Xylocaine Jelly 2%
lidocaine hydrochloride
Jelly

Composition
Active constituent:
1g Xylocaine jelly contains: Lidocaine hydrochloride 20 mg.

Pharmaceutical form
Xylocaine jelly is a clear to almost clear, slightly coloured jelly. The vehicle of the active ingredient consists of water thickened with hydroxypropyl methylcellulose. Xylocaine jelly contains methyl parahydroxybensoate and propyl parahydroxybensoate.

Therapeutic indications
Xylocaine jelly is indicated as a surface anaesthetic and lubricant for:

- The male and female urethra during cystoscopy, catheterisation, exploration by sound and other endourethral procedures.

- Nasal and pharyngeal cavities in endoscopic procedures such as gastroscopy and bronchoscopy.

- During proctoscopy and rectoscopy.

- Tracheal intubation.

Symptomatic treatment of pain in connection with cystitis and urethritis.
To relieve pain after circumcision in children.

Posology and method of administration
Xylocaine jelly 2% provides prompt and profound anaesthesia of mucous membranes, giving effective anaesthesia of long duration (approx. 20-30 min). Anaesthesia usually occurs rapidly (within 5 min depending upon the area of application).

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

Absorption from mucous membranes is variable but especially high from the bronchial tree. The absorption of lidocaine jelly from the nasopharynx is usually lower than with other lidocaine products. Blood concentrations of lidocaine after instillation of the jelly in the intact urethra and bladder in doses up to 800 mg are fairly low and below toxic levels.

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 under the age of 12 years the dose should not exceed 6 mg/kg.

No more than four doses should be given in a 24 hour period.

Urethral anaesthesia
Surface anaesthesia of the male adult urethra: for adequate analgesia in males 20 ml (= 400 mg lidocaine hydrochloride) jelly is required. The jelly is instilled slowly until the patient has a feeling of tension or until almost half the tube (10 ml = 200 mg lidocaine hydrochloride) has been emptied. A penile clamp is then applied for several minutes at the corona, after which the rest of the jelly is instilled.

When anaesthesia is especially important, e.g. during sounding or cystoscopy, a larger quantity of jelly (e.g. 30-40 ml) may be instilled in 3-4 portions and allowed to act for 10 minutes before insertion of the instrument. The jelly instilled into the bladder is also effective for procedures in this region.

Surface anaesthesia of the female adult urethra: instill 5-10 ml in small portions to fill the whole urethra. In order to obtain adequate anaesthesia, several minutes should be allowed to elapse prior to performing urological procedures.

Endoscopy
The instillation of 10-20 ml is recommended for adequate analgesia and a small amount may be applied to the lubricating instrument. When combined with other lidocaine products (e.g. for bronchoscopy), the total dose of lidocaine should not exceed 400 mg.

Proctoscopy and rectoscopy
Up to 20 ml can be used for anal and rectal procedures. The total dose should not exceed 400 mg lidocaine.

Lubrication for endotracheal intubation
About 2 ml applied to the surface of the tube just prior to insertion. Care should be taken to avoid introducing the product into the lumen of the tube.

Contraindications
Known history of hypersensitivity to local anaesthetics of the amide type, or other components of the jelly.

Hypersensitivity to local anaesthetics of the amide type, or to any of the excipients.

Hypersensitivity to methyl and/or propyl parahydroxybensoate (methyl-/propyl paraben), or to their metabolite para amino benzoic acid (PABA). Formulations of lidocaine containing parabens should be avoided in patients allergic to ester local anaesthetics or their metabolite PABA.

Special warnings and precautions for use
Excessive doses of lidocaine products or short intervals between doses, can result in high plasma levels and serious adverse effects. Patients should be instructed to adhere strictly to the recommended dosage (the management of serious adverse reactions may require the use of resuscitative equipment, oxygen and other resuscitative drugs). (See “Overdose”.)

Absorption from wound surfaces and mucous membranes is relatively high and especially high in the bronchial tree. The absorption of lidocaine jelly from the nasopharynx is

variable but usually lower than with other lidocaine products. Following instillation in urethra and bladder, adsorption is low. Lidocaine jelly should be used with caution in patients with traumatized mucosa and/or sepsis in the region of the proposed application.

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.

When used for endotracheal tube lubrication, care should be taken to avoid introduction of the jelly into the lumen of the tube. The jelly may dry on the inner surface leaving a residue which tends to clump with flexion, narrowing the lumen. There have been rare reports in which this residue has caused the lumen to occlude.

Patients being treated with class III antiarrhythmic drugs (e.g. amiodarone) should be closely supervised, and ECG monitoring should be considered, as the effects on the heart can be additive.

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

Xylocaine jelly 20 mg/ml 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
Lidocaine should be used with caution in patients receiving agents structurally related to local anaesthetics, since the toxic effects are additive.
Specific interaction studies with local anaesthetics and class III antiarrhythmic drugs have not been carried out, but caution should be observed.
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 be of no clinical importance following short term treatment with lidocaine 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 malformations.

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

Effects 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 coordination.

Undesirable effects

Local reactions

An increased incidence of postoperative "sore throat" has been reported following endotracheal tube lubrication with lidocaine jelly.

Allergic reactions

Allergic reactions (in most severe instances anaphylactic shock) to local anaesthetics of the amide type are rare (<1/1000). Other constituents of the jelly e.g. methyl parahydroxy bensoate and propyl parahydroxy bensoate may also cause this type of reaction.

Acute systemic toxicity

Lidocaine may have acute toxic effects if high systemic levels occur due to fast absorption or overdosage. (See “Pharmacodynamic properties” and “Overdose”.)

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 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 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

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 drugs.

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.

Pharmacological description
Xylocaine jelly 2% provides prompt and profound anaesthesia of mucous membranes and lubrication which reduces friction. Its water-miscible base, characterized by high viscosity and low surface tension, brings the anaesthetic into intimate and prolonged contact with the tissue, giving effective anaesthesia of long duration (approx. 20-30 min). Anaesthesia usually occurs rapidly (within 5 min, depending upon the area of application).

Pharmacodynamic properties
Pharmacotherapeutic group: Local anaesthetic, ATC code N01BB02

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 (See "Overdose") usually precedes the cardiovascular effects as it occurs at lower plasma concentrations. Direct effects of local anaesthetics on the heart include slow conduction, negative inotropism and possibly cardiac arrest.

Pharmacokinetic properties
Lidocaine is absorbed following topical administration to mucous membranes, its rate and extent of absorption being dependent upon concentration and the 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. Lidocaine is also well-absorbed from the gastrointestinal tract, although little intact drug appears in the circulation because of biotransformation in the liver.

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. 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 lidocaine in human is N-dealkylation to monoethylglycine xylidine (MEGX), followed by hydrolysis to 2,6-xylidine and hydroxylation to 4-hydroxy-2,6-xylidine. MEGX can also be further dealkylated to glycine xylidine (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 10h) than lidocaine and may accumulate during long-term administration. Approximately 90% of the lidocaine administrated intravenously 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 following an intravenous bolus injection is typically 1.5 to 2.0 hours. Because of the rapid rate at which lidocaine is metabolized, 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 µg free base per ml.

Preclinical safety data

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 vivo* or *in vitro* 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-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.

List of excipients
- Hydroxypropyl methylcellulose
- Sodium hydroxide 2 mol/l
  and/or
- Hydrochloric acid 2 mol/l to pH 6.2-6.8
- Methyl parahydroxybensoate
- Propyl parahydroxybensoate
- Water, purified

Special precautions for storage
Do not store above 25°C. Do not freeze.

Shelf-life
Please see outer pack

Pack size
Please see outer pack

Date of revision of the text
January 2009

PAIN.000-061-123.4.0

AstraZeneca AB, Södertälje, Sweden

Manufactured by Recipharm Karlskoga AB, Karlskoga, Sweden for AstraZeneca.