because of their inability to metabolize lidocaine normally. LIDODERM 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. LIDODERM should also be used with caution in pregnant (including labor and delivery) or nursing mothers.
- Allergic reactions, although rare, can occur.
- During or immediately after LIDODERM treatment, the skin at the site of application may develop blisters, bruising, burning sensation, depigmentation, dermatitis, discoloration, edema, erythema, exfoliation, irritation, papules, petechia, pruritis, vesicles, or may be the locus of abnormal sensation. These reactions are generally mild and transient, resolving spontaneously within a few minutes to hours. Other reactions may include dizziness, headache, and nausea.
- When LIDODERM is used concomitantly with local anesthetic products, the amount absorbed from all formulations must be considered.
- Immediately discard used patches or remaining unused portions of cut patches in household trash in a manner that prevents accidental application or ingestion by children, pets, or others.

Before prescribing LIDODERM, please refer to the enclosed full Prescribing Information.

DOSING AND ADMINISTRATION

LIDODERM is easy-to apply with its 3-step application process. See the illustration on page 3. LIDODERM is applied only to intact skin to cover the most painful area.¹⁸ Patients can wear up to 3 patches simultaneously and apply only once for up to 12 hours within a 24-hour period—a regimen of 12 hours on, 12 hours off treatment.^{11,18} Patches may be cut into smaller sizes with scissors before removal of the release liner. Patients can wear clothing over the area of application. Smaller areas of treatment are recommended in a debilitated patient, or a patient with impaired elimination.¹⁸ ■

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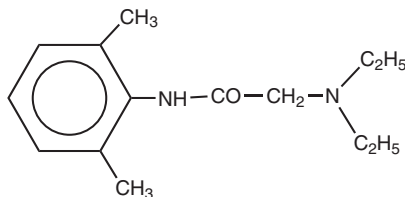
LIDODERM (Lidocaine Patch 5%)

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DESCRIPTION

LIDODERM (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, propylvinyl alcohol, propylene glycol, propylparaben, sodium carboxymethylcellulose, sodium polyacrylate, 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 LIDODERM is sufficient to produce an analgesic effect, but less than the amount necessary to produce a complete sensory block.

Pharmacokinetics

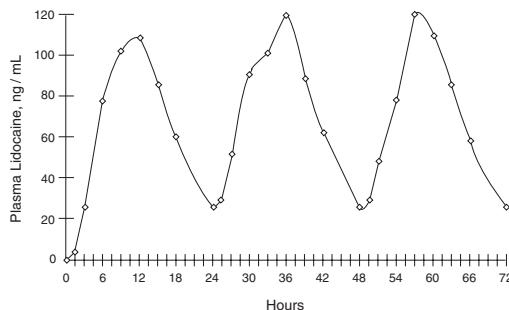
Absorption: The amount of lidocaine systemically absorbed from LIDODERM is directly related to both the duration of application and the surface area over which it is applied. In a pharmacokinetic study, three LIDODERM patches were applied over an area of 420 cm² of intact skin on the back of normal volunteers 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 LIDODERM
Normal volunteers (n = 15, 12-hour wearing time)

LIDODERM Patch	Application Site	Area (cm ²)	Dose Absorbed (mg)	C _{max} (µg/mL)	T _{max} (hr)
3 patches (2100 mg)	Back	420	64 ± 32	0.13 ± 0.06	11 hr

When LIDODERM 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 LIDODERM patches simultaneously for 12 hours per day in healthy volunteers (n = 15).



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 LIDODERM, 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 monoethylglycinexylidide (MEGX) and glycinexylidide (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 LIDODERM (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 LIDODERM 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. LIDODERM performed statistically better than vehicle patch in terms of pain intensity from 4 to 12 hours.

Multiple-dose, two-week treatment with LIDODERM 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 LIDODERM prior to the study. The constant type of pain was evaluated but not the pain induced by sensory stimuli (dysesthesia). Statistically significant differences favoring LIDODERM 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

LIDODERM is indicated for relief of pain associated with post-herpetic neuralgia. It should be applied only to **intact skin**.

CONTRAINDICATIONS

LIDODERM 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* LIDODERM 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 LIDODERM patch, although the risk with this formulation has not been evaluated. It is important for patients to **store and dispose of LIDODERM out of the reach of children, pets and others**. (See HANDLING AND DISPOSAL)

Excessive Dosing

Excessive dosing by applying LIDODERM 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 LIDODERM, 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 (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine. However, LIDODERM 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. LIDODERM is only recommended for use on intact skin.

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

Eye Exposure: The contact of LIDODERM 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: LIDODERM 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 LIDODERM 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 LIDODERM.

Mutagenesis: Lidocaine HCl is not mutagenic in Salmonella/mammalian microsome test nor clastogenic in chromosome aberration assay with human lymphocytes and mouse micronucleus test.

Impairment of Fertility: The effect of LIDODERM on fertility has not been studied.

Pregnancy

Teratogenic Effects: Pregnancy Category B. LIDODERM (lidocaine patch 5%) has not been studied in pregnancy. Reproduction studies with lidocaine have been performed in rats at doses up to 30 mg/kg subcutaneously and have revealed no evidence of harm to the fetus due to lidocaine. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, LIDODERM should be used during pregnancy only if clearly needed.

Labor and Delivery

LIDODERM has not been studied in labor and delivery. Lidocaine is not contraindicated in labor and delivery. Should LIDODERM be used concomitantly with other products containing lidocaine, total doses contributed by all formulations must be considered.

Nursing Mothers

LIDODERM has not been studied in nursing mothers. Lidocaine is excreted in human milk, and the milk:plasma ratio of lidocaine is 0.4. Caution should be exercised when LIDODERM is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

ADVERSE REACTIONS

Application Site Reactions

During or immediately after treatment with LIDODERM (lidocaine patch 5%), the skin at the site of application may develop blisters, bruising, burning sensation, depigmentation, dermatitis, discoloration, edema, erythema, exfoliation, irritation, papules, petechia, pruritus, vesicles, or may be the locus of abnormal sensation. These reactions are generally mild and transient, resolving spontaneously within a few minutes to hours.

Allergic Reactions

Allergic and anaphylactoid reactions associated with lidocaine, although rare, can occur. They are characterized by angioedema, bronchospasm, dermatitis, dyspnea, hypersensitivity, laryngospasm, pruritus, shock, and urticaria. If they occur, they should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.

Other Adverse Events

Due to the nature and limitation of spontaneous reports in postmarketing surveillance, causality has not been established for additional reported adverse events including:

Asthenia, confusion, disorientation, dizziness, headache, hyperesthesia, hypoesthesia, lightheadedness, metallic taste, nausea, nervousness, pain exacerbated, paresthesia, somnolence, taste alteration, vomiting, visual disturbances such as blurred vision, flushing, tinnitus, and tremor.

Systemic (Dose-Related) Reactions

Systemic adverse reactions following appropriate use of LIDODERM are unlikely, due to the small dose absorbed (see CLINICAL PHARMACOLOGY, Pharmacokinetics). Systemic adverse effects of lidocaine are similar in nature 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). Excitatory CNS reactions may be brief or not occur at all, in which case the first manifestation may be drowsiness merging into unconsciousness. Cardiovascular manifestations may include bradycardia, hypotension and cardiovascular collapse leading to arrest.

OVERDOSAGE

Lidocaine overdose from cutaneous absorption is rare, but could occur. If there is any suspicion of lidocaine overdose (see ADVERSE REACTIONS, Systemic Reactions), drug blood concentration should be checked. The management of overdose includes close monitoring, supportive care, and symptomatic treatment. Dialysis is of negligible value in the treatment of acute overdose with lidocaine.

In the absence of massive topical overdose or oral ingestion, evaluation of symptoms of toxicity should include consideration of other etiologies for the clinical effects, or overdosage from other sources of lidocaine or other local anesthetics.

The oral LD₅₀ of lidocaine HCl is 459 (346-773) mg/kg (as the salt) in non-fasted female rats and 214 (159-324) mg/kg (as the salt) in fasted female rats, which are equivalent to roughly 4000 mg and 2000 mg, respectively, in a 60 to 70 kg man based on the equivalent surface area dosage conversion factors between species.

DOSAGE AND ADMINISTRATION

Apply LIDODERM to intact skin to cover the most painful area. Apply up to three patches, only once for up to 12 hours within a 24-hour period. Patches may be cut into smaller sizes with scissors prior to removal of the release liner. (See HANDLING AND DISPOSAL) Clothing may be worn over the area of application. Smaller areas of treatment are recommended in a debilitated patient, or a patient with impaired elimination.

If irritation or a burning sensation occurs during application, remove the patch(es) and do not reapply until the irritation subsides.

When LIDODERM is used concomitantly with other products containing local anesthetic agents, the amount absorbed from all formulations must be considered.

HANDLING AND DISPOSAL

Hands should be washed after the handling of LIDODERM, and eye contact with LIDODERM should be avoided. Do not store patch outside the sealed envelope. Apply immediately after removal from the protective envelope. Fold used patches so that the adhesive side sticks to itself and safely discard used patches or pieces of cut patches where children and pets cannot get to them. LIDODERM should be kept out of the reach of children.

HOW SUPPLIED

LIDODERM (lidocaine patch 5%) is available as the following:

Carton of 30 patches, packaged into individual child-resistant envelopes

NDC 63481-687-06

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

Manufactured for:

Endo Pharmaceuticals Inc.
Chadds Ford, Pennsylvania 19317



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