PACKAGE INSERT

XYLOCAINE® ENDOTRACHEAL

(lidocaine non-aerosol spray)

10mg/Metered Dose

Topical Anesthetic

AstraZeneca Canada Inc.
1004 Middlegate Road
Mississauga, Ontario
L4Y 1M4
www.astrazeneca.ca

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XYLOCAINE® ENDOTRACHEAL

(lidocaine non-aerosol spray)

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Nonmedicinal Ingredients
Oral	Non-aerosol spray, 10mg/Metered Dose	Ethanol, polyethylene glycol 400, essence of banana, menthol (natural), saccharin, purified water

INDICATIONS AND CLINICAL USE

Adults (>18 years of age):

Xylocaine Endotracheal (lidocaine) is indicated for surface anesthesia associated with:

- nasal procedures, e.g. puncture of the maxillary sinus;
- 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.

Geriatrics (> 65 years of age):

Elderly patients should be given reduced doses commensurate with their age and physical condition (see DOSAGE AND ADMINISTRATION-Special Populations).

Pediatrics (<18 years of age):

Children should be given reduced doses commensurate with their age, weight and physical condition (see DOSAGE AND ADMINISTRATION-Special Populations).

Lidocaine should be used with caution in children younger than two years of age as there are insufficient data to support the safety and efficacy of this product in this patient population at this time (see WARNINGS AND PRECAUTIONS-Special Populations).

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CONTRAINDICATIONS

XYLOCAINE Endotracheal (lidocaine) is contraindicated in:

- patients with a known hypersensitivity to local anesthetics of the amide type or to any of the ingredients in the formulation. For a complete listing, see DOSAGE FORMS, COMPOSITION, AND PACKAGING.

WARNINGS AND PRECAUTIONS

General

EXCESSIVE DOSAGE, OR SHORT INTERVALS BETWEEN DOSES, CAN RESULT IN HIGH PLASMA LEVELS OF LIDOCAINE OR ITS METABOLITES AND SERIOUS ADVERSE EFFECTS. Absorption from the 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. This is especially important in children where doses vary with weight. The management of serious adverse reactions may require the use of resuscitative equipment, oxygen and other resuscitative drugs (see OVERDOSAGE).

The lowest dosage that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. Tolerance to elevated blood levels varies with the status of the patient.

Lidocaine should be used with caution in patients with sepsis and/or traumatized mucosa at the area of application, since under such conditions there is the potential for rapid systemic absorption.

XYLOCAINE Endotracheal (lidocaine) should be used with caution in children under the age of 2 as there is insufficient data to support the safety and efficacy of this product in this patient population at this time.

In patients under general anesthesia who are paralyzed, higher plasma concentrations may occur than in spontaneously breathing patients. Unparalyzed 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.

Avoid contact with eyes.

Many drugs used during the conduct of anesthesia are considered potential triggering agents for familial malignant hyperthermia. It has been shown that the use of amide local anesthetics in malignant hyperthermia is safe. However, there is no guarantee that neural blockade will prevent the development of malignant hyperthermia during surgery. It is also difficult to predict the need for supplemental general anesthesia. Therefore a standard protocol for the management of malignant hyperthermia should be available.

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When topical anesthetics are used in the mouth, the patient should be aware that the production of topical anesthesia may impair swallowing and thus enhance the danger of aspiration. Numbness of the tongue or buccal mucosa may enhance the danger of unintentional biting trauma. Food or chewing gum should not be taken while the mouth or throat area is anesthetized. See also Part III: Consumer Information.

XYLOCAINE Endotracheal should not be used on cuffs of endotracheal tubes 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 Endotracheal is ineffective when applied to intact skin.

Lidocaine has been shown to be porphyrinogenic in animal models. XYLOCAINE Endotracheal should only be prescribed to patients with acute porphyria on strong or urgent indications, when they can be closely monitored. Appropriate precautions should be taken for all porphyric patients.

Cardiovascular

Lidocaine should be used with caution in patients with bradycardia or impaired cardiovascular function since they may be less able to compensate for functional changes associated with the prolongation of A-V conduction produced by amide-type local anesthetics.

Lidocaine should be used with caution in patients with severe shock.

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

Neurologic

Epilepsy: The risk of central nervous system side effects when using lidocaine in patients with epilepsy is very low, provided that the dose recommendations are followed (See DOSAGE AND ADMINISTRATION).

Locomotion and Coordination: Topical lidocaine formulations generally result in low plasma concentrations because of a low degree of systemic absorption. However, depending on the dose, local anesthetics may have a very mild effect on mental function and coordination even in the absence of overt CNS toxicity and may temporarily impair locomotion and alertness.

Renal

Lidocaine is metabolized primarily by the liver to monoethylglycinexylidine (MEGX, which has some CNS activity), and then further to metabolites glycinexylidine (GX) and 2,6-dimethylaniline (see ACTION AND CLINICAL PHARMACOLOGY). Only a small fraction (2%) of lidocaine is excreted unchanged in the urine. The pharmacokinetics of lidocaine and its main metabolite were not altered significantly in haemodialysis patients (n=4) who received an intravenous dose of lidocaine. Therefore, renal impairment is not expected to significantly affect the pharmacokinetics of lidocaine when XYLOCAINE Endotracheal is

used for short treatment durations, according to dosage instructions (see DOSAGE AND ADMINISTRATION). Caution is recommended when lidocaine is used in patients with severely impaired renal function because lidocaine metabolites may accumulate during long term treatment (see DOSAGE AND ADMINISTRATION).

Hepatic

Because amide-type local anesthetics such as lidocaine are metabolized by the liver, these drugs, especially repeated doses, should be used cautiously in patients with hepatic disease. Patients with severe hepatic disease, because of their inability to metabolize local anesthetics normally, are at greater risk of developing toxic plasma concentrations.

Sensitivity

Lidocaine should be used with caution in persons with known drug sensitivities.

Special Populations

Debilitated patients, acutely ill patients and patients with sepsis should be given reduced doses commensurate with their age, weight and physical condition because they may be more sensitive to systemic effects due to increased blood levels of lidocaine following repeated doses.

Pregnant Women: There are no adequate and well-controlled studies in pregnant women on the effect of lidocaine on the developing fetus.

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. However, care should be given during early pregnancy when maximum organogenesis takes place.

Labour and Delivery: Should XYLOCAINE Endotracheal be used concomitantly with other products containing lidocaine during labour and delivery, the total dose contributed by all formulations must be kept in mind.

Nursing Women: Lidocaine and its metabolites are excreted in the breast milk. At therapeutic doses the quantities of lidocaine and its metabolites in breast milk are small and generally are not expected to be a risk for the infant.

Pediatrics: Children should be given reduced doses commensurate with their age, weight and physical condition because they may be more sensitive to systemic effects due to increased blood levels of lidocaine following repeated doses (see DOSAGE AND ADMINISTRATION).

XYLOCAINE Endotracheal should be used with caution in children under the age of 2 as there is insufficient data to support the safety and efficacy of this product in this patient population at this time.

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Geriatrics: Elderly patients may be more sensitive to systemic effects due to increased blood levels of lidocaine following repeated doses and may require dose reductions.

Carcinogenesis and Mutagenesis

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. A chronic oral toxicity study of the metabolite 2,6-dimethylaniline (0, 14, 45, 135 mg/kg) administered in feed to rats showed that there was a significantly greater incidence of nasal cavity tumors in male and female animals that had daily oral exposure to the highest dose of 2,6-dimethylaniline for 2 years. The lowest tumor-inducing dose tested in animals (135 mg/kg) corresponds to approximately 45 times the amount of 2,6-dimethylaniline to which a 50 kg subject would be exposed following the application of 40x10 mg/metered dose of lidocaine non-aerosol spray for 24 hours on the mucosa, assuming the highest theoretical extent of absorption of 100%, and 80% conversion to 2,6-dimethylaniline. Based on a yearly exposure (once daily dosing with 2,6-dimethylaniline in animals and 5 treatment sessions with 40x10 mg/metered dose of lidocaine non-aerosol spray in humans), the safety margins would be approximately 3400 times when comparing the exposure in animals to man.

ADVERSE REACTIONS

Adverse experiences following the administration of lidocaine are similar in nature to those observed with other amide local anesthetic agents. These adverse experiences are, in general, dose-related and may result from high plasma levels caused by overdosage or rapid absorption, eg, application to areas below the vocal cords, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels at or above 6.0 μg free base per mL.

Serious adverse experiences are generally systemic in nature. The following types are those most commonly reported:

Central Nervous System: CNS manifestations are excitatory and/or depressant and may be characterized by the following signs and symptoms of escalating severity: circumoral paresthesia, light-headedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, hyperacusis, tinnitus, blurred vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest. The excitatory manifestations (e.g., twitching, tremors, convulsions) may be very brief or may not occur at all, in which case the first manifestation of toxicity may be drowsiness merging into unconsciousness and respiratory arrest.

Drowsiness following the administration of lidocaine is usually an early sign of a high lidocaine plasma level and may occur as a consequence of rapid absorption.

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Cardiovascular System: Cardiovascular manifestations are usually depressant and are characterized by bradycardia, hypotension, arrhythmia, and cardiovascular collapse, which may lead to cardiac arrest.

Allergic: Allergic reactions are characterized by cutaneous lesions, urticaria, edema or, in the most severe cases, anaphylactic shock. Allergic reactions of the amide type are rare (<0.1%) and may occur as a result of sensitivity either to the local anesthetic agent or to other components in the formulation (See DOSAGE FORM, COMPOSITION AND PACKAGING).

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

DRUG INTERACTIONS

Overview

Lidocaine is mainly metabolized in the liver by CYP1A2 and CYP3A4 to its two major metabolites, monoethylglycinexylidine (MEGX) and glycinexylidine (GX), both of which are pharmacologically active. Lidocaine has a high hepatic extraction ratio. Only a small fraction (2%) of lidocaine is excreted unchanged in the urine. The hepatic clearance of lidocaine is expected to depend largely on blood flow.

Strong inhibitors of CYP1A2, such as fluvoxamine, given concomitantly with lidocaine, can cause a metabolic interaction leading to an increased lidocaine plasma concentration. Therefore, prolonged administration of lidocaine should be avoided in patients treated with strong inhibitors of CYP1A2, such as fluvoxamine. When co-administered with intravenous lidocaine, two strong inhibitors of CYP3A4, erythromycin and itraconazole, have each been shown to have a modest effect on the pharmacokinetics of intravenous lidocaine. Other drugs such as propranolol and cimetidine have been reported to reduce intravenous lidocaine clearance, probably through effects on hepatic blood flow and/or metabolism.

When lidocaine is used topically, plasma concentrations are of importance for safety reasons (see WARNINGS AND PRECAUTIONS, General; ADVERSE REACTIONS). However, with the low systemic exposure and short duration of topical application, the abovementioned metabolic drug-drug interactions are not expected to be of clinical significance when XYLOCAINE Endotracheal is used according to dosage recommendations.

Clinically relevant pharmacodynamic drug interactions may occur with lidocaine and other local anesthetics or structurally related drugs, and Class I and Class III antiarrhythmic drugs due to additive effects.

Drug-Drug Interactions

<u>Local anesthetics and agents structurally related to amide-type local anesthetics</u>

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

Antiarryhythmic Drugs

Class I Antiarrhythmic drugs
Class I antiarrhythmic drugs (such as mexiletine) should be used with caution since toxic effects are additive and potentially synergistic.

Class III Antiarrhythmic drugs
Caution is advised when using Class III antiarrhythmic drugs concomitantly with lidocaine due to potential pharmacodynamic or pharmacokinetic interactions with lidocaine, or both. A drug interaction study has shown that the plasma concentration of lidocaine may be increased following administration of a therapeutic dose of intravenous lidocaine to patients treated with amiodarone (n=6). Case reports have described toxicity in patients treated concomitantly with lidocaine and amiodarone. Patients treated with Class III antiarrhythmic drugs (e.g. amiodarone) should be kept under close surveillance and ECG monitoring should be considered, since cardiac effects of these drugs and lidocaine may be additive.

Strong Inhibitors of CYP1A2 and CYP3A4

Cytochrome CYP1A2 and CYP3A4 are involved in the formation of the pharmacologically active lidocaine metabolite MEGX

Fluvoxamine: Strong inhibitors of CYP1A2, such as fluvoxamine, given during prolonged administration of lidocaine to areas with a high extent of systemic absorption (e.g., mucous membranes) can cause a metabolic interaction leading to an increased lidocaine plasma concentration. The plasma clearance of a single intravenous dose of lidocaine was reduced by 41 to 60% during co-administration of fluvoxamine, a selective and potent CYP1A2 inhibitor, to healthy volunteers.

Erythromycin and Itraconazole: Erythromycin and itraconazole, which are strong inhibitors of CYP3A4, have been shown to reduce clearance of lidocaine by 9 to 18%, following a single intravenous dose of lidocaine to healthy volunteers.

During combined co-administration with fluvoxamine and erythromycin the plasma clearance of lidocaine was reduced by 53%.

β-blockers and cimetidine

Following a single intravenous dose of lidocaine, administered to healthy volunteers, the clearance of lidocaine has been reported to be reduced up to 47% when co-administered with propanolol and up to 30% when co-administered with cimetidine. Reduced clearance of lidocaine when co-administered with these drugs is probably due to reduced liver blood flow and/or inhibition of microsomal liver enzymes. The potential for clinically significant interactions with these drugs should be considered during long-term treatment with high doses of lidocaine.

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Drug-Food Interactions
Interactions of lidocaine with food have not been established.

Drug-Herb Interactions
Interactions of lidocaine with herbal products have not been established.

Drug-Laboratory Tests Interactions
Interactions of lidocaine with laboratory tests have not been established.

Drug-Lifestyle Interactions
Interactions of lidocaine with lifestyle have not been established.

DOSAGE AND ADMINISTRATION

Dosing Considerations

General

When XYLOCAINE Endotracheal (lidocaine) is used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind.

Since absorption is variable and especially high in the trachea and bronchi, the maximum recommended doses vary depending on the area of application. Application 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 10 mg lidocaine.

Special Populations

Lidocaine should be used with caution in patients with epilepsy, impaired cardiac conduction, bradycardia, impaired hepatic or renal function and in severe shock (See WARNINGS AND PRECAUTIONS).

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

XYLOCAINE Endotracheal should be used with caution in children under the age of 2 as there is insufficient data to support the safety and efficacy of this product in this patient population at this time.

Mode of Administration

XYLOCAINE Endotracheal

When using the spray for the first time, after attaching the nozzle, the pump must be primed by pressing downwards on the actuator five to ten times. When changing to a new nozzle, the pump need not be re-primed but the air in the nozzle must be voided before a full dose is delivered. This usually requires two actuations.

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The spray nozzle is already bent to its final configuration for use. No further manipulations should be made to the spray nozzle before use. The nozzle must not be shortened, otherwise the spray function will be destroyed. XYLOCAINE Endotracheal should be used in the upright position to ensure proper function. Nozzles should not be reused and should be discarded immediately after use.

XYLOCAINE Endotracheal should not be used on cuffs or endotracheal tubes made of plastic. Lidocaine base in contact with PVC and non-PVC cuffs or endotracheal tubes can damage the cuff (pinholes), which may cause leakage that could lead to pressure loss in the cuff.

Recommended Dose and Dosage Adjustment

Adults

Table 1 Dose Recommendations for Adults

Area	Recommended Dose (mg)	Maximum Dose for Short[1] Procedures (mg)	Maximum Dose for Prolonged[2] Procedures (mg)
Nasal procedures, e.g. puncture of the maxillary sinus.	20-60	500	600
Procedures in the oropharynx, e.g. gastrointestinal endoscopy.	20-200	500	600
Procedures in the respiratory tract, e.g. insertion of instruments and tubes.	50-400	400	600
Procedures in the larynx, trachea and bronchi.	50-200	200[3]	400

[1] For short procedures the drug is given for less than one minute.
[2] For prolonged procedures, the duration of application is more than 5 minutes.
[3] During controlled ventilation the dose should be reduced.

Since absorption is variable and especially high in the trachea and bronchi the maximum recommended doses vary depending on the area of application (see ACTION AND CLINICAL PHARMACOLOGY, Pharmacokinetics).

Pediatrics (<18 years of age)

All children (<18 years of age) should be given doses commensurate with their age, weight and physical condition; however children over 12 years of age considered underweight (i.e., less than 25 kg) should be dosed with caution.

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Under 12 years of age: For laryngotracheal use, the dose should not exceed 3 mg/kg. For nasal and oropharyngeal use, the dose should not exceed 4-5 mg/kg. In neonates and infants, less concentrated lidocaine solutions are recommended.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Acute systemic toxicity from local anesthetics is generally related to high plasma levels encountered during therapeutic use of local anesthetics and originates mainly in the central nervous and the cardiovascular systems (see ADVERSE REACTIONS and WARNINGS AND PRECAUTIONS). It should be kept in mind that clinically relevant pharmacodynamic drug interactions (i.e., toxic effects) may occur with lidocaine and other local anesthetics or structurally related drugs, and Class I and Class III antiarrhythmic drugs due to additive effects (see DRUG INTERACTIONS).

Symptoms

Central nervous system toxicity is a graded response, with symptoms and signs of escalating severity. The first symptoms are circumoral paresthesia, 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 apnea may occur. Acidosis, hyperkalaemia, hypocalcaemia and hypoxia increase and extend the toxic effects of local anesthetics.

Recovery is due to redistribution and metabolism of the local anesthetic drug. Recovery may be rapid unless large amounts of the drug have been administered.

Cardiovascular effects may be 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 anesthetic or is heavily sedated with drugs such as a benzodiazepine or barbiturate.

Treatment

The first consideration is prevention, best accomplished by careful and constant monitoring of cardiovascular and respiratory vital signs and the patient's state of consciousness after each local anesthetic administration. At the first sign of change, oxygen should be administered.

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The first step in the management of systemic toxic reactions consists of immediate attention to the maintenance of a patent airway and assisted or controlled ventilation with oxygen and a delivery system capable of permitting immediate positive airway pressure by mask. This may prevent convulsions if they have not already occurred.

If convulsions occur, the objective of the treatment is to maintain ventilation and oxygenation and support circulation. Oxygen must be given and ventilation assisted if necessary (mask and bag or tracheal intubation). Should convulsions not stop spontaneously after 15-20 seconds, an anticonvulsant should be given iv to facilitate adequate ventilation and oxygenation. Thiopental sodium 1-3 mg/kg iv is the first choice. Alternatively diazepam 0.1mg/kg bw iv 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 1mg/kg bw) will facilitate ventilation, and oxygenation can be controlled. Early endotracheal intubation is required when succinylcholine is used to control motor seizure activity.

If cardiovascular depression is evident (hypotension, bradycardia), ephedrine 5-10 mg i.v. should be given and may be 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 anesthetics. Epinephrine (0.1-0.2 mg as intravenous or intracardial injections) should be given as soon as possible and repeated, if necessary.

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

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Lidocaine stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses, thereby effecting local anesthetic action. Local anesthetics of the amide type are thought to act within the sodium channels of the nerve membrane.

Onset of Action

XYLOCAINE Endotracheal (lidocaine), when applied topically to the oral cavity, acts on mucous membranes to produce local anesthesia. Anesthesia occurs usually within 1-5 minutes and persists for approximately 10-15 minutes. XYLOCAINE Endotracheal is ineffective when applied to intact skin.

Hemodynamics

Lidocaine, like other local anesthetics, may also have effects on excitable membranes in the brain and myocardium. If excessive amounts of drug reach systemic circulation rapidly,

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symptoms and signs of toxicity will appear, emanating from the central nervous and cardiovascular systems.

Central nervous system toxicity (see OVERDOSAGE) usually precedes the cardiovascular effects since it occurs at lower plasma concentrations. Direct effects of local anesthetics on the heart include slow conduction, negative inotropism and eventually cardiac arrest.

Pharmacokinetics

Absorption: The rate and extent of absorption depends upon concentration and total dose administered, the specific site of application and duration of exposure. In general, the rate of absorption of local anesthetic agents, following topical application to wound surfaces and mucous membranes is high, and occurs most rapidly after intratracheal and bronchial administration. Lidocaine is also well absorbed from the gastrointestinal tract, although little intact drug may appear in the circulation because of biotransformation in the liver.

Distribution: Lidocaine has a total plasma clearance of 0.95 L/min and a volume of distribution at steady state of 91 L.

Lidocaine readily crosses the placenta, and equilibrium in regard to free, unbound drug will be reached. Because the degree of plasma protein binding in the fetus is less than in the mother, the total plasma concentration will be greater in the mother, but the free concentrations will be the same.

The plasma binding of lidocaine is dependent on drug concentration, and the fraction bound decreases with increasing concentration. At concentrations of 1 to 4 μg 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.

Metabolism: Lidocaine is metabolized 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. Only 2% of lidocaine is excreted unchanged. Most of it is metabolized first to monoethylglycinexylidide (MEGX) and then to glycinexylidide (GX) and 2,6-dimethylaniline. Up to 70% appears in the urine as 4-hydroxy- 2,6-dimethylaniline.

Excretion: Lidocaine has an elimination half-life of 1.6 h and an estimated hepatic extraction ratio of 0.65. The clearance of lidocaine is almost entirely due to liver metabolism, and depends both on liver blood flow and the activity of metabolizing enzymes.

The elimination half-life following an intravenous bolus injection is typically 1.5 to 2.0 hours. The elimination half-life in neonates (3.2 h) is approximately twice that of adults. 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.

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Special Populations and Conditions

Acidosis increases the systemic toxicity of lidocaine while the use of CNS depressants may increase the levels of lidocaine required to produce overt CNS effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels at or above 6.0 µg free base per mL.

STORAGE AND STABILITY

Store at controlled room temperature (15-30°C). Protect from freezing.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Forms

XYLOCAINE Endotracheal (lidocaine) is a clear or almost clear, slightly coloured liquid with an odour of ethanol, menthol, and banana.

Composition

Active constituent: Each metered dose contains 10 mg of lidocaine.

Non-Medical Ingredients include ethanol, polyethylene glycol 400, essence of banana, menthol (natural), saccharin, purified water.

Packaging

XYLOCAINE Endotracheal is available in a 50 mL non-aerosol glass spray bottle with a metered dose valve and a 12 cm (5") single use plastic nozzle. Additional 12 cm (5”) plastic nozzles are available in packages of 50 nozzles.

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XYLOCAINE® ENDOTRACHEAL
lidocaine non-aerosol spray

PART III:
CONSUMER INFORMATION

This leaflet is part III of a two-part "Prescribing Information" published when XYLOCAINE Endotracheal spray was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about XYLOCAINE Endotracheal spray. Contact your doctor or pharmacist if you have any questions about the drug.

Before using XYLOCAINE Endotracheal spray, read this leaflet carefully.

Please keep this leaflet to refer to until you have used up all your XYLOCAINE Endotracheal spray.

This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

ABOUT THIS MEDICATION

WHAT THE MEDICATION IS USED FOR:
XYLOCAINE Endotracheal spray is used to produce temporary loss of feeling or numbness of the area where it is applied in adults and children, and can be used:

- before certain types of examination and instrumentation are performed by your doctor, e.g., bronchial examination;
- before surgical procedures in the throat, mouth and nose.

WHAT IT DOES:
XYLOCAINE Endotracheal is the brand name for a topical anesthetic that contains the drug lidocaine. Topical anesthetics are used to produce a temporary loss of feeling or numbness on the area where they are applied.

XYLOCAINE Endotracheal should start to work within 5 minutes after it is applied and its effect should last about 10 to 15 minutes.

WHEN IT SHOULD NOT BE USED:
Do not use XYLOCAINE Endotracheal spray if you:

- are allergic to lidocaine, any other "-caine" type anesthetics, or any of the non-medicinal ingredients in the product (see **NONMEDICINAL INGREDIENTS** below).

WHAT THE MEDICINAL INGREDIENT IS:
lidocaine 10 mg/metered dose.

NONMEDICINAL INGREDIENTS:
XYLOCAINE Endotracheal spray also contains ethanol, polyethylene glycol 400, essence of banana, menthol, saccharin and purified water.

Tell your doctor if you think you may be sensitive to any of the medicinal or non-medicinal ingredients.

WHAT DOSAGE FORMS IT COMES IN:
XYLOCAINE Endotracheal spray, 50 mL non-aerosol glass spray bottle with a metered dose valve and a single use plastic nozzle.

WARNINGS AND PRECAUTIONS

BEFORE you use XYLOCAINE Endotracheal spray tell your doctor or dentist:

- about all health problems you have now or have had in the past;
- about other medicines you take, including ones you can buy without a prescription;
- if you are taking other medicines such as drugs used to treat irregular heart activity (anti-arrhythmics);
- if you have ever had a bad, unusual or allergic reaction to XYLOCAINE Endotracheal spray or any other medicines ending with "caine";
- if you think you may be allergic or sensitive to any ingredients in XYLOCAINE Endotracheal spray (see above);
- if there is an infection, skin rash, cut or wound at or near the area you want to apply XYLOCAINE Endotracheal;
- if you have a skin condition that is severe or that covers a large area;
- if you have severe heart, kidney or liver disease (see PROPER USE OF THIS MEDICATION);
- if you have epilepsy (there is very low risk if used as per PROPER USE OF THE MEDICATION section);
- If you or someone in your family has been diagnosed with porphyria;
- if you are experiencing severe shock;
- if you are pregnant, plan to become pregnant or are breastfeeding.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor or dentist about any other drugs you take or have recently taken, including:

- drugs you can buy without a prescription;
- anti-arrhythmic drugs for heart problems (e.g. mexiletine, amiodarone) (see PROPER USE OF THIS MEDICATION);
- other anesthetics (see PROPER USE OF THIS MEDICATION);
- propranolol for heart problems or cimetidine for gastrointestinal problems, if high doses of XYLOCAINE Endotracheal spray will be used for a long time;

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- fluvoxamine, for depression, if high doses of XYLOCAINE Endotracheal spray will be used for a long time.

Usage of such medicines at the same time as XYLOCAINE Endotracheal spray may increase the risk of serious side effects.

PROPER USE OF THIS MEDICATION

USUAL DOSE:
A doctor/dentist/nurse will give you XYLOCAINE Endotracheal spray. The nozzles should not be re-used and should be disposed of immediately after use.

The dose given is decided by the doctor/dentist. If you have the impression that the effect of XYLOCAINE Endotracheal spray is too strong or too weak, talk to your doctor/dentist.

Conditions where dose adjustments may be required:
- elderly patients
- children under 18 years of age
- acutely ill patients
- patients with severe liver disease
- patients with severe kidney disease
- patients also treated with other anesthetics or certain antiarrhythmic drugs (such as amiodarone or mexiletine)

Dose for Adults:
The recommended dose of XYLOCAINE Endotracheal spray is:
- 20-60 mg for nasal procedures. No more than 500 mg for short procedures and no more than 600 mg for longer procedures;
- 20-200 mg for procedures such as gastrointestinal endoscopy. No more than 500 mg for short procedures and no more than 600 mg for longer procedures;
- 50-400 mg for respiratory tract procedures. No more than 400 mg for short procedures and no more than 600 mg for longer procedures;
- 50-200 mg for procedures in the upper respiratory tract. No more than 200 mg for short procedures and no more than 400 mg for longer procedures.

For short procedures the drug is given for less than one minute. For longer procedures, the drug is given for more than 5 minutes.

Dose for Children (Under 18 Years of Age):
The dose depends on the child's age, weight and physical condition, however, children over 12 years of age considered underweight (less than 25 kg) should be dosed with caution. For children under 12 years of age:
- No more than 3 mg/kg of body weight should be used for upper respiratory tract procedures;
- No more than 4-5 mg/kg of body weight should be used for nasal and gastrointestinal procedures;
- In neonates and infants, less concentrated lidocaine solutions are recommended.

OVERDOSE:

In case of drug overdose, contact the regional Poison Control Centre, hospital emergency department or a health care practitioner immediately, even if there are no symptoms.

Early signs of overdosage are light-headedness, dizziness and sometimes blurred vision. In the event of a serious overdosage, trembling, seizures or unconsciousness may occur.

If the early signs of overdosage are noticed and no further XYLOCAINE Endotracheal spray is given, the risk of serious side effects occurring rapidly decreases. If you think you or anyone else is experiencing any of the above signs, contact a doctor or go to the nearest hospital right away.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like any medication, XYLOCAINE Endotracheal spray may cause side effects in some people.

Avoid eating or chewing gum when XYLOCAINE Endotracheal is sprayed in the mouth or throat since numbness in these areas may interfere with swallowing and could potentially cause choking. Numbness of the tongue or gums may also increase the danger of injury due to biting.

Avoid exposure to extreme hot or cold temperatures (e.g. food, drink) until complete sensation has returned.

Avoid contact with the eyes because numbness in the eyes may prevent you from noticing if you get something in your eye.

With the recommended doses, XYLOCAINE Endotracheal spray has no effect on the ability to drive and use machines.

Medicines affect different people in different ways. Just because side effects have occurred in some patients, does not mean that you will get them. If any side effects bother you, or if you experience any unusual effects while you are using XYLOCAINE Endotracheal spray, stop using it and check with your doctor or pharmacist as soon as possible.

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SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency help
		Only if severe	In all cases	
Rare	**Allergic reaction such as:** redness, itching or swelling of your skin, hives, burning, stinging, or any other skin problems, swelling of the neck area, or any difficulty with breathing, not present before using this medicine	**X**		**X**

This is not a complete list of side effects. For any unexpected effects while taking XYLOCAINE Endotracheal, contact your doctor or pharmacist.

XYLOCAINE Endotracheal spray can cause serious side effects if too much is used. These include: drowsiness, numbness of your tongue, light-headedness, ringing in your ears, blurred vision, vomiting, dizziness, unusually slow heart beat, fainting, nervousness, unusual sweating, trembling or seizures.

The above are extremely rare and usually require large amounts of XYLOCAINE Endotracheal spray over a long period of time.

Contact your doctor/dentist or go to the nearest hospital immediately if any of these symptoms appear.

HOW TO STORE IT

Keep XYLOCAINE Endotracheal spray at room temperature. Protect from freezing. Your doctor/dentist or the hospital will normally store XYLOCAINE Endotracheal spray. The staff are responsible for the storing, using and disposing of the solution in the correct way. The nozzles should not be re-used and should be disposed of immediately after use.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701D
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

Important Note: This leaflet alerts you to some of the times you should call your doctor. Other situations which cannot be predicted may arise. Nothing about this leaflet should stop you from calling your doctor with any questions or concerns you have about using XYLOCAINE Endotracheal spray.

NOTE: This CONSUMER INFORMATION leaflet provides you with the most current information at the time of printing.

For the most current information, the Consumer Information Leaflet plus the full Prescribing Information, prepared for health professionals can be found at:
www.astrazeneca.ca or by contacting the sponsor, AstraZeneca Canada Inc. at:
Customer Inquiries – 1 (800) 668-6000,
Renseignements – 1 (800) 461-3787.

This leaflet was prepared by:
AstraZeneca Canada Inc. Mississauga, Ontario L4Y 1M4

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