GP-LIDOCAINE PATCH 5% W/W (700MG/PATCH)

DESCRIPTION

GP-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.

Each adhesive patch (14g) contains 700 mg of lidocaine (50 mg per gram adhesive) in an aqueous base.

It also contains the following ingredients: Urea, Edetate Disodium, Glycerin, Sorbitol Solution, Kaolin, Sodium Polyacrylate, Carboxymethylcellulose Sodium, Sodium Polyacrylate Starch, Polyacrylic Acid, Dihydroxyaluminum Aminoacetate, Propylene Glycol, Polyvinyl Alcohol, Tartaric Acid, Methylparaben, Propylparaben, Purified Water

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 GP-LIDOCAINE PATCH 5% is sufficient to produce an analgesic effect.

Pharmacokinetics

Absorption

When lidocaine 5% medicated plaster is used according to the maximum recommended dose (3 plasters applied simultaneously for 12 h) about 3 ± 2% of the total applied lidocaine dose is systemically available and similar for single and multiple administrations. A population kinetics analysis of the clinical efficacy studies in patients suffering from PHN revealed a mean maximum concentration for lidocaine of 45 ng/ml after application of 3 plasters simultaneously 12 h per day after repeated application for up to one year. This concentration is in accordance with the observation in pharmacokinetic studies in PHN patients (52 ng/ml) and in healthy volunteers (85 ng/ml and 125 ng/ml). For lidocaine and its metabolites monoethylglycinexylidide (MEGX) and glycinexylidide (GX) and 2,6xylidine no tendency for accumulation was found, steady state concentrations were reached within the first four days. The population kinetic analysis indicated that when increasing the number from 1 to 3 plasters worn simultaneously, the systemic exposure increased less than proportionally to the number of used plasters.

Distribution

After intravenous administration of lidocaine to healthy volunteers, the volume of distribution was found to be 1.3 ± 0.4 l/kg (mean ± S.D., n = 15). The lidocaine distribution volume showed no age-dependency; it is decreased in patients with congestive heart failure and increased in patients with liver disease. At plasma concentrations produced by application of the plaster approximately 70 % of lidocaine is bound to plasma proteins. Lidocaine crosses the placental and blood brain barriers presumably by passive diffusion.

Biotransformation

Lidocaine is metabolised rapidly in the liver to a number of metabolites. The primary metabolic route for lidocaine is Ndealkylation to MEGX, GX both of which are less active than lidocaine and available in low concentrations. These are hydrolyzed to 2,6-xylidine, which is converted to conjugated 4-hydroxy-2,6xylidine. The metabolite, 2,6-xylidine, has unknown pharmacological activity but shows carcinogenic potential in rats. A population kinetics analysis revealed a mean maximum concentration for 2,6-xylidine of 9 ng/ml after repeated daily applications for up to one year. This finding is confirmed by a phase I pharmacokinetic study. Data on lidocaine metabolism in the skin are not available.

Elimination

Lidocaine and its metabolites are excreted by the kidneys. More than 85% of the dose is found in the urine in the form of metabolites or active substance. Less than 10% of the lidocaine dose is excreted unchanged. The main metabolite in urine is a conjugate of 4-hydroxy-2,6-xylidine, accounting for about 70 to 80% of the dose excreted in the urine. 2,6-xylidine is excreted in the urine in man at a concentration of less than 1% of the dose. The elimination half-life of lidocaine after plater application in healthy volunteers is 7.6 hours. The excretion of lidocaine and its metabolites may be delayed in cardiac, renal or hepatic insufficiency

CLINICAL STUDIES

Pain management in PHN is difficult. There is evidence of efficacy with lidocaine 5% medicated plaster in the symptomatic relief from the allodynic component of PHN in some cases.

Efficacy of lidocaine patch 5% has been shown in post-herpetic neuralgia studies. Other models of neuropathic pain have not been studied. There were two main controlled studies carried out to assess the efficacy of the lidocaine 5% medicated plaster. In the first study, patients were recruited from a population who were already considered to respond to the product. It was a cross over design of 14 days treatment with lidocaine 5% medicated plaster followed by placebo, or vice versa. The primary endpoint was the time to exit, where patients withdrew because their pain relief was two points lower than their normal response on a six point scale (ranging from worse to complete relief). There were 32 patients, of whom 30 completed. The median time to exit for placebo was 4 days and for active was 14 days (p value < 0.001); none of those on active discontinued during the two week treatment period. In the second study 265 patients with post-herpetic neuralgia were recruited and allocated eight weeks of open label active treatment with lidocaine 5% medicated plaster. In this uncontrolled setting approximately 50% of patients responded to treatment as measured by two points lower than their normal response on a six point scale (ranging from worse to complete relief). A total of 71 patients were randomised to receive either placebo or lidocaine 5% medicated plaster given for 2-14 days. The primary endpoint was defined as lack of efficacy on two consecutive days leading to withdrawal of treatment. There were 9/36 patients on active and 16/35 patients on placebo who withdrew because of lack of treatment benefit. Post hoc analyses of the second study showed that the initial response was independent of the duration of pre-existing PHN. However, the notion that patients with longer duration of PHN (> 12 months) do benefit more from active treatment is supported by the finding that this group of patients was more likely to drop out due to lack of efficacy when switched to placebo during the double-blind withdrawal part of this study.

INDICATION AND USAGE

GP-LIDOCAINE PATCH 5% is indicated for the symptomatic relief of neuropathic pain associated with previous herpes zoster infection (post-herpetic neuralgia, PHN).

DOSAGE AND ADMINISTRATION

Adults and elderly patients

The painful area should be covered with the plaster once daily for up to 12 hours within a 24 hours period. Only the number of plasters that are needed for an effective treatment should be used. When needed, the plasters may be cut into smaller sizes with scissors prior to removal of the release liner. In total, not more than three plasters should be used at the same time. The plaster must be applied to intact, dry, non-irritated skin (after healing of the shingles). Each plaster must be worn no longer than 12 hours. The subsequent plaster-free interval must be at least 12 hours. The plaster must be applied to the skin immediately after removal from the sachet and following removal of the release liner from the gel surface. Hairs in the affected area must be cut off with a pair of scissors (not shaved). Treatment outcome should be re-evaluated after 2-4 weeks. If there has been no response to GP-LIDOCAINE PATCH 5% after this period or if any relieving effect can solely be related to the skin protective properties of the plaster, treatment must be discontinued as potential risks may outweigh benefits in this context. Treatment should be reassessed at regular intervals to decide whether the amount of plasters needed to cover the painful area can be reduced, or if the plaster free period can be extended. Use for patients under the age of 18 is not recommended because of the lack of data in this group.

CONTRAINDICATIONS

GP-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.

The plaster must not be applied to inflamed or injured skin, such as active herpes zoster lesions, atopic dermatitis or wounds.

WARNINGS

If palpitations, dizziness, short term visual disturbances or other arrhythmia like symptoms are present after application, stop use and seek immediate medical attention.

The plaster should not be applied to mucous membranes. Placement of external heat sources, such as heating pads or electric blankets, over GP-LIDOCAINE PATCH 5% is not recommended as this has not been evaluated and may increase plasma lidocaine levels.

Accidental Exposure in Children

Even a used GP-LIDOCAINE PATCH 5% 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 GP-LIDOCAINE PATCH 5%, although the risk with this formulation has not been evaluated. It is important for patients to **store and dispose of GP-LIDOCAINE PATCH 5% out of the reach of children, pets and others**. (See HANDLING AND DISPOSAL)

Excessive Dosing

Excessive dosing by applying GP-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).

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.

PRECAUTIONS

Special populations

The plaster should be used with caution in patients with severe cardiac impairment, severe renal impairment or severe hepatic impairment.

Allergic Reactions

GP-LIDOCAINE PATCH 5% should be used with caution in patients with a history of drug sensitivities, especially if the etiologic agent is uncertain. The plaster contains propylene glycol which may cause skin irritation.

Non-intact Skin

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

Eye Exposure

The contact of GP-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

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

Preclinical Safety Data

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use. In toxicological studies described in the literature using systemic administration of lidocaine, cardiovascular effects (tachycardia or bradycardia, decreases in cardiac output and blood pressure, cardiac arrest) and central nervous system effects (convulsion, coma, respiratory arrest) were observed at exposures considered sufficiently in excess of the maximum human exposure following treatment with lidocaine 5% medicated plaster. This indicates that these effects have little relevance to clinical use. Lidocaine HCl has shown no genotoxicity when investigated in vitro or in vivo. Its hydrolysis product and metabolite, 2,6-xylidine, showed mixed genotoxic activity in several assays particularly after metabolic activation. Carcinogenicity studies have not been performed with lidocaine. Studies performed with the metabolite 2,6-xylidine mixed in the diet of male and female rats resulted in treatment-related cytotoxicity and hyperplasia of the nasal olfactory epithelium and carcinomas and adenomas in the nasal cavity were observed. Tumorigenic changes were also found in the liver and subcutis. Because the risk to humans is unclear, long-term treatment with high doses of lidocaine should be avoided. Lidocaine had no effect on general reproductive performance or female fertility in rats at plasma concentrations up to 130-fold those observed in patients. No adverse effects were seen in an embryofoetal/teratogenicity study in rats at plasma concentrations more than 200-fold that observed in humans. Animal studies are incomplete with respect to effects on pregnancy, embryofoetal development, parturition or postnatal development.

Pregnancy

Teratogenic Effects

Pregnancy Category B.

GP-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, GP-LIDOCAINE PATCH 5% should be used during pregnancy only if clearly needed.

Labor and Delivery

GP-LIDOCAINE PATCH 5% has not been studied in labor and delivery. Lidocaine is not contraindicated in labor and delivery. Should GP-LIDOCAINE PATCH 5% be used concomitantly with other products containing lidocaine, total doses contributed by all formulations must be considered.

Nursing Mothers

GP-LIDOCAINE PATCH 5% 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 GP-LIDOCAINE PATCH 5% 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 GP-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.

Systemic (Dose-Related) Reactions

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. As systemic adverse reactions following appropriate use of GP-LIDOCAINE PATCH 5% are unlikely, due to the small dose absorbed (see CLINICAL PHARMACOLOGY, Pharmacokinetics), please keep to the advised dosage.

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

Hypersensitivity reaction, skin irritation, asthenia, confusion, disorientation, dizziness, headache, hyperesthesia, hypoesthesia, lightheadedness, metallic taste, nausea, nervousness, paresthesia, somnolence, taste alteration, vomiting, visual disturbances such as blurred vision, flushing, tinnitus, and tremor.

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.

HANDLING AND DISPOSAL

Hands should be washed after the handling of GP-LIDOCAINE PATCH 5%, and eye contact with GP-LIDOCAINE PATCH 5% should be avoided. Safely discard used patches or pieces of cut patches where children and pets cannot get to them. GP-LIDOCAINE PATCH 5% should be kept out of the reach of children.

PACKAGING

14g (10x14cm)/patch, 30 patches per box.

STORAGE

Store below 30°C. Keep out of reach of children.

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