

The content of this leaflet was approved by the Ministry of Health in November 2015 and updated according to the guidelines of the ministry of Health in November 2019.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Xylocaine Pump Spray 10%

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Lidocaine 10mg/metered dose.

Excipients with known effect: Each depression also delivers 1mg 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

Non-sterile solution for topical application supplied in a pump spray, with nozzles for single use in an individual patient.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Surface anaesthesia in dental practice otorhinolaryngology, obstetric and anaesthesiology.

4.2. Posology and method of administration

As with any local anaesthetic, the safety and effectiveness of lidocaine depends 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.

The degree of absorption from mucous membranes is variable but especially high from the bronchial tree. Application only to areas below the vocal cords may result in excessive plasma concentrations because of less transfer to the intestine and less first-pass loss.

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

Xylocaine Pump Spray 10% should not be used on cuffs of endotracheal tubes (ETT) made of plastic. (See also section 4.4)

- Otorhinolaryngology: 3 metered doses for puncture of the maxillary sinus or other minor surgical procedures.
- Obstetrics – During delivery: Up to 20 metered doses (200mg lidocaine base).
- Introduction of instruments, tubes and catheters into the respiratory and digestive tract: Up to 20 metered doses (200mg lidocaine base) for procedures in pharynx, larynx and trachea. During prolonged procedures up to 400 mg of lidocaine may be administered. In addition, when combined with other

lidocaine products, the total dose should not exceed 400 mg. With application mainly to the larynx, trachea and bronchi, the dose should not exceed 20 metered doses (200 mg lidocaine base).

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

Debilitated or elderly patients, children over 12 years of age, acutely ill patients or patients with sepsis should be given doses commensurate with their age, weight and physical condition.

In children less than 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 lidocaine solutions are recommended.

4.3. Contraindications

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

4.4. Special warning and precaution 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 Pump Spray 10% 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 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 large proportions 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 anaesthetic, should be used with caution in the following patients who require special attention to prevent potentially dangerous side effects:

- Patients with epilepsy.
- Patients with cardiovascular disease, 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 eyes.

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

Xylocaine Pump Spray 10% 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 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 10% 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 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 mexiletin and tocainide, since the toxic effects are additive.

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

Drugs that reduce the clearance of lidocaine (e.g. cimetidine or betablockers) 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 Pump Spray 10%) at recommended doses.

4.6. 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 and animal studies have shown no hazard. If drug therapy is needed in pregnancy, this drug can be used if there is no safer alternative.

Lactation

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 Pump Spray 10% 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

Allergic reaction

In extremely rare cases amide-type local anaesthetic preparations have been associated with allergic reaction (in the most severe instances anaphylactic shock).

Local reactions

Local irritations at the application site have 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 10% provides surface anaesthesia during endotracheal procedure but does not prevent post-intubation soreness.

Acute systemic toxicity

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 cords), 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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form <https://sideeffects.health.gov.il>

In addition, you can report to Perrigo via the following address: www.perrigo-pharma.co.il

4.9. Overdose

Acute systemic toxicity

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

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 disturbances and muscular tremors are more serious and precede the onset of generalized convulsions. Unconsciousness and grand mal convulsions may follow, which may last for 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 anaesthetic.

Cardiovascular effects are only seen in cases with high systematic 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 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 body-weight i.v. may be used although its action will be slower.

Prolonged convulsions may jeopardise the patient's ventilation and oxygenation. If so, injection of a muscle relaxant (e.g. succinylcholine 1 mg/kg body-weight) 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 minutes.

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 microgram 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 2.0 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 6.0 microgram free base per ml.

5.3 Preclinical safety data

Lidocaine is a well-established active ingredient.

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

Genotoxicity tests with lidocaine showed no evidence of mutagenic potential. A metabolite of lidocaine, 2,6-dimethylaniline, showed weak evidence of activity in some genotoxicity tests. The metabolite 2,6-dimethylaniline 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

Polyethylene glycol 400, Ethanol 96%, , Essence of banana (contains propylene glycol), Saccharin , Purified water ,Levomenthol,

6.2. Incompatibilities

Not applicable.

6.3. Shelf-life

The expiry date of the product is indicated on the packaging materials.

Shelf life after first opening: Until the end of shelf life.

6.4. Special precautions for storage

Do not store above 25°C. Do not freeze. During storage at temperatures below 8°C precipitation may occur. This prescription is dissolved when warming up in room temperature.

6.5. Nature and content of container

50 ml glass spray bottles (approx. 500 spray doses) with a metering spray pump.

The package includes a single-use spray nozzle approximately 120mm long.

Additional short spray nozzles are available separately.

Each depression of the metered spray pump delivers 10 mg lidocaine base. 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. The nozzles should be handled using gloves and the box of 50 should be kept closed between procedures.

Nozzles should not be reused, and should be discarded after use.

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

7. REGISTRATION HOLDER

Perrigo Israel Agencies Ltd.
1 Rakefet St., Shoham, Israel

8. MANUFACTURER

AstraZeneca AB, Södertälje, Sweden for Aspen.

9. MARKETING AUTHORISATION NUMBER

116-41-25500

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