

1. NAME OF THE MEDICINAL PRODUCT

Xylocaine 10 mg/delivered dose Mucosal Spray

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each depression of the valve delivers 10 mg of lidocaine.

Excipient(s) with known effect

Each depression also delivers 1 mg of propylene glycol (an excipient of the banana essence). Also contains ethanol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Mucosal Spray.

A clear or almost clear, slightly coloured liquid with an odour of banana, ethanol and menthol.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For the prevention of pain associated with the following procedures:

Otorhinolaryngology

- Anaesthesia prior to minor surgical procedures in the nasal cavity, maxillary sinus, pharynx and epipharynx.
- Paracentesis.

Obstetrics

As supplementary pain control during labour (before episiotomy and perineal suturing).

Introduction of instruments and catheters into the respiratory and digestive tract

Provides surface anaesthesia for the oropharyngeal and tracheal areas to reduce reflex activity, attenuate haemodynamic response and to facilitate insertion of the catheter or the passage of instruments during endotracheal intubation, laryngoscopy, bronchoscopy and oesophagoscopy.

Dental practice

Before minor dental procedures, dental impressions, X-ray photography, and removal of calculus.

4.2 Posology and method of administration

This product is **non-sterile** and therefore not recommended for use prior to procedures that require aseptic techniques.

As with any local anaesthetic, reactions and complications are best averted by employing the minimal effective dosage. Debilitated or elderly patients and children should be given doses commensurate with their age and physical condition.

Paediatric population

In children under the age of 12 years doses should not exceed 3 mg/kg.

Xylocaine Spray should not be used on cuffs of endotracheal tubes (ETT) made of plastic (see also section 4.4). Concomitant use of lidocaine via any other routes should be borne in mind. Total dosage in any one session of use should not exceed 3 mg/kg or 200 mg lidocaine base when used without adrenaline.

Each activation of the metered dose valve delivers 10 mg lidocaine base. It is unnecessary to dry the site prior to application. No more than 20 spray applications should be used in any adult to produce the desired anaesthetic effect.

The number of sprays depend on the extent of the area to be anaesthetised.

- Dental practice
- 1–5 applications to the mucous membranes.
- Otorhinolaryngology
- 3 applications for puncture of the maxillary sinus.
- During delivery
- Up to 20 applications (200 mg lidocaine base).
- Introduction of instruments and catheters into the respiratory and digestive tract
- Up to 20 applications (200 mg lidocaine base) for procedures in pharynx, larynx, and trachea.

Method of administration

Nozzles are non-sterile single patient single use only. Appropriate measures should be taken to avoid cross-contamination (see Section 6.6).

4.3 Contraindications

Hypersensitivity to the active substance, to any of the excipients listed in section 6.1 or to local anaesthetics of the amide type.

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 of toxic symptoms, such as convulsions. Xylocaine Spray should be used with caution in patients with wounds or traumatised 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 drugs (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. This is particularly important in children because of their frequency of eating. Numbness of the tongue or buccal mucosa may increase the danger of biting trauma.

If the dose or site of administration is likely to result in high blood levels, lidocaine, in common with other local anaesthetics, should be used with caution in the following patients who will require special attention to prevent potentially dangerous side effects:

- Patients with epilepsy.
- Patients with cardiovascular disease and heart failure.
- Patients with impaired cardiac conduction or bradycardia.
- Patients with severe renal dysfunction.
- Patients with impaired hepatic function.
- Patients in severe shock.
- The elderly and patients in poor general health.

Avoid contact with the eyes.

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

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

Xylocaine 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 Interaction with other medicinal products and other forms of interaction

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

Specific interaction studies with lidocaine and antiarrhythmic drugs class III (e.g. amiodarone) have not been performed, but caution is advised (see also section 4.4).

Drugs that reduce the clearance of lidocaine (e.g. cimetidine or beta-blockers) may cause potentially toxic plasma concentrations when lidocaine is given in repeated high doses over a long time period. Such interactions should therefore be of no clinical importance following short term treatment with lidocaine (e.g. Xylocaine Spray) at recommended doses.

4.6 Fertility, pregnancy and lactation

Pregnancy

There is no or inadequate evidence of safety of the drug in human pregnancy but it has been in wide use for many years without apparent ill consequence; animal studies have shown no hazard. If drug therapy is needed in pregnancy, this drug can be used if there is no safer alternative.

Breast-feeding

Lidocaine enters the mother's milk, but in such small quantities that there is generally no risk of the child being affected at therapeutic dose levels.

4.7 Effects on ability to drive and use machines

Xylocaine Spray has minor influence on the 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

Frequencies are defined as very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$) or not known (cannot be estimated from the available data).

System Organ Class	Frequency Classification	Adverse Drug Reaction
Immune system disorders	Rare	Hypersensitivity
Nervous system disorders	Not known	Aphonia, Seizure, Neurotoxicity, Nervousness, Dizziness, Loss of consciousness
Respiratory, thoracic and mediastinal disorders	Not known	Dysphonia, Oropharyngeal pain
	Not known	Cough
General disorders and administration site conditions	Not known	Application site irritation
Cardiac disorders	Not known	Hypotension, Myocardial depression, Bradycardia, Cardiac arrest

Description of selected adverse reactions

Systemic adverse reactions are rare and may result from high plasma levels due to excessive dosage or rapid absorption (e.g. following application to areas below the vocal chords) or from hypersensitivity, idiosyncrasy or reduced tolerance on the part of the patient. Such reactions involve the central nervous system and/or the cardiovascular system.

CNS reactions are excitatory and/or depressant and may be characterised by nervousness, 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 manifestations of toxicity may be drowsiness, merging into unconsciousness and respiratory arrest.

Cardiovascular reactions are depressant and may be characterised by hypotension, myocardial depression, bradycardia and possibly cardiac arrest.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via:

HPRA Pharmacovigilance

Earlsfort Terrace
Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

4.9 Overdose

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 generalized 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.

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 drugs such as a benzodiazepine or barbiturate.

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

Treatment of acute toxicity

Treatment of acute toxicity should be instituted at the latest when twitches occur. The necessary drugs and equipment should be immediately available. The objectives of treatment are to maintain oxygenation, stop the convulsions and support the circulation. Oxygen must be given and, if necessary, assisted ventilation (mask and bag).

An anticonvulsant should be given i.v. if the convulsions do not stop spontaneously in 15–30 sec. Thiopentone sodium 1–3 mg/kg i.v. will abort the convulsions rapidly. Alternatively diazepam 0.1 mg/kg *bw* i.v. may be used, although its action will be slow. Prolonged convulsions may jeopardise the patient's ventilation and oxygenation. If so, injection of a muscle relaxant (e.g. succinylcholine 1 mg/kg *bw*) will facilitate ventilation, and oxygenation can be controlled. Early endotracheal intubation must be considered in such situations.

If cardiovascular depression is evident (hypotension, bradycardia), ephedrine 5–10 mg i.v. should be given and repeated, if necessary after 2–3 min.

Should circulatory arrest occur, immediate cardiopulmonary resuscitation should be instituted. Optimal oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance, since hypoxia and acidosis will increase the systemic toxicity of local anaesthetics.

Children should be given doses commensurate with their age and weight.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group (ATC code): N01B B02

Lidocaine, 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.

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

Central nervous system toxicity 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

Absorption

Lidocaine 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 duration of exposure. In general, the rate of absorption of local anaesthetic agents following topical application is most rapid after intratracheal and bronchial administration. Lidocaine is also well-absorbed from the gastrointestinal tract, although little of the intact drug appears in the circulation because of biotransformation in the liver.

Distribution

The plasma protein binding of lidocaine is dependent on the drug concentration, and the fraction bound decreases with increasing concentration. At concentrations of 1 to

4 micrograms of free base per ml, 60 to 80 percent of lidocaine is protein-bound. Binding is also dependent on the plasma concentration of the alpha-1-acid glycoprotein.

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

Biotransformation

Lidocaine is metabolised rapidly by the liver, and metabolites and unchanged drug are excreted by the kidneys. Biotransformation includes oxidative N-dealkylation, ring hydroxylation, cleavage of the amide linkage and conjugation. N-dealkylation, a major pathway of biotransformation, yields the metabolites monoethylglycinexylidide and glycinexylidide. The pharmacological/toxicological actions of these metabolites are similar to, but less potent than, those of lidocaine. Approximately 90% of lidocaine administered is excreted in the form of various metabolites, and less than 10% is excreted unchanged. The primary metabolite in urine is a conjugate of 4-hydroxy-2,6-dimethylaniline.

Elimination

The elimination half-life of lidocaine following an intravenous bolus injection is typically 1.5 to 2 hours. Because of the rapid rate at which lidocaine is metabolised, any condition that affects liver function may alter lidocaine kinetics. The half-life may be prolonged two-fold or more in patients with liver dysfunction. Renal dysfunction does not affect lidocaine 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 lidocaine required to produce overt systemic effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6 micrograms free base per ml.

5.3 Preclinical safety data

Genotoxicity tests with lidocaine showed no evidence of mutagenic potential. A metabolite of lidocaine, 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 lidocaine, 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 (96%)
Macrogol 400
Essence of Banana
Levomenthol
Saccharin

Water purified

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. During storage at temperatures below +8°C precipitation may occur. The precipitate dissolves on warming up to room temperature.

6.5 Nature and contents of container

A 50 ml Type I Ph. Eur. neutral glass spray bottle with a metering spray pump. The package includes a single use PP spray nozzle approximately 120 mm long. Additional short spray nozzles are available separately.

The contents of the spray bottles are sufficient to provide approximately 500 sprays.

6.6 Special precautions for disposal and other handling

The spray nozzle is bent to ensure correct spray function. Do not try to alter the shape as this could affect its performance.

The nozzle must not be shortened, as it will affect the spray function.

Nozzles are non-sterile single patient single use and national/local procedures should be adhered to in order to prevent cross contamination. Nozzles should not be reused and should be discarded immediately after use.

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

7. MARKETING AUTHORISATION HOLDER

Aspen Pharma Trading Limited
3016 Lake Drive
Citywest Business Campus
Dublin 24
Ireland.

8. MARKETING AUTHORISATION NUMBER

PA1691/028/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 01 April 2010

10. DATE OF REVISION OF THE TEXT

August 2023