2% XYLOCAINE® Dental with Adrenaline 1:80,000

PRODUCT INFORMATION

NAME OF THE MEDICINE

2% XYLOCAINE® Dental with Adrenaline 1:80,000

contains lignocaine hydrochloride and adrenaline acid tartrate as the active substances. The product also contains sodium chloride, sodium metabisulfite, water for injections, and may contain sodium hydroxide and/or hydrochloric acid for pH adjustment to 3.3-5.0.

Lignocaine

The CAS number for lignocaine is 137-58-6.
The chemical name for lignocaine hydrochloride is 2-Diethylaminoaceto-2’,6’-xylidide hydrochloride. The BP name and International Non-proprietary Name (INN) for lignocaine is lidocaine.

The Australian Approved Name (AAN) is lignocaine hydrochloride.

Lignocaine base has a pKa of 7.85 (25°C) and a molecular weight of 234.3.

The chemical structure of lignocaine hydrochloride is:

![Chemical structure of lignocaine hydrochloride]

Adrenaline

The CAS number for adrenaline acid tartrate is 51-42-3.
The chemical name for adrenaline is (R)-1-(3,4-Dihydroxyphenyl)-2-methylaminoethanol. The salt used in this product is adrenaline acid tartrate. Adrenaline is also known as epinephrine.

The Australian Approved Name is adrenaline acid tartrate.
The chemical structure of adrenaline is:

\[
\text{HO} \quad \text{H} \quad \text{OH} \\
\text{HO} \quad \text{N} \quad \text{NHCH}_3
\]

**DESCRIPTION**

Lignocaine is classed as a membrane stabilising agent, and is a local anaesthetic of the amide type. Lignocaine hydrochloride is a white crystalline powder with a molecular weight of 288.8. It is very soluble in water and freely soluble in alcohol and chloroform. It must be protected from light.

Adrenaline is a potent sympathomimetic. Adrenaline acid tartrate is a white to greyish-white crystalline powder with a molecular weight of 333.3. It is freely soluble in water and slightly soluble in alcohol.

**PHARMACOLOGY**

Lignocaine stabilises the neuronal membrane and reversibly prevents the initiation and conduction of nerve impulses thereby producing local anaesthesia.

The onset and duration of anaesthesia depend on the route of administration and the dosage (volume and concentration) employed. The addition of adrenaline reduces the rate of absorption of lignocaine from the site of injection, thereby increasing the duration of action.

Lignocaine is metabolised mainly in the liver and excreted via the kidneys. Approximately 90% of administered lignocaine is excreted in the form of various metabolites while less than 10% is excreted unchanged. Lignocaine has an elimination half life of approximately 1.8 hours in healthy adults, depending on the site of injection.

**INDICATIONS**

Lignocaine solutions are indicated for the production of local anaesthesia in routine dental procedures and oral surgery by means of infiltration and nerve block techniques.

Lignocaine solutions with adrenaline are recommended for oral surgery requiring prolonged duration of anaesthesia and haemostasis.

**CONTRAINDICATIONS**

1. Allergy or hypersensitivity to amide type local anaesthetics or other components of the injection solution which may be present eg. sodium metabisulfite (see note under PRESENTATION AND STORAGE CONDITIONS).
2. Local anaesthetic techniques must not be used when there is inflammation and/or sepsis in the region of the proposed injection.

The following are additional contraindications for solutions with adrenaline:

3. Solutions with adrenaline should not be used in patients with a known sensitivity to sympathomimetic amines.

4. Solutions with adrenaline should not be used in most patients with cerebral arteriosclerosis.

See also INTERACTIONS WITH OTHER MEDICINES

PRECAUTIONS

1. WHEN ANY LOCAL ANAESTHETIC AGENT IS USED, RESUSCITATIVE EQUIPMENT AND DRUGS, INCLUDING OXYGEN, SHOULD BE IMMEDIATELY AVAILABLE IN ORDER TO MANAGE POSSIBLE ADVERSE REACTIONS INVOLVING THE CARDIOVASCULAR, RESPIRATORY OR CENTRAL NERVOUS SYSTEMS.

2. INJECTION SHOULD ALWAYS BE MADE SLOWLY WITH FREQUENT ASPIRATIONS TO AVOID INADVERTENT INTRAVASCULAR INJECTION WHICH CAN PRODUCE TOXIC EFFECTS. MULTIPLE INJECTIONS SHOULD BE ADMINISTERED AT SPACED INTERVALS.

3. The safety and effectiveness of lignocaine depend on proper dosage, correct technique and adequate precautions. Standard textbooks should be consulted regarding specific techniques and precautions for various anaesthetic procedures.

4. Lignocaine should be given with great caution to patients with severe bradycardia, cardiac conduction disturbances or severe digitalis intoxication.

5. Lignocaine and/or its metabolites may accumulate during prolonged or repeated administration in patients with hepatic, renal or cardiac diseases. However, this is unlikely to occur at the doses normally used in dentistry.

6. Adrenaline-containing solutions should be used with extreme caution in patients with severe or untreated hypertension, arteriosclerotic heart disease, heart block, cerebral vascular insufficiency, thyrotoxicosis, advanced diabetes or any other pathological condition that might be aggravated by the effects of adrenaline. Adrenaline may induce anginal pain in patients suffering from ischaemic heart disease. The use of CITANEST-OCTAPRESSIN solutions may be preferable in these conditions.

7. Lignocaine should be used with caution in patients with known drug sensitivities. Patients allergic to ester derivatives of para-aminobenzoic acid (procaine, tetracaine, benzocaine etc.) have not shown cross
sensitivity to agents of the amide type.

8. Lignocaine should be used with caution in patients with genetic predisposition to malignant hyperthermia as the safety of amide local anaesthetic agents in these patients has not been fully established.

9. The patient should be advised to exert caution to avoid inadvertent trauma to the lips, tongue, cheek mucosa or soft palate when these structures are anaesthetised. Eating and drinking hot liquids should therefore be postponed until normal function returns.

10. Although the dose of Xylocaine with adrenaline administered in dental practice is generally small, some patients eg. the elderly and patients in poor general health, may require special attention to reduce the risk of dangerous side effects.

11. Lignocaine with adrenaline solutions contain sodium metabisulfite, a sulfite that may cause allergic type reactions including anaphylactic symptoms and life threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than non-asthmatic people.

**Carcinogenicity/Mutagenicity/Impairment of Fertility**

A two-year oral toxicity study of 2,6-xylidine, a metabolite of lignocaine, has shown that in both male and female rats, 2,6-xylidine in daily doses of 900 mg/m² (150 mg/kg) resulted in carcinomas and adenomas of the nasal cavity. No nasal tumours were observed in the low dose (15 mg/kg or control animals). In addition, the compound also caused subcutaneous fibromas and fibrosarcomas in male and female rats (significant at 150 mg/kg).

The genotoxic potential of 2,6-xylidine has been studied with mixed results: Positive results were reported in assays for gene mutations (weakly positive in the Ames test with metabolic activation and in the mouse lymphoma assay) and chromosomal damage (chromosomal aberrations in Chinese hamster ovary cells at concentrations at which the drug precipitated from solution). No evidence of genotoxicity was found in *in vivo* assays for chromosomal damage (micronucleus assay) and DNA damage (unscheduled DNA synthesis). Covalent binding studies of DNA from liver and ethmoid turbinates in rats indicate that 2,6-xylidine may be genotoxic under certain conditions *in vivo*.

**USE IN PREGNANCY** Category A

The safe use of lignocaine during pregnancy has not been established. Lignocaine has, however, been used extensively for dental procedures during pregnancy with no reports of ill effects to mother or foetus.

**USE DURING LACTATION**

Lignocaine passes into breast milk. The amount of lignocaine appearing in breast milk from a nursing mother
receiving parenteral lignocaine is unlikely to lead to a significant accumulation of the parent drug in the breast-fed infant. The remote possibility of an idiosyncratic or allergic reaction in the breast-fed infant from lignocaine remains to be determined.

**Effects on ability to drive and operate machinery**
Depending on dosage, local anaesthetics may have a very mild effect on mental function and may temporarily impair locomotion and coordination.

**INTERACTIONS WITH OTHER MEDICINES**

1. **Antiarrhythmic drugs**
Local anaesthetics of the amide type should be used with caution in patients receiving anti-arrhythmic drugs eg. mexiletine, or any other agents structurally related to local anaesthetics, since potentiation of cardiac effects may occur.

2. **Amiodarone**
Amiodarone has been reported to reduce the clearance of lignocaine in two case reports, although a small prospective study of combined therapy on lignocaine pharmacokinetics found no change in clearance or other pharmacokinetic factor.
This combination has been reported to precipitate seizures and to lead to severe sinus bradycardia and a long sinoatrial arrest. Until more experience with concurrent use of lignocaine and amiodarone becomes available, patients receiving the combination should be monitored carefully.

3. **Anticonvulsive agents**
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.

4. **Inhalational anaesthetics**
Lignocaine decreases the minimum effective concentration of inhalational anaesthetics, e.g. nitrous oxide.

The following interactions may occur with adrenaline-containing solutions:

5. **CNS acting drugs**
Solutions containing adrenaline should be used with extreme caution in patients receiving tricyclic antidepressants since severe hypertension may result, or phenothiazines and butyrophenones which may reduce or reverse the pressor effects of adrenaline, giving rise to hypotensive response and tachycardia.

6. **Oxytocic drugs of the ergot-type**
Adrenaline-containing solutions should not be used in the presence of oxytocic drugs of the ergot-type as they are known to interact to produce severe, persistent hypertension and its subsequent sequelae.
7. Adrenergic neuron blocking agents
Solutions containing adrenaline should be used with caution in the presence of adrenergic neuron blocking agents (e.g., guanethidine, debrisoquine, bethanidine).

8. Inhalation anaesthetics
Serious cardiac arrhythmias may occur if preparations containing adrenaline are employed in patients during or following the administration of chloroform, halothane, cyclopropane, trichlorethylene, or other halogenated compounds.

9. Cardiac glycosides
Solutions containing adrenaline may interact with cardiac glycosides resulting in arrhythmias.

10. Quinidine
Solutions with adrenaline may interact with quinidine resulting in cardiac arrhythmias.

11. Hypoglycaemics
Adrenaline-induced hyperglycaemia may lead to loss of blood sugar control in diabetic patients treated with hypoglycaemic agents.

12. Beta-blockers
Non-cardioselective betablockers such as propanolol enhance the pressor effect of adrenaline, which may lead to severe hypertension and bradycardia.

ADVERSE EFFECTS
Reactions to lignocaine are very rare in the doses used in dental procedures. If adverse reactions occur, they are similar in character to those observed with other local anaesthetics of the amide type.

Adverse reactions may be due to high plasma levels as a result of excessive dosage, rapid absorption, delayed elimination or metabolism, or inadvertent intravascular injection. Such reactions are systemic in nature and involve the central nervous system and/or the cardiovascular system (see OVERDOSAGE). Pronounced acidosis or hypoxia may increase the risk and severity of toxic reactions.

The following adverse events have been observed during use of lignocaine medical injections and have not necessarily been associated with the dental use of lignocaine.

More common reactions
Nervousness, dizziness, blurred vision, tremor, drowsiness, tinnitus, numbness, disorientation, nausea and vomiting.

Less common reactions
More serious but less common reactions that reflect an overdosage of lignocaine are convulsions,
unconsciousness, respiratory depression or arrest, hypotension, cardiovascular collapse and bradycardia which may lead to cardiac arrest.

**Allergy**
Allergy to amide type local anaesthetics is very rare but may present as allergic dermatitis, bronchospasm or anaphylaxis. However, sodium metabisulfite (which is in the adrenaline containing products) may cause this type of reaction.

**Neurological reactions**
The incidence of adverse neurological reactions directly caused by the use of local anaesthetics is very low.

Neurological reactions may be related to the total dose of the local anaesthetic administered and are also dependent upon the particular drug used, the route of administration and the physical status of the patient. Many of these effects may be related to local anaesthetic techniques, with or without contribution from the drug.

Neurological reactions following regional nerve blocks have included persistent numbness, paraesthesia and sensory disturbances.

**DOSAGE AND ADMINISTRATION**

The lowest dosage that results in effective anaesthesia for the planned treatment should be used. The dosage will also depend on the area of the oral cavity to be anaesthetised, the vascularity of the oral tissues and the technique of anaesthesia.

**Adults**

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<td>1.5 - 5 mL</td>
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<td>90 min</td>
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<tr>
<td>Soft tissue</td>
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**Note**

1. **Recommended doses**
Toxic doses vary widely between patients and toxic effects may occur after any local anaesthetic procedure. Careful observation of the patient must therefore be maintained. It is recommended that the dose of lignocaine at any one time should not exceed 7mg/kg (adrenaline containing solutions). However, the dose administered must be tailored to the individual patient and procedure, and the maximum doses here quoted should be used as
2. **Safe dose**

The safe dose for people with acute or chronic disease, especially those on medications, may be substantially less.

**Paediatric**

For children, the dose may have to be reduced commensurate with body weight.

**OVERDOSAGE**

Systemic toxicity to amide type local anaesthetics is initially manifested as CNS excitation and may result in a slow onset of nervousness, dizziness, blurred vision and tremors followed by drowsiness, convulsions, unconsciousness and possibly respiratory arrest.

Toxic cardiovascular reactions to local anaesthetics are usually depressant in nature, may occur rapidly and with little warning and can lead to peripheral vasodilation, hypotension, myocardial depression, bradycardia and possibly cardiac arrest.

Treatment of a patient with toxic symptoms consists of ensuring a patent airway and supporting ventilation with oxygen and assisted or controlled respiration as required. This usually will be sufficient in the management of most reactions.

Further treatment depends on diagnosis. Medical assistance should be summoned.

If convulsions occur, intravenous diazepam should be administered incrementally. Sodium thiopentone (5 mg/kg) may be used if diazepam is unavailable or ineffective. If convulsions interfere with breathing and/or are not rapidly controlled by specific anticonvulsant medication, suxamethonium (1-2 mg/kg) may be used to paralyse the patient. Artificial ventilation must then be instituted.

If ventricular fibrillation or cardiac arrest occurs, effective cardiovascular resuscitation treatment must be instituted and maintained for a prolonged period if necessary.

**PRESENTATION AND STORAGE CONDITIONS**

**2% XYLOCAINE Dental with adrenaline 1:80,000**

Lignocaine hydrochloride 46.9 milligram/2.2 mL + adrenaline acid tartrate 49.9 microgram/2.2 mL

Excipients: sodium chloride, sodium metabisulfite, water for injections
May contain sodium hydroxide and/or hydrochloric acid for pH adjustment to 3.0-5.0

2.2 mL standard and self-aspirating cartridges
Note:

1. Adrenaline-containing solutions contain the antioxidant sodium metabisulphite, 1.1 mg/2.2 mL.

2. All Dentsply Xylocaine dental cartridges (with adrenaline) are paraben free and for single use in a single patient only. Remaining unused contents should be discarded.

2% XYLOCAINE® Dental with Adrenaline 1:80,000 should be stored at 2°C to 8°C (Refrigerate. Do not freeze) and protected from light.

Once removed from refrigeration for use, store below 25°C and use within 4 weeks. Do not return to refrigerator.

Excursions outside the recommended storage temperature are permitted during transport.

Local anaesthetics react with certain metals and cause the release of their respective ions which, if injected, may cause severe local irritation. Adequate precautions should be taken to avoid prolonged contact between lignocaine solutions and metal surfaces e.g. cartridges should not be preloaded and connected to needles until just prior to use.

Cartridges showing discolouration or cracks should be discarded. Adrenaline-containing solutions should not be autoclaved. Surface sterilisation using pure, undiluted isopropyl alcohol (91%) or 70% ethyl alcohol (USP) may be carried out if desired.

Xylocaine® is a registered trademark used under licence from AstraZeneca AB.

NAME AND ADDRESS OF THE SPONSOR
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POISON SCHEDULE OF THE MEDICINE
Australian Poisons Schedule: S4
New Zealand Medicine Classification: Prescription Medicine

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS
(the ARTG)
February 28, 2005

DATE OF MOST RECENT AMENDMENT
4 March 2014