**Name of the Medicine**
Lignocaine.

The structural formula is represented below.

![ Structural formula of Lignocaine ]

Molecular formula: $\text{C}_{14}\text{H}_{22}\text{N}_{2}\text{O}$  
Molecular weight: 234.3  
CAS No: 137-58-6

**Description**
Lignocaine is 2-(diethylamino)-$N$-(2,6-dimethylphenyl) acetamide. It is a white to almost white crystalline powder that is practically insoluble in water, very soluble in alcohol and in methylene chloride.

Lignocaine 2% Gel is a clear, colourless, sterile, preservative-free water-soluble gel containing 20mg/mL lignocaine, propylene glycol, hydroxyethyl cellulose, glacial acetic acid, sodium hydroxide (for pH adjustment) and water for injections (in bulk).

**Pharmacology**

**Class of drug:** Local anaesthetic/anti-arrhythmic.  
**Mechanism of action:** Lignocaine is a local anaesthetic of the amide type. It produces a reversible loss of sensation by preventing or diminishing the conduction of sensory nerve impulses near the site of application.

**Pharmacokinetics**

Lignocaine is readily absorbed from mucous membranes and damaged skin producing rapid, local anaesthesia in these areas. Absorption from intact skin is poor. The rate of absorption and amount of dose absorbed is dependent upon concentration, the total dose administered, the specific site of application and the duration of exposure.

Lignocaine is metabolised rapidly by the liver, with both metabolites and unchanged drug excreted by the kidney. Approximately 90% of lignocaine is excreted as metabolites and less than 10% is excreted as unchanged drug. Excessive blood levels of lignocaine may cause changes in cardiac output, total peripheral resistance and mean arterial pressure. These changes may be attributed to a direct depressant effect of the anaesthetic agent on various components of the cardiovascular system. The pharmacological/toxicological actions of the metabolites are similar to, but less potent than those of lignocaine. The plasma binding of lignocaine is dependent on drug concentration, and the fraction bound decreases with increasing concentration. At concentrations of 1 to 4 microgram 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.

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 doubled in patients with hepatic dysfunction. Renal dysfunction does not affect lignocaine kinetics, but may increase the accumulation of metabolites.
Acidosis and the use of CNS stimulants and depressants affect the CNS levels of lignocaine required to produce systemic effects. Adverse reactions become increasingly apparent with venous plasma levels above 6.0 microgram free base/mL.

**Indications**
- Local anaesthesia and lubrication during catheterisation, exploration by sound and other endourethral operations and examinations.
- Cystoscopy and symptomatic treatment of painful cystitis and urethritis.

**Contraindications**
Known hypersensitivity to amide type local anaesthetics or to any of the excipients.

**Precautions**
Not for injection.

**Warning:** Excessive dosage, or short intervals between doses, can result in high serum levels of lignocaine or its metabolites and serious adverse effects, therefore the recommended dosage and administration guidelines should be strictly followed. Where possible the lowest dose that results in effective anaesthesia should be used to avoid high plasma levels and serious adverse effects.

**Dose reduction:** Care is required with debilitated, elderly, acutely ill patients and children who should be given reduced doses relative to their age and physical status.

**Excessive absorption:** As absorption from wound surfaces and mucous membranes is relatively high and tolerance to elevated blood levels varies with the status of the patient, use with caution in patients with severely traumatised mucosa and/or sepsis in the region of 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, severe shock and patients with severe renal dysfunction.

**Antiarrhythmic drugs class III:** Patients treated with antiarrhythmic drugs class III (e.g., amiodarone) should be kept under close surveillance and electrocardiogram (ECG) monitoring considered, since cardiac effects may be additive.

**Porphyric patients:** Lignocaine 2% Gel is probably porphyrogenic 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.

**Carcinogenesis, mutagenesis, impairment of fertility:** 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 fetal tissues. When used for surface anaesthesia, lignocaine blood levels following normal administration are low thus minimal drug is available for placental transfer. No specific disturbances to the reproductive process have so far been reported.

**Use in lactation:** Lignocaine enters the breast milk, but in such small quantities at therapeutic dose levels that there is generally no risk when breastfeeding.
Effect on ability to drive or operate machinery: Depending on the dose administered, local anaesthetics may have a very mild effect on mental function and may temporarily impair locomotion and coordination.

Interactions with other medicines
Antiarrhythmic drugs: Lignocaine should be used with caution in patients receiving antiarrhythmic drugs such as mexiletine, since the toxic effects are additive. Specific interaction studies with lignocaine and antiarrhythmic drugs class III (e.g., amiodarone) have not been performed, but caution is advised.
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. Caution should be taken if administered concurrently with lignocaine. However, such interactions should be of no clinical importance following short-term treatment with Lignocaine 2% Gel at the recommended dosage. 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.

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

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, sensation of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness and possibly respiratory arrest. The excitatory reactions may be very 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 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 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, pruritus, rash, oedema, rhinitis, increased sweating, urticaria, sleepiness, dizziness, paraesthesia and, in the most severe instances, anaphylactic shock.

Effects on the blood: Methaemoglobinaemia may occur, probably due to the metabolism of lignocaine to an aniline-like structure. Infants (during the first 3 months of life) are particularly susceptible to induced methaemoglobinaemia, probably due to their limited enzyme capacity.

Dosage and administration
As with any local anaesthetic, reactions and complications are best averted by employing the minimum effective dosage. Debilitated or elderly patients and children should be given doses according to their age and physical condition. 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. The following dosage recommendations should be regarded as a guide. The
clinician’s experience and knowledge of the patient’s physical status are of importance in calculating the required dose. 1mL of Lignocaine 2% Gel is approximately equal to 1g of Lignocaine 2% Gel.

- **Males:** The usual dose required for adequate analgesia is 20mL (equiv. lignocaine 400mg). The gel is instilled slowly into the urethra until it reaches the external sphincter, proximal to the prostate, where a certain resistance is felt. Compression is then applied for several minutes at the corona. The remaining gel is administered, filling the length of the urethra. For procedures such as sounding or cystoscopy, a larger quantity of gel (up to 40mL) may be required. This amount should be instilled in three to four portions and anaesthesia allowed to take effect for five to ten minutes before insertion of the instrument.

- **Females:** Instil 5 to 10mL in small portions to fill the whole urethra. In order to obtain adequate anaesthesia, three to five minutes should be allowed prior to performing urological procedures.

- **Children:** In children under the age of 12 years up to 6mg/kg can be used.

**Overdosage**
Lignocaine is absorbed from mucous membranes and serious toxicity has been reported following the use of lignocaine preparations for urethral anaesthesia. Lignocaine intoxication affects the CNS and cardiovascular system. Overdose symptoms include: severe hypotension, asystole, bradycardia, apnoea, cardiac arrest, respiratory arrest, seizures, coma and possibly death.

*Management of local anaesthetic emergencies:* The first consideration is prevention, which is 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:* If convulsions occur, immediate attention is required for the maintenance of a patent airway and assisted or controlled ventilation with oxygen. 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 ultrashort acting barbiturate (e.g., thiopentone) or a benzodiazepine (e.g., diazepam) may be administered intravenously.

Hypotension may be initially managed by the use of intravenous fluids and by vaspressors if the problem persists.

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

Contact the Poisons Information Centre for advice on the management of an overdose.

**Presentation and storage conditions**
AUST R 155647. Lignocaine 2% Gel 10g is supplied in a plastic syringe with an applicator nozzle for easy application. It is contained in an outer, sterile bag to allow assembly of syringe and nozzle under aseptic conditions. Pack size: 10 syringes.

Store below 30˚C. Single use only. Discard unused portion.

The expiry date (month/year) is stated on the package after the word EXP.
Name and address of the sponsor

Sponsor in Australia  Manufacturer  Distributed in Australia by:
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Poison schedule of the medicine
Australia – S2.

Date of approval
This information was approved by the TGA on 08 October 2008.