

AUSTRALIAN PRODUCT INFORMATION

2% Xylocaine® DENTAL with adrenaline (epinephrine) 1:80,000

(lidocaine (lignocaine) hydrochloride and adrenaline (epinephrine) acid tartrate)

1 NAME OF THE MEDICINE

lidocaine (lignocaine) hydrochloride
adrenaline (epinephrine) acid tartrate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

2% Xylocaine® DENTAL with adrenaline (epinephrine) 1:80,000 is a clear, colourless sterile aqueous solution that contains lidocaine (lignocaine) hydrochloride 2% (21.3 mg/mL) and adrenaline (epinephrine) acid tartrate (22.7 mcg/mL) in a 1:80,000 strength.

Lidocaine (lignocaine) is classed as a membrane stabilising agent, and is a local anaesthetic of the amide type. Lidocaine (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 (epinephrine) is a potent sympathomimetic.

Adrenaline (epinephrine) 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.

2% Xylocaine® DENTAL with adrenaline (epinephrine) 1:80,000 injection contains the excipient with known effect, sodium metabisulfite. For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

2% Xylocaine® DENTAL with adrenaline (epinephrine) 1:80,000

Lidocaine (lignocaine) hydrochloride 46.9 milligram/2.2 mL + adrenaline (epinephrine) acid tartrate 49.9 microgram/2.2 mL

2.2 mL standard and self-aspirating cartridges

Note:

1. Adrenaline (epinephrine)-containing solutions contain the antioxidant sodium metabisulphite, 1.1 mg/2.2 mL.
2. All Dentsply Sirona Xylocaine dental cartridges (with adrenaline (epinephrine)) are paraben free and for single use in a single patient only. Remaining unused contents should be discarded.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Lidocaine (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.

Lidocaine (lignocaine) solutions with adrenaline (epinephrine) are recommended for oral surgery requiring prolonged duration of anaesthesia and haemostasis.

4.2 DOSE AND METHOD OF 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

RECOMMENDED DOSAGES FOR LIDOCAINE (LIGNOCAINE) 2% (20mg/mL) WITH ADRENALINE (EPINEPHRINE) 1:80,000 (12.5 microgram/mL) IN THE AVERAGE, HEALTHY 70kg ADULT		
	Infiltration	Block
Suggested dosage	1-2 mL	1.5 - 5 mL
Onset of action (approx)	1.5 minutes	4 minutes
Duration of action		
Pulp	60 minutes	90 minutes
Soft tissue	3 hours	3 hours

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 lidocaine (lignocaine) at any one time should not exceed 7mg/kg (adrenaline (epinephrine) 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 a guide only.

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.

4.3 CONTRAINDICATIONS

1. Allergy or hypersensitivity to amide type local anaesthetics or other components of the injection solution which may be present e.g. sodium metabisulfite (see note under Section 3 Pharmaceutical Form).
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 (epinephrine):

3. Solutions with adrenaline (epinephrine) should not be used in patients with a known sensitivity to sympathomimetic amines.
4. Solutions with adrenaline (epinephrine) should not be used in most patients with cerebral arteriosclerosis.

See also Section 4.5 Interactions with Other Medicines and Other Forms of Interactions

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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 lidocaine (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. Lidocaine (lignocaine) should be given with great caution to patients with severe bradycardia, cardiac conduction disturbances or severe digitalis intoxication.
5. Lidocaine (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 (epinephrine)-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 (epinephrine). Adrenaline (epinephrine) 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 (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 (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. Lidocaine (lignocaine) with adrenaline (epinephrine) 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.
11. 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 lidocaine (lignocaine) solutions and metal surfaces e.g. cartridges should not be preloaded and connected to needles until just prior to use.
12. Cartridges showing discolouration or cracks should be discarded. Adrenaline (epinephrine)-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.

Use in the elderly

Although the dose of Xylocaine with Adrenaline (epinephrine) administered in dental practice is generally small, some patients e.g. the elderly and patients in poor general health, may require special attention to reduce the risk of dangerous side effects.

Paediatric use

See Section 4.2 Dose and Method of Administration.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

1. Antiarrhythmic drugs

Local anaesthetics of the amide type should be used with caution in patients receiving anti-arrhythmic drugs e.g. 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 lidocaine (lignocaine) in two case reports, although a small prospective study of combined therapy on lidocaine (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 lidocaine (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 lidocaine (lignocaine) but the significance of this effect is not known. Phenytoin and lidocaine (lignocaine) have additive cardiac depressant effects.

4. Inhalational anaesthetics

Lidocaine (lignocaine) decreases the minimum effective concentration of inhalational anaesthetics, e.g. nitrous oxide.

The following interactions may occur with adrenaline (epinephrine)-containing solutions:

5. CNS acting drugs

Solutions containing adrenaline (epinephrine) 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 (epinephrine), giving rise to hypotensive response and tachycardia.

6. Oxytocic drugs of the ergot-type

Adrenaline (epinephrine)-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 (epinephrine) 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 (epinephrine) are employed in patients during or following the administration of chloroform, halothane, cyclopropane, trichlorethylene, or other halogenated compounds.

9. Cardiac glycosides

Solutions containing adrenaline (epinephrine) may interact with cardiac glycosides resulting in arrhythmias.

10. Quinidine

Solutions with adrenaline (epinephrine) may interact with quinidine resulting in cardiac arrhythmias.

11. Hypoglycaemics

Adrenaline (epinephrine)-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 propranolol enhance the pressor effect of adrenaline, which may lead to severe hypertension and bradycardia.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy

Category A

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

Use in lactation

Lidocaine (lignocaine) passes into breast milk. The amount of lidocaine (lignocaine) appearing in breast milk from a nursing mother receiving parenteral lidocaine (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 lidocaine (lignocaine) remains to be determined.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Reactions to lidocaine (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 Section 4.9 Overdose). Pronounced acidosis or hypoxia may increase the risk and severity of toxic reactions.

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

Reporting suspected adverse effects

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 www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia) and 0800 764 766 (New Zealand).

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.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Lidocaine (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 (epinephrine) reduces the rate of absorption of lidocaine (lignocaine) from the site of injection, thereby increasing the duration of action.

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

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

No data available.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

The genotoxic potential of 2,6-xylylidine, a metabolite of lidocaine (lignocaine), 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-xylylidine may be genotoxic under certain conditions *in vivo*.

Carcinogenicity

A two-year oral toxicity study of 2,6-xylylidine, has shown that in both male and female rats, 2,6-xylylidine 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 or fibrosarcomas in male and female rats (significant at 150 mg/kg).

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

2% Xylocaine® DENTAL with adrenaline (epinephrine) 1:80,000 contains sodium chloride, sodium metabisulfite, water for injections, and may contain sodium hydroxide and/or hydrochloric acid for pH adjustment.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

2% Xylocaine® DENTAL with adrenaline (epinephrine) 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.

6.5 NATURE AND CONTENTS OF CONTAINER

Presentation	Fill Size	Pack Size	Cartridge Type*
2% Xylocaine® DENTAL with adrenaline (epinephrine) 1:80,000	2.2mL	50, 100	Standard and self-aspirating cartridges

*Type I glass cartridges

Not all pack sizes/presentations are being distributed.

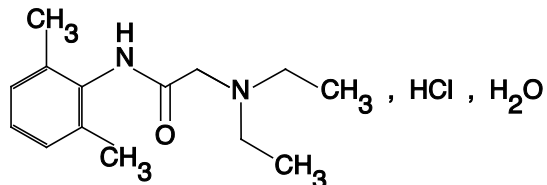
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

The chemical structure of lidocaine (lignocaine) hydrochloride is:

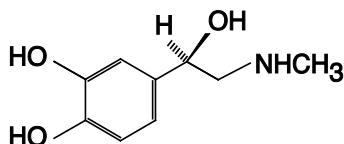


The chemical name for lidocaine (lignocaine) hydrochloride is 2-Diethylaminoaceto-2',6'-xylylide hydrochloride. The BP name and International Non-proprietary Name (INN) for lignocaine is lidocaine.

The Australian Approved Name (AAN) is lidocaine (lignocaine) hydrochloride.

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

The chemical structure of adrenaline (epinephrine) is:



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

The Australian Approved Name is adrenaline (epinephrine) acid tartrate.

CAS Number

The CAS number for lidocaine (lignocaine) is 137-58-6.

The CAS number for adrenaline (epinephrine) acid tartrate is 51-42-3.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Australian Poisons Schedule: S4 – Prescription Only Medicine
New Zealand Medicine Classification: Prescription Medicine

8 SPONSOR

Australia

Dentsply Sirona Pty Ltd
11-21 Gilby Road
Mount Waverley, VIC 3149
Australia
www.dentsplysirona.com.au

New Zealand

Dentsply Sirona (N.Z.) Limited
c/o- Lowndes Jordan
Level 15, PWC Tower
188 Quay Street
Auckland 1010
New Zealand
www.dentsplysirona.co.nz

9 DATE OF FIRST APPROVAL

13 August 1991

10 DATE OF REVISION

26 October 2018

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

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All sections	<ul style="list-style-type: none">• Updated PI format according to the new requirements• Updated the expression of the Drug Product and Drug Substances
Section 8	Updated sponsor information