Xylocaine

Lidocaine

Spray 10mg/dose

Pump spray for topical anaesthesia of mucous membrane

Qualitative and quantitative composition

Active constituent:
1 dose XYLOCAINE pump spray contains lidocaine base 10 mg.
For excipients see *List of excipients*.

Pharmaceutical form

XYLOCAINE is presented as cutaneous spray, solution.
XYLOCAINE pump spray is a clear to almost clear, slightly coloured liquid with menthol and banana flavour. The active ingredient is dissolved in a mixture of water, ethanol and polyethylene glycol 400.

Therapeutic indications

For the prevention of pain associated with the following procedures:

- Nasal procedures, e.g. puncture of the maxillary sinus
- Oral and dental procedures, e.g. prior to injection
- Procedures in the oropharynx, e.g. gastrointestinal endoscopy
- Procedures in the respiratory tract, e.g. insertion of instruments and tubes
- Procedures in the larynx, trachea and bronchi
- Procedures in obstetrics and gynaecology, e.g. vaginal delivery, suturing of ruptures in the mucosa and cervical biopsies

Posology and method of administration

XYLOCAINE pump spray is intended for use on mucous membranes and provides efficient surface anaesthesia, 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, reaction 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 conditions.

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 spray depends 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
Obstetrics	: up to 20 applications (200 mg lidocaine base) during delivery.

Introductions of instruments and catheters into the respiratory and digestive tract up to 20 applications (200 mg lidocaine base) for procedures in the pharynx, larynx and trachea.

XYLOCAINE spray 10% should not be used on cuffs of endotracheal tubes (ETT) made of plastic.

Dose recommendations for adults

Area	Recommended dose (mg)
Nasal procedures, e.g. puncture of the maxillary sinus	30
Oral and dental procedures, e.g. prior to injection	10-50
Procedures in the oropharynx e.g. gastrointestinal endoscopy	20-200
Procedures in the respiratory tract, e.g. insertion of instruments and tubes	50-200
Procedures in the larynx, trachea and bronchi	50-200
Procedures in obstetrics and gynaecology, e.g. vaginal delivery, suturing of ruptures in the mucosa and cervical biopsies	50-200

Since absorption is variable and especially high in the trachea and bronchi (see *Undesirable effects* and *Pharmacokinetic properties*) the maximum recommended doses vary depending on the area of application.

For children 3 to 12 years of age the dose should not exceed 3 mg/kg. When used mainly in the larynx and trachea the dose should be reduced to 1.5 mg/kg.

For children below 3 years of age less concentrated lidocaine solutions are recommended.

Contraindications
XYLOCAINE is contraindicated in patients who have known history of hypersensitivity to local anaesthetics of the amide type or to other components of the spray solution.

Special warnings and special 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.

Lidocaine 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 drugs (see *Overdose*).

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 with low protein binding capacity or
- nephrotic syndrome
- patients with epilepsy, impaired cardiac conduction or bradycardia, impaired hepatic function, severe shock

Avoid contact with the 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 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 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.

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 also *Special warnings and special precautions for use*).

Drugs that reduce the clearance of lidocaine (e.g. cimetidine and betablockers) may cause potentially toxic plasma concentration 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.

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. No specific disturbances to the reproductive process have so far been reported, e.g. no increased incidence of malformation.

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

Effect on ability to drive or operate machinery
Depending on the dose, local anaesthetics may have a very mild effect on mental function and may temporarily impair locomotion and coordination.

Undesirable effects
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 spray provides surface anaesthesia during an endotracheal procedure but does not prevent post-intubation soreness.

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

Acute systemic toxicity
Lidocaine 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 *Pharmacokinetic properties* and *Overdose*).

Systemic adverse reactions are extremely rare and may result from high plasma levels due to excessive dosage or rapid absorption 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 possible 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.

Overdose
Acute systemic toxicity
Toxic reactions originate mainly in the central nervous 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 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.

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.

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.

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 IV if the convulsions do not stop spontaneously in 15-20 seconds. Thiopentone sodium 1-3 mg/kg IV will abort the convulsions rapidly. Alternatively diazepam 0.1 mg/kgbw IV may be used although its action is slower.

Prolonged convulsions may jeopardise the patient's ventilation and oxygenation. If so, injection of muscle relaxant (e.g. succinylcholine 1 mg/kgbw) will facilitate ventilation, and oxygenation can be controlled. Early endotracheal intubation must be considered in such situations. Suxamethonium will stop the muscle convulsions rapidly, but will require tracheal intubation and artificial ventilation, and should only be used by those familiar with these procedures. If cardiovascular depression is evident (hypotension, bradycardia), ephedrine 5-10 mg IV 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. Adrenaline (0.1-0.2 mg as intravenous or intracardiac injections) should be given as soon as possible and repeated, if necessary.

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

Pharmacological properties
Pharmacodynamic properties
Pharmacotherapeutic group: Local anaesthetic.
ATC Code: N01BB02.

XYLOCAINE pump spray is intended for use on mucous membranes and provides an efficient surface 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 depolarization and repolarization 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 depolarization 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 drug ionizes again and enters the sodium channel to exert an inhibitory effect on sodium influx and, consequently, on impulse conduction.

Pharmacokinetic properties
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 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. Lidocaine is well absorbed from the gastrointestinal tract, but undergoes extensive first-pass metabolism.

Normally about 65% of the lidocaine 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.

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

The main elimination pathway of lidocaine is by liver metabolism. The primary route of metabolism of lidocaine in humans is 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 lidocaine. GX has a longer half-life (about 10 hours) than lidocaine and may accumulate during prolonged administration. Approximately 90% of the lidocaine 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 lidocaine and MEGX following an intravenous bolus dose are approx. 1.5-2 and 2.5 hours respectively. On account of the rapid hepatic metabolism, the kinetics are sensitive to all alternation in liver function. The half-life can be more than doubled in patients with impaired liver function. Impaired renal function does not affect the kinetics, but can 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 from 6.0 µg free base per ml.

Pharmaceutical particulars
List of excipients
Ethanol, Polyethylene glycol 400, Essence of banana, Menthol, Saccharin, Purified water

Special precautions for storage
Do not store above +25°C. During storage at temperatures below +8°C precipitation may occur. This precipitation is dissolved when warming up in room temperatures.

Instructions for use/handling
The spray nozzle is already bent to its final appearance and no further action 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.

Presentations
XYLOCAINE spray 10%, 10 mg/dose, pump spray of 50 ml is available in bottle made of glass with a metering spray pump.
The package includes a plastic spray nozzle.
Reg. No.: DKI2137200384A1

Shelf life
3 years

HARUS DENGAN RESEP DOKTER

Manufactured by:
Aspen Bad Oldesloe GmbH
Bad Oldesloe, Germany

Imported by:
PT Mitsubishi Tanabe Pharma Indonesia
Bandung, Indonesia

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