NEW ZEALAND DATA SHEET

1 PRODUCT NAME

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

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

2% Xylocaine® DENTAL with adrenaline (epinephrine) 1:80,000 consists of lidocaine (lignocaine) hydrochloride 2% (21.3 mg/mL) and adrenaline (epinephrine) acid tartrate (22.7 mcg/mL) in a 1:80,000 strength.

2% Xylocaine® DENTAL with adrenaline (epinephrine) 1:80,000 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 is a sterile aqueous solution. The pH of the solution is 3.3 – 5.0.

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

The cartridges are free from preservatives and are intended for single use only.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Lidocaine (lignocaine) solutions are indicated for the production of local nerve 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

2% Xylocaine® DENTAL with adrenaline (epinephrine) 1:80,000 has a rapid onset of action after infiltration, averaging 2-3 minutes. Inferior alveolar nerve block requires 5 minutes or more to take full effect. The duration of effective anaesthesia varies in individuals and depends on the type of anaesthetic technique. The average duration of useful anaesthesia after infiltration is 60 minutes. After successful regional anaesthesia, e.g. inferior alveolar nerve block, anaesthesia lasts for 2 hours or longer.

Injections should always be made slowly, with careful aspiration before and intermittently during injection, to avoid inadvertent intravascular injection, which may have toxic effects.

The lowest dose that results in effective anaesthesia should be used. The dose will also depend on the area of the oral tissues to be anaesthetised, the vascularity of the oral tissues and the technique of anaesthesia. The total dose must be adjusted to the age, size and physical status of the patient.

For effective local anaesthesia in most dental procedures, an adequate dose of 2% Xylocaine® DENTAL with adrenaline (epinephrine) 1:80,000 solution injected into the tissues is as follows.

Adults
In normal healthy adults: 1-5 mL (equivalent to 20-100 mg lidocaine (lignocaine) hydrochloride). For routine dental procedures, a dose of 10 mL (equivalent to 200 mg lidocaine (lignocaine) hydrochloride) should not be exceeded.

Children under 10 years of age
1-2 mL (equivalent to 20-40 mg lidocaine (lignocaine) hydrochloride)

A rapid rate of injection may lead to complications due to the high concentration (see Section 4.9 Overdose) even after injection of small amounts. This is more likely following accidental intravascular injection. The injected medicine could be transported in a retrograde manner along a blood vessel and, in cases of intra-arterial injection in the head and neck area, reach the brain.

Instructions for Use/Handling
Adequate precautions should be taken to avoid prolonged contact between local anaesthetic solutions containing adrenaline (epinephrine) (low pH) and metal surfaces (e.g. needles or metal parts of syringes) since dissolved metal ions, particularly copper ions, may cause severe local irritation (swelling, oedema) at the site of injection and accelerate the degradation of adrenaline (epinephrine).

Surface sterilisation using pure, undiluted isopropyl alcohol (91%) or 70% ethyl alcohol may be carried out if desired. Do not soak or autoclave.

The solutions which are free from preservative should be used immediately after opening of the container. Any unused solution should be discarded.

Aspiration (preferably by the use of passive-type aspiration systems) prior to injection is recommended since this reduces the possibility of intravascular injection, thereby keeping the incidence of side effects and anaesthetic failure to a minimum.

In order to avoid traumatic nerve injuries leading to paraesthesia in conjunction with dental nerve block, an atraumatic technique should be used. Dental cartridge systems may generate high pressures during injection, leading to local anaesthetics distributing in a retrograde manner along a nerve in cases of intraneural injection. If an accidental traumatic nerve injury has occurred, the adrenaline (epinephrine) content in 2% Xylocaine® DENTAL with adrenaline (epinephrine) 1:80,000 may aggravate the local neurotoxicity by decreasing the intraneural blood circulation.

4.3 Contraindications

Known hypersensitivity to local anaesthetics of the amide type, or other components of the solution, e.g. sodium metabisulfite in solutions containing adrenaline (epinephrine).

4.4 Special warnings and precautions for use

The safety and effectiveness of the local anaesthetic agent, lidocaine (lignocaine) hydrochloride, depends on the proper dosage, correct injection technique, adequate precautions and readiness for emergencies.

Before administering a local anaesthetic medicine, make sure that resuscitative equipment, such as equipment required for oxygenation and assisted ventilation, and medicines for the treatment of toxic reactions are immediately available.

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. The ingestion of food should therefore be postponed until normal function and sensation returns.

In the head and neck area, due to the proximity of the CNS, the intravascular injection of even small doses of local anaesthetics may cause systemic adverse reactions similar to those seen after the inadvertent intravascular injection of larger doses in other parts of the body.

Even if the dose of 2% Xylocaine® DENTAL with adrenaline (epinephrine) 1:80,000 used in dental practice is generally small, some patients may require special attention to reduce the risk of dangerous side effects:

- Patients with partial or complete heart block, due to the fact that local anaesthetics may depress myocardial conduction.
- Patients with advanced liver disease or severe renal dysfunction.
- The elderly and patients in poor general condition.

Local anaesthetics, especially those containing adrenaline (epinephrine), should be administered with caution to patients with severe or untreated hypertension, severe heart disease, advanced diabetes, severe anaemia or circulatory failure from whatever cause, thyrotoxicosis 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. Local anaesthetics should be avoided when there is infection in the region of the proposed injection.

2% Xylocaine® DENTAL with adrenaline (epinephrine) 1:80,000 contains 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 in non-asthmatic people.

4.5 Interaction with other medicines and other forms of interaction

Lidocaine (lignocaine) should be used with caution in patients receiving agents structurally related to local anaesthetics e.g. tocainide, since the toxic effects are additive.

Solutions containing adrenaline (epinephrine) should generally be avoided or used with care in patients receiving tricyclic antidepressants since severe, prolonged hypertension may be the result. In addition, the concurrent use of adrenaline (epinephrine)-containing solutions and oxytocic medicines of the ergot type may cause severe, persistent hypertension and possibly cerebrovascular and cardiac accidents. Phenothiazines and butyrophenones may reduce or reverse the pressor effect of adrenaline (epinephrine), giving rise to hypertensive response and tachycardia.

Non-cardioselective betablockers such as propranolol enhance the pressor effects of adrenaline (epinephrine), which may lead to severe hypertension and bradycardia.

Serious cardiac arrhythmias may occur if preparations containing a vasoconstrictor, such as adrenaline (epinephrine), are employed during or following the administration of volatile inhalation anaesthetics such as halothane.

4.6 Fertility, pregnancy and lactation

Pregnancy

It is reasonable to assume that a large number of pregnant women and women of child-bearing age have been given lidocaine (lignocaine) with or without adrenaline (epinephrine). No specific disturbances to the reproductive process have so far been reported, e.g. no increased incidence of malformations, or other direct or indirect harmful effects on the foetus.

Breast-feeding
Lidocaine (lignocaine) may enter the mother's milk, but in such small amounts that there is generally no risk of this affecting the neonate. It is not known whether adrenaline (epinephrine) enters breast milk or not, but it is unlikely to affect the breast-fed child.

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 co-ordination.

4.8 Undesirable effects

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

Allergic Reactions
Allergic reactions (in the most severe instances anaphylactic shock) to local anaesthetics of the amide type are rare. However, other constituents of the solutions, e.g. sodium metabisulfite, may cause this type of reaction.

Neurological Complications
The incidence of adverse neurological reactions (e.g. persistent neurological deficit) associated with the use of local anaesthetics is very low. Neurological reactions may be dependent upon the particular medicine used, the route of administration and the physical status of the patient. Many of these effects may be linked to the injection techniques, with or without a contribution by the medicine (see Section 4.2 Dose and method of administration, Instructions for use/handling). Neurological reactions following regional nerve blocks have included persistent numbness, paraesthesia and other sensory disturbances.

Acute Systemic Toxicity
Lidocaine (lignocaine) may cause acute toxic effects if high systemic levels occur due to accidental intravascular injection or overdosage. (See Section 4.9 Overdose and 5.1 Pharmacodynamic properties)

Reporting of suspected adverse effects
Reporting suspected adverse reactions after authorization of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

Acute emergencies are, in general, dose-related and may result from high plasma levels caused by excessive dosage, rapid absorption (i.e. rate of increase of plasma concentration) or unintentional intravascular injection, or may result from hypersensitivity or diminished tolerance on the part of the patient.

Acute Systemic Toxicity
CNS reactions are excitatory or depressant and may be characterised by nervousness, twitching, tinnitus, euphoria, drowsiness, blurred or double vision, dizziness, convulsions, unconsciousness and possibly respiratory arrest. The excitatory reactions may be very brief or may not occur at all, in which case the first manifestation of toxicity is drowsiness merging into unconsciousness and even respiratory arrest.

Cardiovascular reactions are depressant and may be characterised by hypotension, myocardial depression, bradycardia and possibly cardiac arrest. Signs and symptoms of depressed cardiovascular function may commonly result from a vasovagal reaction, particularly if the patient is in an upright position. Less commonly, they may occur as a direct effect of the medicine. Failure to recognise premonitory signs such as sweating, a feeling of faintness, changes in pulse or sensorium may result in progressive cerebral hypoxia and seizure or serious cardiovascular collapse.

Cardiovascular effects are usually only seen in the most severe cases and are generally preceded by signs of toxicity in the central nervous system.

Acidosis or hypoxia in the patient may increase the risk and severity of toxic reactions. Such reactions involve the central nervous system and the cardiovascular system.

Treatment of Acute Toxicity

1. Put the patient in a supine position. Raise the legs 30°-45° above the horizontal level.
2. Ensure a patent airway. If ventilation is inadequate, ventilate the patient, with oxygen if available. This is important since toxicity increases with acidosis.
3. The treatment of convulsions consists of ensuring a patent airway and arresting convulsions. Should convulsions persist despite adequate ventilation, diazepam 0.1 mg/kg or thiopentone sodium 1-3 mg/kg should be administered intravenously to arrest the convulsions. Since this treatment may also depress respiration, a means of mechanically supporting or controlling ventilation should be available.
4. Supportive treatment of circulatory depression may require the administration of intravenous fluids and, when appropriate, a vasopressor (e.g. ephedrine 5-10 mg IV and repeated, if necessary, after 2-3 min), as governed by the clinical situation.
5. If the patient is unresponsive and the carotid pulse rate is totally absent, start external cardiac massage and mouth to mouth resuscitation.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Amides, ATC code: N01BB52

Lidocaine (lignocaine), like other local anaesthetics, causes a reversible blockade of impulse propagation along nerve fibres by preventing the inward movement of sodium ions through the nerve membrane. Local anaesthetics of the amide type are thought to act within the sodium channels of the nerve membrane.

The addition of adrenaline (epinephrine) decreases the rate of absorption of lidocaine (lignocaine) from the site of injection, increasing the duration of effect.

Local anaesthetic medicines may have similar effects on excitable membranes in the brain and myocardium. If excessive amounts of medicine reach the systemic circulation rapidly, symptoms and signs of toxicity will appear, emanating mainly from the central nervous and cardiovascular systems.

Central nervous system toxicity (see OVERDOSAGE) usually precedes the cardiovascular effects since it occurs at lower plasma concentrations. Direct effects of local anaesthetics on the heart include slow conduction, negative inotropism and eventually cardiac arrest.

5.2 Pharmacokinetic properties

Lidocaine (lignocaine) has a pKa of 7.9, an oil/water partition coefficient of 2.9, and is 65% protein-bound (mainly to alpha-1-acid glycoprotein) in plasma.

Lidocaine (lignocaine) has a total plasma clearance of 0.95 L/min, a volume of distribution at steady state of 91 L, an elimination half-life of 1.6 h and an estimated hepatic extraction ratio of 0.65. The clearance of lidocaine (lignocaine) is almost entirely due to liver metabolism, and depends both on liver blood flow and the activity of metabolising enzymes.

The elimination half-life in neonates (3.2 h) is approximately twice that of adults.

Lidocaine (lignocaine) readily crosses the placenta and equilibrium in regard to free, unbound medicine will be reached. Because the degree of plasma protein binding in the foetus is less than in the mother, the total plasma concentration will be greater in the mother, but the free concentrations will be the same.

Lidocaine (lignocaine) is excreted in breast milk, but in such small quantities that there is no risk of affecting the child with therapeutic doses.

Only 2% of lidocaine (lignocaine) is excreted unchanged. Most is metabolised first to monoethylglycinexylidide (MEGX) and then to glycinexylidide (GX) and 2,6-xylidine. Up to 70% appears in the urine as 4-hydroxy-2,6-xylidine.

5.3 Preclinical safety data

No data available.

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

24 months

6.4 Special precautions for storage

Store at 2°C to 8°C (Refrigerate. Do not freeze.). Protect 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 <and special equipment for use, administration or implantation>

Glass Aspirating Dental Cartridge Pack sizes of 50 and 100, 2.2 mL cartridges.
Glass Standard Dental Cartridge Pack sizes of 50 and 100, 2.2 mL cartridges.
Not all pack sizes/presentations are being distributed.

6.6 Special precautions for disposal <and other handling>

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE

Prescription Medicine.

8 SPONSOR

Dentsply Sirona (N.Z.) Limited
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9 DATE OF FIRST APPROVAL

31 December 1969

10 DATE OF REVISION OF THE TEXT

11 December 2018

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

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All sections	• Updated Data Sheet format according to the new requirements • Updated expression of the Drug Product and Drug Substance to ensure consistency of the ingredient name with the International Nonproprietary Name for therapeutic substances
Section 8	Updated sponsor information