XYLOCAINE® 4% TOPICAL SOLUTION

Lignocaine

PRODUCT INFORMATION

NAME OF DRUG

Xylocaine 4% Topical Solution contains lignocaine hydrochloride as the active ingredient.

The CAS number for lignocaine is 137-58-6.

The chemical structure of lignocaine is:

\[
\text{CH}_3 \text{CH}_3 \text{NCOCH}_2 \text{N(C}_2\text{H}_5)_2 \\
\text{CH}_3
\]

Molecular Formula: C\(_{14}\)H\(_{22}\)N\(_2\)O

Molecular Weight: 234.3

The chemical name for lignocaine is 2-diethylamino-2',6'-dimethylacetanilide.

DESCRIPTION

Xylocaine 4% Topical Solution is a colourless, aqueous, topical anaesthetic solution for use on mucous membranes.

Each mL of solution contains: lignocaine hydrochloride 42.8 mg (equivalent to lignocaine hydrochloride anhydrous 40 mg), methyl hydroxybenzoate, sodium hydroxide or hydrochloric acid (for pH adjustment) and water for injections.

PHARMACOLOGY

Pharmacodynamics

Lignocaine, the active ingredient of Xylocaine Topical Solution, stabilises the neuronal membrane and prevents the initiation and conduction of nerve impulses, thereby effecting local anaesthetic action.

Pharmacokinetics

Xylocaine Topical Solution acts intact on mucous membranes to provide prompt local anaesthetic action. Anaesthesia usually occurs within 1-5 minutes and the
effect lasts for approximately 15-30 minutes. It is ineffective when applied to intact skin.

Lignocaine may be absorbed following topical administration to mucous membranes, its rate of absorption and amount of dose absorbed depending upon concentration and total dose administered, the specific site of application and duration of exposure.

In general, the rate of absorption occurs most rapidly after intratracheal administration. Lignocaine is well absorbed from the gastrointestinal tract, but little intact drug appears in the circulation because of biotransformation in the liver. Lignocaine is metabolised rapidly by the liver, and metabolites and unchanged drug are excreted by the kidney.

Excessive blood levels may cause changes in cardiac output, total peripheral resistance and mean arterial pressure. These changes may be attributable to a direct depressant effect of the anaesthetic agent on various components of the cardiovascular system.

Biotransformation includes oxidative N-dealkylation, ring hydroxylation, cleavage of the amide linkage and conjugation. The pharmacological / toxicological actions of the metabolites are similar to, but not less potent than, those of lignocaine. Approximately 90% of lignocaine is excreted in the form of various metabolites, and less than 10% is excreted unchanged. The primary metabolite in urine is a conjugate of 4-hydroxy-2,6-dimethylaniline.

The plasma binding of lignocaine is dependent on drug concentration, and the fraction bound decreases with increasing concentration. At concentrations of 1 to 4 μg of free base/mL, 60 to 80% of lignocaine is protein bound. Binding is also dependent on the plasma concentrations of the alpha-1-acid glycoprotein.

Lignocaine crosses the blood-brain and placental barriers, presumably by passive diffusion.

Studies of lignocaine metabolism following iv bolus injection have shown that the elimination half-life is usually 1.5 to 2 hours. The half-life may be prolonged 2-fold or more in patients with liver dysfunction. Renal dysfunction does not affect lignocaine kinetics, but may increase the accumulation of metabolites.

Factors such as acidosis and the use of CNS stimulants and depressants affect the CNS levels of lignocaine required to produce overt systemic effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6.0 μg free base/mL. In the rhesus monkey arterial blood levels of 18 to 21 μg/mL have been shown to be the threshold for convulsive activity.

INDICATIONS

Anaesthesia of mucous membranes of the oropharyngeal, tracheal and bronchial areas e.g. in bronchoscopy, bronchography, laryngoscopy, oesophagoscopy and endotracheal intubation.
CONTRAINDICATIONS

Known history of hypersensitivity to lignocaine or other local anaesthetics of the amide or ester type or to other components of the solution.

Hypersensitivity to methyl and/or propyl hydroxybenzoate (paraben) or to their metabolite para aminobenzoic acid (PABA).

Xylocaine 4% Topical Solution is intended for topical use only and must not be used for injection.

PRECAUTIONS

Patients should not exceed the recommended dose or use Xylocaine 4% Topical Solution for prolonged periods except on the advice of their physician. The lowest dose that results in effective anaesthesia should be used to avoid high plasma levels and serious adverse effects. Tolerance to elevated blood levels varies with the status of the patient.

Dosage reduction

Debilitated, elderly and/or acutely ill patients, and children should be given reduced doses commensurate with their age and physical status.

Excessive absorption

Absorption from wound surfaces and mucous membranes is relatively high, especially in the bronchial tree. This should be taken into consideration when the solution is used in children for treatment of large areas. Because of the possibility of significant systemic absorption, Xylocaine Topical Solution should be used with caution in patients with traumatised mucosa and/or sepsis in the region of the proposed application.

If the dose or site of administration is likely to result in high blood levels, lignocaine, in common with other local anaesthetics, should be used with caution in patients with epilepsy, impaired cardiac conduction, bradycardia, impaired hepatic function, in severe shock, patients in poor general health, patients with severe renal dysfunction and the elderly.

Eating and drinking

The use of topical anaesthetic agents in the oral cavity may interfere with swallowing and thus enhance the danger of aspiration of food or drink. For this reason, food or drink should not be ingested within 60 minutes of using local anaesthetics in the mouth or throat area. Numbness of the tongue or buccal mucosa may increase the danger of biting or heat trauma. Food, chewing gum or hot drinks should not be taken while the mouth or throat area is anaesthetised.

Contact with the eyes

Xylocaine Topical Solution is not intended for ophthalmological use. If Xylocaine Topical Solution inadvertently comes into contact with the eyes, rinse immediately with copious amounts of water for at least 15 minutes and seek medical advice.
Paralysed patients
In paralysed patients under general anaesthesia, higher blood concentrations may occur than in spontaneously breathing patients. Unparalysed patients are more likely to swallow a large proportion of the dose which then undergoes first-pass hepatic metabolism following absorption from the gut.

Malignant hyperthermia
Many drugs used during the conduct of anaesthesia are considered potential triggering agents for familial malignant hyperthermia. It has been shown that the use of amide local anaesthetics in malignant hypothermia patients is generally safe, but cases of malignant hyperthermia have occasionally been documented after use.

Gargling
The use of Xylocaine Topical Solution as a gargle is not indicated. The use of concentrated Xylocaine Topical Solution 4% for gargling increases the risk of systemic toxicity due to overdosing and rapid uptake over the mucosa and/or ingestion.

Porphyric patients
Xylocaine 4% Topical Solution is probably porphyrinogenic and should only be used on patients with acute porphyria where there are strong or urgent indications. Appropriate precautions should be taken for all porphyric patients.

Carcinogenic and Mutagenic Potential
Genotoxicity tests with lignocaine are inconclusive. In genotoxicity studies, a metabolite of lignocaine, 2,6-xylidine, showed evidence of activity in some tests but not in other tests. This metabolite has been shown to have carcinogenic potential (nasal and subcutaneous tumours) in preclinical toxicological studies evaluating chronic exposure.

Use in pregnancy - Category A
Lignocaine crosses the placental barrier and may be taken up by foetal tissues. When used for surface anaesthesia, lignocaine blood levels after normal doses are low so little drug is available for placental transfer.

There are, however, no adequate and well-controlled studies in pregnant women. Reproduction studies have been performed in rats at doses of 500 mg/kg/day and have revealed no evidence of harm to the foetus caused by lignocaine.

It is reasonable to assume that a large number of pregnant women and women of child bearing age have used lignocaine. No specific disturbances to the reproduction process have so far been reported.

Labour and delivery
Lignocaine is not contraindicated in labour and delivery.
Use in lactation

Lignocaine enters breast milk, but in such small quantities that there is generally no risk of affecting the child at therapeutic dose levels.

Interactions with other drugs

Antiarrhythmic drugs

Lignocaine should be used with caution in patients receiving antiarrhythmic drugs, such as mexiletine, since the toxic effects are additive.

Enzyme inducing drugs

Drugs that reduce the clearance of lignocaine (e.g. cimetidine or beta-blockers) may cause potentially toxic plasma concentrations when lignocaine is given in repeated high doses over a long time period. Such interactions should therefore be of no clinical importance following short-term treatment with lignocaine (e.g. Xylocaine Spray) at recommended doses. Caution should be taken if administered concurrently with lignocaine.

Phenytoin and other antiepileptic drugs such as phenobarbitone, primidone and carbamazepine appear to enhance the metabolism of lignocaine but the significance of this effect is not known. Phenytoin and lignocaine have additive cardiac depressant effects.

Incompatibilities

The solubility of lignocaine is limited at pH > 6.5. This must be taken into consideration when alkaline solutions, i.e. carbonates, are added since precipitation might occur.

Effects on ability to drive and operate machines

Depending on the dose, local anaesthetics may have a very mild effect on mental function and may temporarily impair locomotion and coordination.

ADVERSE REACTIONS

Systemic adverse reactions are rare and may result from high plasma levels caused by excessive dosage or rapid absorption, or may result from a hypersensitivity, idiosyncrasy or reduced tolerance on the part of the patient. Such reactions are systemic in nature and involve the central nervous system and/or the cardiovascular system.

Central Nervous System

CNS reactions are excitatory and/or depressant and may be characterised by lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness and possibly respiratory arrest. The excitatory reactions may be brief or may not occur at all, in which case the first manifestations of toxicity may be drowsiness, progressing to unconsciousness and respiratory arrest.
Drowsiness following administration of lignocaine is usually an early sign of a high blood level of the drug and may occur as a result of rapid absorption.

**Cardiovascular**

Cardiovascular reactions are usually depressant and may be characterised by hypotension, myocardial depression, bradycardia and possibly cardiac arrest.

**Allergic reactions**

Allergic reactions may occur as a result of sensitivity either to the local anaesthetic agent or to other ingredients in the formulation. Allergic reactions as a result of sensitivity to lignocaine are extremely rare. The detection of sensitivity by skin testing is of doubtful value.

The extremely rare cases of allergy to local anaesthetic preparations have included bronchospasm, chest pain, dyspnoea, pruritis, rash, rhinitis, increased sweating, urticaria, sleepiness, dizziness, paraesthesia, oedema, and in the most severe instances anaphylactic shock. Several cases of contact dermatitis have been reported with the use of lignocaine.

**DOSAGE AND ADMINISTRATION**

XYLOCAINE 4% TOPICAL SOLUTION IS NOT TO BE USED FOR INJECTION.

As with any local anaesthetic, reactions and complications are best averted by employing the minimal effective dosage. Debilitated, acutely ill or elderly patients and children should be given doses commensurate with their age and physical condition.

**Anaesthesia of the mucous membranes of the oropharyngeal, tracheal and bronchial areas:**

The recommended dosage for a procedure in adults is 1 to 5mL Xylocaine topical solution (40 to 200 mg lignocaine HCl).

**Maximum dosage:**

*Adults:* no more than 5mL (200mg lignocaine HCl) should be used at any one time.

*Children:* the maximum single dose should not exceed 3mg/kg of bodyweight.

The dose of topical lignocaine should be taken into consideration in estimating the total dose of lignocaine if parenteral lignocaine is to be administered concomitantly.

Xylocaine Topical Solution may be applied with cotton applicators or packs and by instillation into a cavity or onto a surface. For laryngoscopy and bronchoscopy, Xylocaine Topical Solution should be used as a spray. The pharynx and larynx may also be sprayed prior to endotracheal intubation.
OVERDOSAGE

In the event of an overdose, contact the Poisons Information Centre on 13 11 26.

Management of Local Anaesthetic Emergencies

The first consideration is prevention, best accomplished by careful and constant monitoring of cardiovascular and respiratory vital signs and the patient's state of consciousness after each local anaesthetic administration. At the first sign of change, oxygen should be administered.

Treatment

Should symptoms of acute systemic toxicity occur, the signs are anticipated to be similar in nature to those following the administration of local anaesthetics by other routes. Local anaesthetic toxicity is manifested by symptoms of nervous system excitation and, in severe cases, central nervous and cardiovascular depression.

If circulatory arrest should occur, immediate cardiopulmonary resuscitation should be instituted. Optimal oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance.

If convulsions or other severe neurological symptoms occur, such as CNS depression, then immediate attention is required for the maintenance of a patent airway and assisted or controlled ventilation with oxygen, via a positive airway pressure delivery system mask. Adequacy of the circulation should then be evaluated, bearing in mind that drugs used to treat convulsions depress the circulation when administered iv.

Should convulsions persist despite adequate respiratory support, and if the status of the circulation permits, appropriate anticonvulsant medication such as an ultra-short acting barbiturate or a benzodiazepine may be administered iv. The clinician should be familiar with these anticonvulsant drugs prior to use of local anaesthetics.

Dialysis is of negligible value in the treatment of acute overdosage with lignocaine.

PRESENTATION

Xylocaine 4% Topical Solution, 30 mL bottle.

POISONS SCHEDULE OF THE DRUG

S2

STORAGE

Store below 25°C.
NAME AND ADDRESS OF SPONSOR

AstraZeneca Pty Ltd
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Alma Road,
North Ryde NSW  2113 Australia

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