New Zealand Data Sheet

1 PRODUCT NAME

XYLESTESIN-A 1/80 000 solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Component	1 mL solution for injection contains	1.7 mL solution for injection contains
Active ingredients		
Lidocaine (lignocaine) hydrochloride *(as monohydrate)*	20 mg	34 mg
Adrenaline (epinephrine) hydrochloride *(equivalent to Adrenaline (epinephrine)*	15 micrograms *12.5 micrograms*	25.5 micrograms *21.25 micrograms*
Excipients with known effect		
Sodium sulfite (E 221)	0.6 mg	1.02 mg
Sodium*	1.71 mg	2.91 mg

*Sodium content of sodium sulfite and sodium chloride
For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection

The solution is a clear, not opalescent, colourless liquid with a pH value of 3.6 to 4.4.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Local anaesthesia (infiltration and nerve-block anaesthesia) in dentistry.
Xylestesin-A is indicated in adults, children and adolescents.

4.2 Dose and method of administration

Xylestesin-A is exclusively recommended for use in dentistry.

Dose

The smallest possible volume of solution which will lead to an effective anaesthesia should be used.

Adults:

The dosage should be determined on an individual basis according to the technique used and particularities of the specific case.

In oral infiltration and/or mandibular block, initial dosages of 1.0 – 4.0 mL are usually sufficient.

Special populations:

Elderly population: Increased plasma levels of Xylestesin-A can occur in older patients due to diminished metabolic processes and reduced distribution volume. The risk of accumulation of Xylestesin-A is particularly increased after repeated.

Dosages should be reduced from adult recommendations, taking into consideration any cardiac or liver disease (see section 4.4).

Patients with hepatic impairment: Lidocaine (lignocaine) is metabolised in the liver. Lower doses of lidocaine (lignocaine) may be required in patients with hepatic dysfunction due to prolonged effects and systemic accumulation. (see section 4.4).

Patients with renal impairment: Lidocaine (lignocaine) and its metabolites are mainly eliminated in urine. Lower doses of lidocaine (lignocaine) may be required in patients with severe renal dysfunction due to prolonged effects and systemic accumulation (see section 4.4)

Other relevant special populations: The dose has to be similarly reduced in patients with certain pre-existing diseases (angina pectoris, arteriosclerosis, see section 4.3 and 4.4) and patients concurrently taking medications known to interact with lidocaine (lignocaine) and/or adrenaline (epinephrine) see section 4.4 and 4.5).

Dose recommendation for special populations: A lower dosage range is thus recommended in all such cases (i.e. minimum volume of Xylestesin-A for sufficient anaesthetic effect).

Paediatric population:

Xylestesin-A is indicated in adults, children and adolescents. Special care has to be exercised when treating children below 4 years. The quantity to be injected should be determined by the age and weight of the child and the magnitude of the operation. The anaesthesia technique should be selected carefully. Painful anaesthesia techniques should be avoided. The behaviour of the child during treatment has to be monitored carefully. The average dose to be used is in the range of 20 mg to 30 mg lidocaine (lignocaine) hydrochloride per session. The dose in mg of lidocaine (lignocaine) hydrochloride which can be administered in children may alternatively be calculated from the expression: child's weight (in kilograms) x 1.33.

Dose recommendation for children and adolescents:

Body weight (kg)	**Recommended dosage**	
	lidocaine (lignocaine) hydrochloride mg/child	solution for injection mL/child
20 - <30	5-20	0.25 mL – 1 mL
30- <40	10-40	0.5 mL – 2 mL
40 - <50		
50 - < 60	10 – 60 mg	0.5 mL – 3 mL
60 - < 70	20 – 80 mg	1 mL – 4 mL
70 - < 80		

Due to the fact that lidocaine (lignocaine) diffuses rapidly into tissues and the density of bones is lower in children compared to adults, infiltration anaesthesia instead of conduction anaesthesia can be preferred in paediatric population.

Maximum Recommended Dosage:

Adults:

For healthy adults, the maximum dose of the active ingredient lidocaine (lignocaine) hydrochloride with vasoconstrictor admixture is 7mg/kg body weight.

Example: The maximum dose for a 70 kg patient is 500 mg. However, due to the addition of adrenaline (epinephrine) 1:80,000, the maximum administered quantity of 16 mL solution for injection or 9 cartridges (equivalent to 0.2 mg adrenaline (epinephrine), maximum dose) must not be exceeded.

Children:

The quantity to be injected should be determined by the age and weight of the child and the magnitude of the operation. Do not exceed the equivalent of 5 mg lidocaine (lignocaine) hydrochloride /kg BW or 0.250 mL Xylestesin-A/kg BW.

Maximum recommended dosage of Xylestesin-A in children and adolescents:

Body weight (kg) (Corresponding paediatric age groups according to ± limits of growth tables)	**Maximum** allowed dose based on 5 mg/kg BW	
	Lidocaine (lignocaine) hydrochloride mg/child	solution for injection mL/child
20 - <30	100	5
30- <40	150	7.5
40 - <50	200	10.0
50 - <60	250	12.5
60 - <70	300	15.0
70 - <80	350	16.0

Method of administration

Dental use

To avoid intravascular injection, aspiration control at least in two planes (rotation of the needle by 180°) must always be carefully undertaken, although a negative aspiration result does not safely rule out an unintentional and unnoticed intravascular injection.

The injection rate should not exceed 0.5 mL in 15 seconds, i.e. 1 cartridge per minute.

Major systemic reactions as a result of accidental intravascular injection can be avoided in most cases by an appropriate injection technique – after aspiration of slow injection of 0.1 – 0.2 mL and slow application of the rest –after allowing an interval of at least 20 – 30 seconds later.

Opened cartridges must not be used in other patients. Residues must be discarded (see section 6.6).

4.3 Contraindications

Xylestesin-A must not be used in the event of

- hypersensitivity to the active substances, sodium sulphite (E221) or to any of the excipients listed in section 6.1,

Due to the active substance lidocaine (lignocaine), Xylestesin-A must not be used in the event of

– known allergy or hypersensitivity to local anaesthetics of the amide type,
– severe, uncontrolled or untreated excitation and conduction disorders of the heart (e.g. grade II and III AV block, pronounced bradycardia),
– acutely decompensated heart failure,
– severe hypotension

Due to the content of adrenaline (epinephrine) as a vasoconstrictor admixture, Xylestesin-A must not be used in the event of

– Heart diseases such as:
  - unstable angina pectoris,
  - recent myocardial infarction,
  - recent coronary artery bypass surgery,
  - refractory arrhythmia and paroxysmal tachycardia or high-frequency, continuous arrhythmia,
  - untreated or uncontrolled severe hypertension,
  - untreated or uncontrolled congestive heart failure,
– concomitant treatment with monoamine oxidase (MAO) inhibitors or tricyclic antidepressants (see section 4.5).
– Xylestesin-A must not be used in acra of extremities

Due to the content of sulphite as excipient, Xylestesin-A must not be used in the event of

- allergy or hypersensitivity to sulphite,
- severe bronchial asthma.

Xylestesin-A can provoke acute allergic reactions with anaphylactic symptoms (e.g. bronchospasm).

4.4 Special warnings and precautions for use

Special warnings

Xylestesin-A must be used with particular caution in the event of

– severely impaired renal and hepatic function,
– angina pectoris (see sections 4.2 and 4.3),
– arteriosclerosis,
– considerably impaired blood coagulation or concomitant treatment with anticoagulants or platelet aggregation inhibitors. The overall risk of bleeding is increased.
– haemorrhagic diathesis – increased bleeding risk particularly with nerve-block anaesthesia,
– uncontrolled or untreated hyperthyroidism,
– narrow-angle glaucoma,
– diabetes mellitus,
– lung diseases – particularly allergic bronchial asthma,
– phaeochromocytoma,

– methaemoglobinaemia,
– impaired cardiovascular function due to decreased ability to compensate prolonged A-V conduction,
– epilepsy (Avoid high doses!),
– blood screening tests on athletes as Xylestesin-A may show positive results. Lidocaine (lignocaine) is not listed in the current WADA list. The listed adrenaline (epinephrine) can be used as a vasoconstrictor in local anaesthetics.

This medicinal product contains less than 1 mmol (23 mg) sodium per 1.7 mL, i.e. essentially “sodium free”.

Precautions for use:

- Information for patients: The patient should be advised to exert caution to avoid inadvertent trauma to the lips, tongue, cheek mucosae or soft palate while these structures are anaesthetised. The patient should therefore avoid eating until the anaesthetic has worn off.

- The lower blood flow in the pulp tissue due to the content of adrenaline (epinephrine) and thus the risk of overlooking an opened pulp, has to be taken into account regarding cavity or crown preparations.

- Injection into an inflamed area should be avoided. The reduced penetration of lidocaine (lignocaine) into inflamed tissue can result in failure of anaesthesia.

- Inadvertent intravascular application must be avoided (see section 4.2). Accidental intravascular injection or accidental overdose may be associated with convulsions, followed by central nervous system depression or cardiorespiratory arrest (see section 4.9).

- Dental practitioners who employ local anaesthetic agents should be well versed in diagnosis and management of emergencies which may arise from their use.

- Each time a local anaesthetic is used the following medicines/therapy as well as an indwelling venous cannula set should be available:

  - Anti-convulsant medicines (benzodiazepines e.g. diazepam), muscle relaxants, glucocorticoids, antihistamine, atropine and vasopressors or adrenaline (epinephrine) as well as an electrolyte solution for a severe allergic or anaphylactic reaction.
  - Resuscitation equipment (in particular a source of oxygen) enabling artificial ventilation if necessary.

- Cardiovascular and respiratory (adequate oxygen supply) vital signs and the patient's state of consciousness should be carefully and constantly monitored after each local anaesthetic injection. Restlessness, anxiety, tinnitus, dizziness, visual disturbances, tremors, depression, or drowsiness may be early warning signs of central nervous system toxicity (see section 4.9).

4.5 Interaction with other medicines and other forms of interaction

Interactions affecting the use of this medicine:

- Contraindications of concomitant use:
  Patients taking MAO inhibitors or tricyclic antidepressants
  The sympathomimetic effect of adrenaline (epinephrine) can be intensified by the simultaneous intake of MAO inhibitors or tricyclic antidepressants (see also section 4.3).

- Concomitant use is not recommended in:
  Patients taking phenothiazines and butyrophenones
  Phenothiazines and butyrophenones may reduce or reverse the pressor effect of adrenaline (epinephrine).
  Concurrent use of these agents should generally be avoided. In situations where concurrent therapy is necessary, careful patient monitoring is essential.

  Patients taking non-selective beta-blockers

  The concomitant administration of non-cardioselective ß-blockers can lead to an increase in blood pressure due to the adrenaline (epinephrine) in Xylestesin-A.

  Inhalational anaesthetics
  Certain inhalational anaesthetics, such as halothane, can sensitise the heart to catecholamines and therefore induce arrhythmias following administration of Xylestesin-A.
  The use of Xylestesin-A during or following treatment with general anaesthesia should be avoided, if possible.

  Patients taking vasopressor and ergot-type oxytocic medicines

  Lidocaine (lignocaine) hydrochloride with adrenaline (epinephrine) 1:80,000 or other vasopressors should not be used concomitantly with ergot-type oxytocic medicines, because a severe persistent hypertension may occur.

Precautions including dose adjustment:

Local anaesthetics
Caution is advised if lidocaine (lignocaine) with adrenaline (epinephrine) is used concurrently with other local anaesthetics. The toxic effects of local anaesthetics are additive.
Lithium carbonate
The duration of the local anaesthetic effect of lidocaine (lignocaine) may be prolonged in patients taking lithium carbonate. Lithium may interact with the sodium channels by replacing extracellular sodium.

Interactions resulting in clinically relevant changes in the use of other medicines:

- Concomitant use is not recommended in:
  Patients taking oral antidiabetics
  Adrenaline (epinephrine) can inhibit insulin release in the pancreas and thus diminish the effect of oral antidiabetics.

Paediatric population
No significant differences can be expected between the adult and paediatric populations with regard to medicine interactions.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is limited data available on the use of Xylestesin-A in pregnant women. Lidocaine (lignocaine) animal studies do not indicate directly or indirectly harmful effects with respect to reproductive toxicity (see section 5.3). Animal studies carried out with adrenaline (epinephrine) have shown reproductive toxicity (see section 5.3). The potential risk for humans is unknown. Caution should be exercised when administering to pregnant women. Xylestesin-A should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Breast-feeding
A small ratio of lidocaine (lignocaine) is excreted into the breast milk but no effects on breast-fed neonates are likely at therapeutic doses. It is not known whether adrenaline (epinephrine) is excreted into the breast milk.

A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with Xylestesin-A should be made taking into account the benefit of breast-feeding to the child and the benefit of Xylestesin-A therapy to the woman. Therefore, following anaesthesia with Xylestesin-A, breast-feeding mothers should discard the first human milk output before resuming breast-feeding.

Fertility
Animal studies with high doses of lidocaine (lignocaine) or adrenaline (epinephrine) showed an effect on fertility (see section 5.3). At therapeutic doses of Xylestesin-A, however, no effects on male or female fertility are likely.

4.7 Effects on the ability to drive and use machines

In sensitive patients, injection of Xylestesin-A can lead to a transient impairment of responsiveness, e.g. when driving a vehicle. The physician must decide on an individual basis whether the patient may drive or operate machinery. The patient should not leave the dental practice earlier than 30 minutes after the injection.

4.8 Undesirable effects

a) Summary of the safety profile:

In general, the therapeutic use of Xylestesin-A can be regarded as very safe. The causality assessment in case of adverse events is difficult, as they may be due to the underlying dental disease, the dental procedure or the local anaesthetic and a clear differentiation is not possible. The description of the safety profile of Xylestesin-A is based on data identified in published clinical studies and on the postmarketing surveillance data of the manufacturer.
In clinical studies, the most frequently observed adverse events were medicine ineffective, pain and procedural pain. In clinical studies, only few nerve disturbances (e.g. hypoaesthesia, paraesthesia/paraesthesia oral and neuralgia) were reported. Postmarketing surveillance data confirm the pattern described in published clinical studies in general, but indicated a lower overall incidence of adverse events. However, it has to be considered that spontaneous reporting systems do not allow incidence calculation.
The overall risk of nerve disturbances (e.g. hypoaesthesia, paraesthesia, taste disorders) is low according to the postmarketing experience. In the case of suspected hypersensitivity reactions, allergy testing is recommended including testing of the individual components of the medicine.

b) Tabulated summary of adverse reactions:

The tabulated summary is based on data from published controlled clinical studies and completed by postmarketing surveillance data :

Very common (> 1/10)
Common (≥ 1/100, <1/10)
Uncommon (≥ 1/1'000, < 1/100)
Rare (≥ 1/10´000, < 1/1´000)
Very rare (< 1/10'000)
Not known (frequency cannot be estimated from the available data)

System organ class	
Infections and infestations	*Uncommon* alveolar osteitis
	Rare infection, oral herpes
Immune system disorders	*Not known** anaphylactic reaction, anaphylactic shock, type I hypersensitivity, type IV hypersensitivity reaction
Psychiatric disorders	*Not known** confusional state
Nervous system disorders	*Uncommon* headache, dizziness, somnolence, hypoaesthesia
	Rare paraesthesia, neuralgia
	*Not known** facial palsy, paresis, syncope, presyncope, dysarthria, tremor, loss of consciousness
Eye disorders	*Not known** accommodation disorder, blindness, diplopia, eye swelling, vision blurred, eyelid ptosis, mydriasis, ophthalmoplegia
Cardiac disorders	*Rare* palpitations
Vascular disorders	*Rare* haematoma
	*Not known** pallor
	*Not known**

System organ class	
Respiratory, thoracic and mediastinal disorders	bronchospasm, laryngeal oedema, respiratory failure, throat tightness, wheezing, dyspnoea, cough

Gastrointestinal disorders	*Uncommon* *nausea, oral pain, vomiting, gingivitis, mouth haemorrhage*
	Rare Diarrhoea, abdominal pain, paraesthesia oral
	*Not known** tongue oedema, dysphagia
Skin and subcutaneous tissue disorders	*Uncommon* erythema
	Rare rash, hyperhidrosis, pruritus, haemorrhage subcutaneous
	*Not known** dermatitis bullous, dermatitis contact, hypoaesthesia facial, swelling face, urticaria, angioedema
Musculoskeletal and connective tissue disorders	*Rare* myalgia, temporomandibular joint syndrome, trismus, arthralgia
General disorders and administration site conditions	*Common* medicine ineffective, pain
	Uncommon injection site swelling, face oedema, injection site haematoma
	Rare injection site pain, asthenia, chest pain, chills, injection site inflammation
Investigations	*Rare* ECG signs of myocardial ischaemia
	*Not known** Allergy test positive, heart rate increased, heart rate irregular
Injury, poisoning and procedural complications	*Common* procedural pain
	Rare mouth injury

* data from postmarketing surveillance

c) Description of selected adverse events:

Two types of adverse events are of special clinical interest, but these are not the most frequently reported adverse events. The presentation is based mainly on postmarketing surveillance data.

Nerve disturbances

Nerve disturbances in dentistry may have different reasons, caused by underlying dental disease, by the dental procedure, but also by direct adverse events of dental local anaesthetics. With an observation frequency of one event per 10 million of sold cartridges the risk of such disturbances is low. In the data compilation given above the most frequently reported nerve disturbance in clinical studies was hypoaesthesia. During postmarketing surveillance, cases of facial palsy, hypoaesthesia facial and various adverse events affecting the eye (e.g. diplopia, accommodation disturbances) were identified indicating possibly anaesthesia related nerve disturbances. All of these adverse events were reversible.

Hypersensitivity reactions
Hypersensitivity reactions were only rarely identified in the postmarketing surveillance. Mostly the reactions were non-serious, but life-threatening reactions cannot be fully excluded. The reactions included anaphylactic reactions/shock, skin reactions and respiratory symptoms.
In the case of suspected hypersensitivity reaction, allergy testing is recommended including testing of the individual components of the medicinal product.
Sodium sulfite (E221): May rarely cause severe hypersensitivity reactions and bronchospasm.

d) Paediatric population

The observation during postmarketing surveillance does not reveal differences in the safety profile in children compared with that in adults.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose

Acute emergencies from local anaesthetics are generally related to high plasma levels encountered during therapeutic use or unintended and rapid intravascular administration of local anaesthetics. Symptoms of overdose may appear either immediately, caused by accidental intravascular injection or abnormal absorption conditions, e.g. in inflamed or -well vascularised tissue, or later, caused by genuine overdose following an injection of excessive quantity of anaesthetic solution, and manifest themselves as central nervous and/or vascular symptoms.

No case of overdose has been reported during post-marketing surveillance.

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

Symptoms probably caused by lidocaine (lignocaine):

Cardiovascular symptoms (SOC Cardiac disorders, Vascular disorders, Investigations): blood pressure decreased, bradycardia, cardiac arrest, conduction disorder.

Central nervous symptoms (SOC Psychiatric disorders, Nervous system disorders, Ear and labyrinth disorders, Gastrointestinal disorders, Musculoskeletal and connective tissue disorders, Investigations): anxiety, coma, confusional state, dizziness, dysgeusia, grand mal convulsions, muscle twitching, nausea, respiratory paralysis, respiratory rate increased, restlessness, somnolence, tinnitus, tremor, vomiting.

The most dangerous symptoms regarding the outcome of such an event are:

blood pressure decreased, cardiac arrest, conduction disorder, grand mal convulsions, respiratory paralysis and somnolence/coma.

Symptoms probably caused by adrenaline (epinephrine):

Pressure symptoms (SOC Vascular disorders, Investigations): blood pressure systolic increased, blood pressure diastolic increased, venous pressure increased, pulmonary arterial pressure increased, hypotension.

Cardiac symptoms (SOC Cardiac disorders): bradycardia, tachycardia, arrhythmia (eg. atrial tachycardia, atrioventricular block, ventricular tachycardia, premature ventricular contractions).
These symptoms can result in life threatening situations as well as pulmonary oedema, cardiac arrest, kidney failure, and metabolic acidosis.

Therapy

If symptoms of overdose arise the application of the local anaesthetic has to be stopped.

General basic measures:

Diagnostics (respiration, circulation, consciousness), resuscitation and/or maintenance of the vital functions (respiration and circulation), administration of oxygen, intravenous access.

Special measures:

Hypertension: Elevation of the upper body, if necessary sublingual nifedipine.

Convulsions: Protect patients from concomitant injuries, if necessary benzodiazepines (e.g. diazepam iv).

Hypotension: Horizontal position, if necessary intravenous infusion of a physiological electrolyte solution, vasopressors (e.g. etilefrine IV).

Bradycardia: Atropine iv.

Anaphylactic shock: Contact emergency physician, in the meantime shock positioning, generous infusion of a physiological electrolyte solution, if necessary adrenaline (epinephrine) IV,), cortisone IV, antihistamines IV.

Cardiovascular arrest: Immediate cardiopulmonary resuscitation, contact emergency physician.

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anaesthetics, local, ATC code N01B B52

Mechanism of action:
Xylestesin-A contains lidocaine (lignocaine) a local anaesthetic of the amide type used in dentistry and leads to a reversible inhibition of the irritability of vegetative, sensory and motor nerve fibres. The blocking of voltage dependent Na^+ channels on the membrane of the nerve fibre is thought to be the mechanism of action of lidocaine (lignocaine).
Adrenaline (epinephrine) leads locally to vasoconstriction and reduced blood supply, whereby the absorption of lidocaine (lignocaine) is delayed. The result is a higher concentration of the local anaesthetic at the site of action, over a longer period, as well as the reduction of systemic adverse side effects.

Pharmacodynamic effects:
Onset of local anaesthetic effects of Xylestesin-A occurs after a short latency period of 1-3 minutes with infiltration and after a somewhat longer latency period with nerve block anaesthesia (2 to 4 minutes after injection). The duration of complete anaesthesia with Xylestesin-A in pulpal anaesthesia is 30 to 60 minutes, and in soft-tissue anaesthesia 120 to 180 minutes.

Clinical efficacy and safety:
Success rates of anaesthesia with Xylestesin-A differ, depending on the type of anaesthesia and the above-mentioned factors. In general, success rates of about 90% or higher may be expected after single use if the medicine is administered as indicated. The inferior alveolar nerve block has the greatest failure rate. Repeated or supplementary injections may be necessary in the event of failed anaesthesia or in the event of prolonged dental procedures and surgery. Particular circumstances, e.g. acute irreversible pulpitis of mandibular molars, may require special or alternative anaesthetic techniques. Articaine 4% with adrenaline (epinephrine) may provide better clinical efficacy in such cases as reported by different authors. Although Xylestesin-A is usually tolerated, adverse reactions cannot be fully excluded (see section 4.8), particularly in the event of overdose (see section 4.9).

Paediatric population:
The use of Xylestesin-A in the paediatric population is considered for routine treatment. Dosages in the paediatric population should be reduced taking into account age, body weight, physical condition and the magnitude of the treatment (see section 4.2), together with complex measures to prevent a painful experience and to reduce anxiety, including sedation.
Since paediatric patients relatively often suffer traumatic injury to their still (residual) anaesthetised soft tissue following local anaesthesia administration in the dental practice (reportedly 13% of all cases), local anaesthesia providing the appropriate duration of efficacy should be used.

5.2 Pharmacokinetic properties

Absorption:
Lidocaine (lignocaine) is rapidly and extensively absorbed. The maximum plasma level of lidocaine (lignocaine) from intraoral injection is achieved after 10 – 20 minutes. Exogenously administered adrenaline (epinephrine), including in dental use, may increase the adrenaline

(epinephrine) serum concentration in a dose dependent manner with a decline within a few minutes of administration.

Distribution:
Lidocaine (lignocaine) is bound up to 60 to 80 % in the serum to plasma proteins. Lidocaine (lignocaine) and adrenaline (epinephrine) are widely distributed within the organism.

Biotransformation and elimination:
Lidocaine (lignocaine) is largely metabolised in the liver and any alteration in liver function or hepatic blood flow can have a significant effect on its pharmacokinetics and dosage requirements. Metabolism in the liver is rapid and about 90 % of the given dose is dealkylated to form monoethylglycinexylidide and glycinexylidide. Less than 10 % is excreted unchanged. The primary metabolite in urine is a conjugate of 4-hydroxy-2,6-dimethylaniline. The elimination half-life is 1.5 to 2 hours.
Lidocaine (lignocaine) crosses the blood-brain and placental barriers.
Adrenaline (epinephrine) is rapidly catabolised in the liver and other tissues. The metabolites are excreted renally.

Special populations:
Effect of age: Lidocaine (lignocaine) has been extensively investigated in elderly patients. A significantly longer half-life was found for lidocaine (lignocaine) in elderly patients. Reduced clearance was detected only in elderly men, while the values in elderly women did not differ significantly from younger individuals. Dose reduction was sometimes suggested for elderly patients (reduction by approximately 1/3 to ½).
Depending on the age of the child, differences compared with adults regarding metabolism and distribution volume should be considered.
For children it seems preferable to use medicines with higher protein binding and a faster metabolism such as articaine.

Renal and hepatic insufficiency:
The elimination half-life of lidocaine (lignocaine) following an intravenous bolus injection is typically 1.5 to 2.0 hours. Because of the rapid rate at which lidocaine (lignocaine) is metabolised, any condition that affects liver function may alter lidocaine (lignocaine) kinetics. The half-life may be more than doubled in patients with liver dysfunction. Renal dysfunction does not affect lidocaine (lignocaine) kinetics but may lead to the accumulation of metabolites.

5.3 Preclinical safety data

There is evidence that 2,6-xylidine, a metabolic product arising from lidocaine (lignocaine), can have mutagenic effects in the rat, and possibly also in man. This evidence is obtained from in-vitro tests in which the said metabolite was used at very high, almost toxic concentrations. There is no reason to believe at this time that the parent substance, lidocaine (lignocaine), is itself also mutagenic.
A carcinogenicity study of transplacental exposure and postnatal treatment of animals for two years with 2,6-xylidine in rats demonstrated malignant and benign tumors predominantly in the nasal cavities (ethmoturbinalia) by means of this highly sensitive test system (transplacental exposure and postnatal treatment of animals for two years with very high doses). It does not seem totally unlikely that these findings will be relevant to humans. For this reason, high doses of Xylestesin-A (lidocaine (lignocaine)) should not be

administered over longer periods.
Lidocaine (lignocaine) has evidently no teratogenic potential if used in recommended doses (see section 4.6).
Adrenaline (epinephrine) was potentially teratogenic in rats albeit at doses 25 times the human therapeutic dose (see section 4.6).
While supratherapeutic doses of lidocaine (lignocaine) and adrenaline (epinephrine) administered under *in vitro* or *in vivo* experimental conditions to laboratory animals may affect fertilisation and foetal development, harmful or other effects on female or male fertility is not expected based on animal studies at therapeutic doses of lidocaine (lignocaine) and adrenaline (epinephrine) (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium sulfite (E221)
Sodium chloride
Hydrochloric acid 14% (for pH adjustment)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf-life

2 years

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package in order to protect from light.

6.5 Nature and contents of container

Cartridge made of colourless neutral glass I.
Stopper and rubber disc are made of butyl rubber.
Aluminium cap made of aluminium-iron-silicon-alloy.

Tin with 50 cartridges of 1.7 mL each.

6.6 Special precautions for disposal and other handling

Prior to administration, the product should be inspected visually for particulate matter, discolouration or damage to the container. The product should not be used if such defects are observed.

The product is for single use only. Any unused product and waste material should be disposed of immediately after first use in accordance with local requirements.

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

CARSL Consulting
PO Box 766
Hastings 4156
New Zealand

9 DATE OF FIRST APPROVAL

14 August 1984

10 DATE OF REVISION OF THE TEXT

23 February 2026

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
4.8	Updated the reporting of adverse reactions website address
4.9	Included the overdose advice statement and Poisons number
6.5	Removing ‘Green coloured’ from the container description
8	Updated sponsor address