NEW ZEALAND DATA SHEET

1. PRODUCT NAME

XYLOCAINE PUMP SPRAY

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One spraydose of XYLOCAINE PUMP SPRAY contains lignocaine base 10 mg.
For excipients see section 6.1.

3. PHARMACEUTICAL FORM

XYLOCAINE PUMP SPRAY is a clear or almost clear, slightly coloured liquid with an odour of ethanol, menthol and banana. The active ingredient is dissolved in a mixture of water, ethanol and polyethylene glycol 400.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For the prevention of pain associated with the following procedures:

Otorhinolaryngology

- Puncture of the maxillary sinus and minor surgical procedures in the oral and nasal cavity, pharynx and epipharynx.

Obstetrics

- During the final stages of delivery and before episiotomy and perineal suturing as supplementary pain control.

Introduction of instruments, tubes and catheters into the respiratory and digestive tract

- Provides surface anaesthesia for the oropharyngeal and tracheal areas to reduce reflex activity, attenuate haemodynamic responses and facilitate insertion of the tube or the passage of instruments during endotracheal intubation and endoscopic procedures of the airways and upper gastrointestinal tract.

Dental practice

- Before injections, dental impressions, X-ray photography, removal of calculus.

4.2 DOSAGE AND METHOD OF ADMINISTRATION

XYLOCAINE PUMP SPRAY provides prompt and profound anaesthesia of mucous membranes which lasts for approximately 10-15 minutes. The anaesthesia usually occurs within 1-3 minutes, depending on the area of application.

As with any local anaesthetic, the safety and effectiveness of lignocaine depend on the proper dosage, the correct technique, adequate precautions and readiness for emergencies.

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.

Each actuation of the metered-dose valve delivers 10 mg lignocaine base. It is unnecessary to dry the site prior to application.

XYLOCAINE PUMP SPRAY should not be used on cuffs of endotracheal tubes (ETT) made of plastic (see Section 4.4).

- **Otorhinolaryngology:** 3 metered doses for puncture of the maxillary sinus or other minor surgical procedures.

- **During delivery:** Up to 20 metered doses (200 mg lignocaine base).

- **Introduction of instruments, tubes and catheters into the respiratory and digestive tract:** Up to 20 metered doses (200 mg lignocaine base) for procedures in pharynx, larynx and trachea. During prolonged procedures up to 400 mg of lignocaine may be administered. In addition, when combined with other lignocaine products, the total dose should not exceed 400 mg. With applications mainly to the larynx, trachea and bronchi, the dose should not exceed 20 metered doses (200 mg lignocaine base).

- **Dental practice:** 1-5 metered doses to the mucous membranes.

Since absorption is variable and especially high in the trachea and bronchi (see Section 4.8 and 5.2) the maximum recommended doses vary depending on the area of application.

Debilitated or elderly patients, acutely ill patients or patients with sepsis should be given doses commensurate with their age, weight and physical condition.

Children

Children over 12 years of age weighing less than 25 kg should be given doses commensurate with their weight and physiological condition.

In children under the age of 12 years of age the dose should not exceed 3 mg/kg (e.g. 6 metered doses in an infant weighing 20 kg). When used mainly in the larynx and trachea the dose should be reduced to 1.5 mg/kg.

In children less than 3 years of age less concentrated lignocaine solutions are recommended.

4.3 CONTRAINDICATIONS

Known hypersensitivity to local anaesthetics of the amide type or to any of the excipients.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Excessive dosage, or short intervals between doses, may result in high plasma levels and serious adverse effects. Absorption from mucous membranes is variable but is especially high from the bronchial tree. Such applications may therefore result in rapidly rising or excessive plasma concentrations, with an increased risk for toxic symptoms, such as convulsions. Lignocaine spray should be used with caution in patients with wounds or traumatized mucosa in the region of the proposed application. A damaged mucosa will permit increased systemic absorption. The management of serious adverse reactions may

require the use of resuscitative equipment, oxygen and other resuscitative agents (see Section 4.9).

In paralysed patients under general anaesthesia, higher blood concentrations may occur than in spontaneously breathing patients. Unparalysed patients are more likely to swallow a large proportion of the dose which then undergoes considerable first-pass hepatic metabolism following absorption from the gut.

The oropharyngeal use of topical anaesthetic agents may interfere with swallowing and thus enhance the danger of aspiration. Numbness of the tongue or buccal mucosa may increase the danger of biting trauma.

If the dose or administration is likely to result in high blood levels, some patients require special attention to prevent potentially dangerous side effects:

- Patients with cardiovascular disease and heart failure.
- Patients with partial or complete heart block.
- The elderly and patients in poor general health.
- Patients with severe renal dysfunction.
- Patients with advanced liver disease.

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

Avoid contact with the eyes.

XYLOCAINE PUMP SPRAY should not be used on cuffs of endotracheal tubes (ETT) made of plastic. Lignocaine base in contact with both PVC and non-PVC cuffs of endotracheal tubes may cause damage of the cuff. This damage is described as pinholes, which may cause leakage that could lead to pressure loss in the cuff.

XYLOCAINE PUMP SPRAY is probably porphyrinogenic and should only be prescribed to patients with acute porphyria on strong or urgent indications. Appropriate precautions should be taken for all porphyric patients.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

Lignocaine should be used with caution in patients receiving other local anaesthetics or agents structurally related to amide-type local anaesthetics, e.g. anti-arrhythmics such as mexiletine and tocainide, since the toxic effects are additive.

Specific interaction studies with lignocaine and anti-arrhythmic medicines class III (e.g. amiodarone) have not been performed, but caution is advised (see Section 4.4).

Medicines that reduce the clearance of lignocaine (e.g. cimetidine or betablockers) may cause potentially toxic plasma concentrations when lignocaine is given in repeated high doses over a long period of time. Such interactions should therefore be of no clinical importance following short term treatment with lignocaine (e.g. XYLOCAINE PUMP SPRAY) at recommended doses.

4.6 FERTILITY, PREGNANCY AND LACTATION

It is reasonable to assume that a large number of pregnant women and women of child-bearing age have been given lignocaine. No specific disturbances to the reproductive process have so far been reported, e.g. no increased incidence of malformations.

Like other local anaesthetics lignocaine may enter the mother's milk, but in such small amounts that there is generally no risk of this affecting the neonate.

4.7 EFFECT ON ABILITY TO DRIVE AND USE MACHINES

Depending on the dose, local anaesthetics may have a very mild effect on mental function and may temporarily impair locomotion and co-ordination.

4.8 UNDESIRABLE EFFECTS

4.8.1 Local reactions

Local irritation at the application site has been described. Following application to laryngeal mucosa before endotracheal intubation, reversible symptoms such as "sore throat", "hoarseness" and "loss of voice" have been reported. The use of XYLOCAINE PUMP SPRAY provides surface anaesthesia during an endotracheal procedure but does not prevent post-intubation soreness.

4.8.2 Allergic reactions

Allergic reactions (in the most severe instances anaphylactic shock) to local anaesthetics of the amide type are rare (<0.1%).

4.8.3 Acute systemic toxicity

Lignocaine may cause acute toxic effects if high systemic levels occur due to rapid absorption, e.g. application to areas below the vocal cords, or overdosage (see Section 5.2 and Section 4.9).

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://nzphvc.otago.ac.nz/reporting/

4.9 OVERDOSAGE

4.9.1 Acute systemic toxicity

Toxic reactions originate mainly in the central nervous and the cardiovascular systems.

Central nervous system toxicity is a graded response with symptoms and signs of escalating severity. The first symptoms are circumoral paraesthesia, numbness of the tongue, light-headedness, hyperacusis and tinnitus. Visual disturbance and muscular tremors are more serious and precede the onset of generalised convulsions. Unconsciousness and grand mal convulsions may follow, which may last from a few seconds to several minutes. Hypoxia and hypercarbia occur rapidly following convulsions due to the increased muscular activity, together with the interference with normal respiration. In severe cases apnoea may occur. Acidosis increases the toxic effects of local anaesthetics.

Recovery is due to redistribution and metabolism of the local anaesthetic agent from the central nervous system. Recovery may be rapid unless large amounts of the agent have been administered.

Cardiovascular effects are only seen in cases with high systemic concentrations. Severe hypotension, bradycardia, arrhythmia and cardiovascular collapse may be the result in such cases.

Cardiovascular toxic effects are generally preceded by signs of toxicity in the central nervous system, unless the patient is receiving a general anaesthetic or is heavily sedated with agents such as a benzodiazepine or barbiturate.

4.9.2 Treatment of acute toxicity

Should symptoms of systemic toxicity occur, the signs are anticipated to be similar in nature to those following the administration of local anaesthetics by other routes. Local anaesthetic toxicity is manifested by symptoms of nervous system excitation and, in severe cases, central nervous and cardiovascular depression.

Severe neurological symptoms (convulsions, CNS depression) must be treated symptomatically by respiratory support and the administration of anticonvulsive medicines.

If circulatory arrest should occur, immediate cardiopulmonary resuscitation should be instituted. Optimal oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance.

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

Local anaesthetic, pharmacotherapeutic group: ATC code N01BB02

XYLOCAINE PUMP SPRAY provides prompt and profound anaesthesia, which lasts for approximately 10-15 minutes. The anaesthesia usually occurs within 1-3 minutes depending on the area of application.

Local anaesthesia is defined as a loss of feeling or sensation that is confined to a certain area of the body. All local anaesthetics have a common mode of action. To produce their effect, they must block the propagation of impulses along nerve fibres. Such impulses are transmitted by rapid depolarisation and repolarisation within the nerve axons. These changes in polarity are due to the passage of sodium and potassium ions across the nerve membrane, through ionic channels within the membrane. Local anaesthetics prevent the inward movement of sodium ions which initiate depolarisation and, as a consequence, the nerve fibre cannot propagate any impulses. The mechanisms behind the activity of local anaesthetics are not fully understood but a possible explanation is that the lipid-soluble base form diffuses across the lipid membrane into the cell. Inside the cell a proportion of the medicine ionises again and enters the sodium channel to exert an inhibitory effect on sodium influx and, consequently, on impulse conduction.

5.2 PHARMACOKINETIC PROPERTIES

Lignocaine is absorbed following topical administration to mucous membranes, its rate and extent of absorption being dependent upon the concentration and total dose administered, the specific site of application, and the duration of exposure. In general, the rate of absorption of local anaesthetic agents following topical application is most rapid after intratracheal and bronchial administration. Such applications may therefore result in rapidly

rising or excessive plasma concentrations, with an increased risk of toxic symptoms, such as convulsions. Lignocaine is also well-absorbed from the gastrointestinal tract, although little of the intact medicine appears in the circulation because of biotransformation in the liver.

Normally about 65% of the lignocaine is bound to plasma proteins. Amide local anaesthetics are mainly bound to alpha-1 acid glycoprotein but also to albumin. The alpha-1 acid glycoprotein has high-affinity, low-capacity sites and albumin has quantitatively less important low-affinity, high-capacity sites.

Lignocaine crosses the blood-brain and placental barriers, presumably by passive diffusion.

The main elimination pathway of lignocaine is by liver metabolism. The primary route of metabolism of lignocaine in humans in N-dealkylation to monoethylglycine xylidide (MEGX), followed by hydrolysis to 2,6-xylidine and hydroxylation to 4-hydroxy-2,6-xylidine. MEGX can also be further N-dealkylated to glycine xylidide (GX). The pharmacological/toxicological actions of MEGX and GX are similar to, but less potent than, those of lignocaine. GX has a longer half-life (about 10 hours) than lignocaine and may accumulate during prolonged administration. Approximately 90% of the lignocaine administered is excreted in the form of various metabolites and less than 10% is excreted unchanged in the urine. The primary metabolite in urine is a conjugate of 4-hydroxy-2,6-xylidine, accounting for about 70-80% of the dose excreted in the urine.

The elimination half-life of lignocaine following an intravenous bolus injection is typically 1.5 to 2.0 hours. Because of the rapid rate at which lignocaine is metabolised, any condition that affects liver function may alter lignocaine kinetics. The half-life may be prolonged two-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 from 6.0 µg free base per mL.

5.3 PRECLINICAL SAFETY DATA

In animal studies the toxicity noted after high doses of lignocaine consisted of effects on the central nervous and cardiovascular systems. No medicine-related adverse events were seen in reproduction toxicity studies, neither did lignocaine show a mutagenic potential in either *in vitro* or *in vivo* mutagenicity tests. Cancer studies have not been performed with lignocaine, due to area and duration of therapeutic use for this medicine.

Genotoxicity tests with lignocaine showed no evidence of mutagenic potential. A metabolite of lignocaine, 2,6-xylidine, showed weak evidence of activity in some genotoxicity tests. The metabolite 2,6-xylidine has been shown to have carcinogenicity potential in preclinical toxicological studies evaluating chronic exposure. Risk assessments comparing the calculated maximum human exposure from intermittent use of lignocaine, with the exposure used in preclinical studies, indicate a wide margin of safety for clinical use.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

- Ethanol
- Polyethylene glycol 400
- Essence of banana

- Menthol
- Saccharin
- Water, purified

6.2 INCOMPATIBILITIES

Not applicable

6.3 SHELF-LIFE

36 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at temperatures below 25°C. During storage at temperatures below 8°C precipitation may occur. This precipitation is dissolved when warming up in room temperature.

6.5 NATURE AND CONTENTS OF CONTAINER

Bottle (50 mL) made of glass with a metering spray pump. The package includes a plastic spray nozzle.

Additional nozzles for single use are available separately.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

The spray nozzle is already bent to its final appearance and no further actions should be done before using the spray nozzle. The nozzle must not be shortened, otherwise the spray function will be destroyed. Nozzles should not be reused and should be discarded immediately after use.

7. MEDICINE SCHEDULE

Pharmacy Medicine.

8. SPONSOR

Pharmacy Retailing (NZ) Limited Trading as Healthcare Logistics
58 Richard Pearse Drive
Airport Oaks
Auckland
New Zealand
Telephone: (09) 918 5100
Email: aspen@aspenpharma.co.nz

9. DATE OF FIRST APPROVAL

31 December 1969

10. DATE OF REVISION OF THE TEXT

21 Mar 2018

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
	Update to the SPC-style format and minor editorial changes