PRODUCT INFORMATION

LIDOCAINE HYDROCHLORIDE 4% TOPICAL SOLUTION
LIDOCAINE (LIGNOCAINE) HYDROCHLORIDE

This product is an unapproved therapeutic good in Australia. It is manufactured in a TGA approved pharmaceutical manufacturing facility in Australia and is provided under Schedule 5A – subregulation 12(1A) of the Therapeutic Goods Act and Regulations. The product is supplied under contract between a public or private hospital or public institution and the licensed manufacturer in Australia in accordance with a specified formulation.

Approval for use is required from the hospital pharmacist and / or drug committee as appropriate. Informed consent should be obtained in accordance with good medical practice where applicable and practicable. Records of the use of the product should be fully detailed and include dose, route of administration, duration of treatment, clinical, biochemical, haematological and immunological monitoring as appropriate. Adverse events and reactions must be reported to Phebra Pty Ltd and the Therapeutic Goods Administration.

The responsibility for the use of this product remains with the prescriber and the institution. The following product information has not been evaluated or approved by the Therapeutic Goods Administration. Physicians should consult the medical literature for the most recent advice concerning the appropriate dose, route of administration, warnings and adverse effects.

1 NAME OF THE MEDICINE
Lidocaine (lignocaine) hydrochloride

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each mL of solution contains: lidocaine (lignocaine) hydrochloride monohydrate 42.8 mg (equivalent to lidocaine (lignocaine) hydrochloride 40 mg) and water for injections.

3 PHARMACEUTICAL FORM
Lidocaine Hydrochloride 4% Topical Solution is a colourless, aqueous, topical anaesthetic solution for use on mucous membranes.

4 CLINICAL PARTICULARS
4.1 THERAPEUTIC INDICATIONS
Anaesthesia of mucous membranes of the oropharyngeal, tracheal and bronchial areas e.g. in bronchoscopy, bronchography, laryngoscopy, oesophagoscopy and endotracheal intubation.
4.2 Dose and Method of Administration

LIDOCAINE HYDROCHLORIDE 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 5 mL Lidocaine Hydrochloride 4% Topical Solution (40 to 200 mg lidocaine (lignocaine) HCl).

Maximum dosage:

Adults: no more than 5 mL (200 mg lidocaine (lignocaine) HCl should be used).
Children: the maximum single dose should not exceed 3 mg/kg of bodyweight.

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

Lidocaine Hydrochloride 4% Topical Solution may be applied with cotton applicators or packs and by instillation into a cavity or onto a surface. For laryngoscopy and bronchoscopy, Lidocaine Hydrochloride 4% Topical Solution should be used as a spray. The pharynx and larynx may also be sprayed prior to endotracheal intubation.

Lidocaine Hydrochloride 4% Topical Solution contains no preservatives. Product is for single use in one patient only. Discard after use.

4.3 Contraindications

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

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

4.4 Special Warnings and Precautions for Use

Must not be used for injection. Patients should not exceed the recommended dose or use Lidocaine Hydrochloride 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.

Dose 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, Lidocaine Hydrochloride 4% 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, lidocaine (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

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

Porphyric patients

Lidocaine Hydrochloride 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.
4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Antiarrhythmic drugs

Lidocaine (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 lidocaine (lignocaine) (e.g. cimetidine or beta-blockers) may cause potentially toxic plasma concentrations when lidocaine (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 lidocaine (lignocaine) (e.g. Lidocaine Hydrochloride 4% Topical Solution) at recommended doses. Caution should be taken if administered concurrently with lidocaine (lignocaine).

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

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy – Category A

Lidocaine (lignocaine) crosses the placental barrier and may be taken up by fetal tissues. When used for surface anaesthesia, lidocaine (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 fetus caused by lidocaine (lignocaine).

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

Use in labour and delivery

Lidocaine (lignocaine) is not contraindicated in labour and delivery.

Use in lactation

Lidocaine (lignocaine) enters breast milk, but in such small quantities that there is generally no risk of affecting the child at therapeutic dose levels.
4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

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 light-headedness, 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 lidocaine (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 lidocaine (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 lidocaine (lignocaine).

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at http://www.tga.gov.au/reporting-problems.
4.9 Overdose

For information on the management of overdose, contact the Poison Information Centre on 13 11 26 (Australia).

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 intravenously.

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 intravenously. 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 lidocaine (lignocaine).

5 Pharmacological Properties

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Anaesthetics, Local.

ATC code: N01B

Mechanism of action

Lidocaine (lignocaine), the active ingredient of Lidocaine Hydrochloride 4% Topical Solution, stabilises the neuronal membrane and prevents the initiation and conduction of nerve impulses, thereby effecting local anaesthetic action.

Clinical trials

No data available.
5.2 **PHARMACOKINETIC PROPERTIES**

**Absorption**

Lidocaine Hydrochloride 4% Topical Solution acts on intact 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.

Lidocaine (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. Lidocaine (lignocaine) is well absorbed from the gastrointestinal tract, but little intact drug appears in the circulation because of biotransformation in the liver.

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.

**Distribution**

The plasma binding of lidocaine (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 lidocaine (lignocaine) is protein bound. Binding is also dependent on the plasma concentrations of the alpha-1-acid glycoprotein. Lidocaine (lignocaine) crosses the blood-brain and placental barriers, presumably by passive diffusion.

Factors such as acidosis and the use of CNS stimulants and depressant affect the CNS levels of lidocaine (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.

**Metabolism**

Lidocaine (lignocaine) is metabolised rapidly by the liver, and the metabolites and unchanged drug are excreted by the kidney.

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 lidocaine (lignocaine).

**Excretion**

Studies of lidocaine (lignocaine) metabolism following intravenous 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 lidocaine (lignocaine) kinetics, but may increase the accumulation of metabolites. Approximately 90% of lidocaine (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.
5.3  PRECLINICAL SAFETY DATA

Genotoxicity
Genotoxicity tests with lidocaine (lignocaine) are inconclusive.

Carcinogenicity
In genotoxicity studies, a metabolite of lidocaine (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.

6  PHARMACEUTICAL PARTICULARS

6.1  LIST OF EXCIPIENTS
Water for Injections

6.2  INCOMPATIBILITIES
The solubility of lidocaine (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.

6.3  SHELF LIFE
The expiry date can be found on the packaging.

6.4  SPECIAL PRECAUTIONS FOR STORAGE
Store below 25°C.

6.5  NATURE AND CONTENTS OF CONTAINER
Lidocaine Hydrochloride 4% Topical Solution, 5 pack of 5 mL vials.

Phebra product code: SOL055

6.6  SPECIAL PRECAUTIONS FOR DISPOSAL
In Australia, any unused medicine or waste material should be disposed of by taking it to your local pharmacy.
6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Structural formula of lidocaine (lignocaine):

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\text{[Chemical structure image]}
\]

Molecular formula of lidocaine (lignocaine): \( \text{C}_{14}\text{H}_{22}\text{N}_{2}\text{O} \).

The molecular weight of lidocaine (lignocaine) is 243.3 g/mol.

CAS number

137-58-6

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 2 – Pharmacy Medicine

8 SPONSOR

Phebra\(^1\) Pty Ltd
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Telephone: 1800 720 020

9 DATE OF REVISION

17 January 2018

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