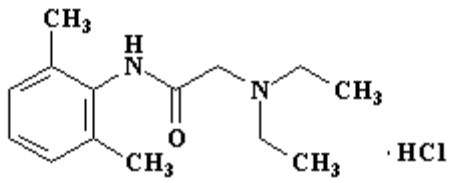
PRODUCT NAME
Cathejell Lignocaine 2% sterile lubricant gel

NAME OF THE MEDICINE
Lidocaine (Lignocaine) hydrochloride monohydrate



Molecular Formula: $C_{14}H_{23}ClN_2O$
Molecular Weight: 270.8
CAS Number: 6108-05-0

DESCRIPTION

Cathejell Lignocaine 2% is a topical anesthetic for urological and endoscopic procedures and lubrication of endotracheal tubes and endoscopes.

The active ingredient is lignocaine hydrochloride. Cathejell Lignocaine 2% is a sterile gel product. Each gram of Cathejell Lignocaine 2% contains lidocaine (lignocaine) hydrochloride monohydrate 21.3 mg (equivalent to lidocaine (lignocaine) hydrochloride 20 mg), Glycerol, Hydroxyethyl cellulose, Hydrochloric acid & Sodium hydroxide (for pH adjustment) and Water for injections.

PHARMACOLOGY

Lignocaine, the active ingredient of Cathejell Lignocaine 2%, stabilises the neuronal membrane and prevents the initiation and conduction of nerve impulses, thereby effecting local anaesthetic action.

Cathejell Lignocaine 2% provides prompt anaesthesia of mucous membranes and lubrication which reduces friction. Lignocaine is absorbed following application to mucous membranes, with anaesthesia usually occurring rapidly (within 3 to 5 minutes, depending upon the area of application).

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 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 in urine. 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.

Cathejell Lignocaine 2% is ineffective when applied to intact skin.

Its water miscible base, characterised by high viscosity and low surface tension, brings the anaesthetic into intimate and prolonged contact with the tissue giving effective anaesthesia of short duration (approx. 20 - 30 minutes.).

Blood concentrations of lignocaine after instillation in the urethra of doses up to 800 mg are low and well below toxic levels.

INDICATIONS

Surface anaesthesia and lubrication for:

- The male and female urethra during cystoscopy, catheterization, exploration by sound and other endourethral operations.
- Nasal and pharyngeal cavities in endoscopic procedures such as gastroscopy and bronchoscopy.
- Proctoscopy and rectoscopy.

- Tracheal intubation
- Cytoscopy and symptomatic treatment of painful cystitis and urethritis

CONTRAINDICATION

Known history of hypersensitivity to local anaesthetics of the amide type or other components of the gel.

PRECAUTIONS

Warning:

Excessive dosage, or short intervals between doses, can result in high levels of lignocaine or its metabolites and serious adverse effects. Patients should be instructed to strictly adhere to the recommended dosage and administration guidelines (the management of serious adverse reactions may require the use of resuscitative equipment, oxygen and other resuscitative drugs).

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. Because of the possibility of significant systemic absorption, Cathejell Lignocaine 2% 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, severe shock and patients with severe renal dysfunction.

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.

Endotracheal tube lubrication
When used for endotracheal tube lubrication, care should be taken to avoid introduction of the gel into the lumen of the tube. The gel may dry on the inner surface leaving a residue which tends to clump with flexion, narrowing the lumen. It has been reported rarely that this residue

has caused the lumen to occlude.

Anti-arrhythmic drugs class III
Patients treated with anti-arrhythmic drugs class III (e.g., amiodarone) should be kept under close surveillance and ECG monitoring considered, since cardiac effects may be additive.

Porphyric patients
Cathejell Lignocaine 2% 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 up 500mg/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.

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.

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.

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 lidocaine and anti-arrhythmic 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 Cathejell Lignocaine 2% at recommended doses.

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 may result from 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, sensation 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 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, rhinitis, increased sweating, urticaria, sleepiness, dizziness, paraesthesia, oedema, and in the most severe instances, anaphylactic shock.

Local reactions

An increased incidence of postoperative ‘sore throat’ has been reported following endotracheal tube lubrication with Cathejell Lignocaine 2%.

There have been rare reports of endotracheal tube occlusion associated with the presence of dried gel residue in the inner lumen of the tube. (See also **Precautions**)

DOSAGE AND ADMINISTRATION

As with any local anaesthetic, reactions and complications are best averted by employing the minimal effective dosage. Debilitated or elderly patients and children should be given doses commensurate with 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. When fully compressed each 1 x 12.5 g accordion syringe will express approximately 10.0 g (corr. to 9.4 mL) of Cathejell Lignocaine sterile gel (equivalent to 200 mg of lidocaine (lignocaine) hydrochloride).

Urethral anaesthesia
Surface Anesthesia of the Male Adult Urethra

For adequate analgesia in males, 20 g gel (2 syringes; equiv. 400 mg lignocaine hydrochloride) is usually required.

The gel is instilled slowly into the urethra until it reaches the external sphincter, proximal to the prostate, where a certain resistance is felt (approximately 10g of gel (1 accordion syringe)). A penile clamp is then applied for several minutes at the corona. The remaining gel (10 g of gel (1 accordion syringe)) is administered, filling the length of the urethra.

For procedures such as sounding or cystoscopy, a larger quantity of gel (up to 40 g gel (4 syringes; equiv. 800 mg lignocaine hydrochloride) may be required. This amount should be instilled in 3-4 portions and anaesthesia allowed to take effect for 5-10 minutes before insertion of the instrument.

To anesthetize only the anterior male urethra, e.g., for catheterization, small volumes (e.g. 5-10 g gel, (½ to 1 syringe; equiv. 100-200 mg lignocaine hydrochloride)) are usually adequate for lubrication.

For Surface Anesthesia of the Female Adult Urethra

Instill 5-10 g gel (½ to 1 syringe; equiv. 100-200 mg lignocaine hydrochloride) in small portions to fill the whole urethra. In order to obtain adequate anesthesia, 3-5 minutes should be allowed prior to performing urological procedures.

Endoscopy (Upper and lower airways and rectal)

Instillation of 10-20 g gel (1-2 syringes) into the appropriate body cavity is recommended for adequate analgesia and a small amount should be applied to lubricate the endoscope. When combined with other lignocaine products (e.g., for bronchoscopy), the total dose of lignocaine

hydrochloride should not exceed 400 mg (20 g gel; 2 syringes).

Lubrication for Endotracheal Intubation

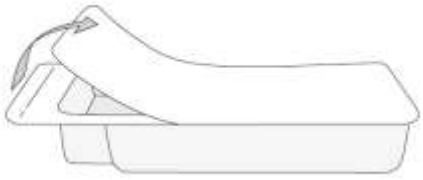
Apply approximately 2 g of gel to the external surface of the endotracheal tube prior to insertion. Care should be taken to avoid introducing the product into the lumen of the tube (see also PRECAUTIONS). Do not use the gel to lubricate endotracheal stylettes.

Children (Under 12 Years)

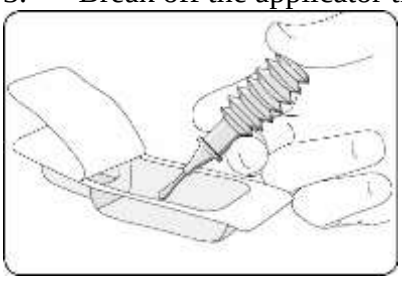
In children under the age of 12 years up to 6mg/kg can be used.

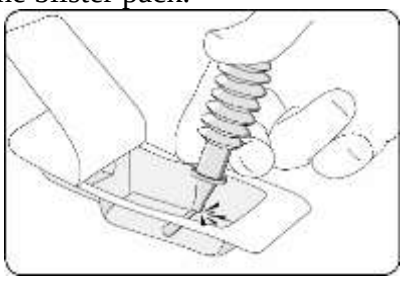
SPECIAL HANDLING INSTRUCTIONS

1. Clean and disinfect the affected area if possible.
2. Peel off the paper cover from the transparent blister pack. Inspect mixture visually for clarity, particulate matter, precipitation, discolouration and leakage prior to administration.

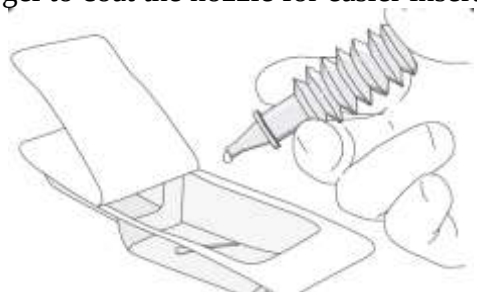


3. Break off the applicator tip in the blister pack.





4. Remove the applicator tip completely.
5. Release one drop of the gel to coat the nozzle for easier insertion.



6. Instillation is completed by applying slight but steady pressure to the collapsible syringe.
7. To avoid suction, keep the collapsible syringe compressed whilst removing from the affected area.

OVERDOSAGE

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

If convulsions occur 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 AND STORAGE CONDITIONS

Cathejell Lignocaine 2%.is available in polypropylene, collapsible accordion-type syringes with an applicator cone. Each accordion syringe is labelled and blistered individually.
Pack sizes: 5 x 12.5 g and 25 x 12.5 g.

STORAGE CONDITIONS: Store below 25˚C. Single use only. Discard unused portion.

NAME AND ADDRESS OF THE SPONSOR

Sponsor: KSJ Pharmatech

Distributed in Australia by
InterPharma Pty Ltd
Suite 103, 39 East Esplanade
Manly NSW 2095
Ph: 02 9976 6876

Distributed in New Zealand by
InterPharma Pty Ltd
C/- Healthcare Logistics
58 Richard Pearse Drive
Airport Oaks, Mangere 2022, Ph: 09 918 5100

POISON SCHEDULE OF THE MEDICINE

PHARMACY ONLY MEDICINE S2.

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (The ARTG) : 01 / August/2016.