

PRESCRIBING INFORMATION

pms-LIDOCAINE VISCOUS 2%

Lidocaine Hydrochloride Oral Topical Solution, USP

20 mg/mL

Oral Topical Anesthetic

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pms-LIDOCAINE VISCOUS 2%

Lidocaine Hydrochloride Oral Topical Solution, USP

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	All Nonmedicinal Ingredients
Oral Topical	Liquid 2% (20 mg/mL) lidocaine hydrochloride	Artificial cherry flavor, FD&C Red No.2, glycerin, methylparaben, propylene glycol, propylparaben, purified water, sodium saccharin and sodium carboxymethylcellulose. Citric acid and sodium citrate to adjust pH

INDICATIONS AND CLINICAL USE

Adults (≥18 years of age):

pms-LIDOCAINE VISCOUS 2% (Lidocaine Hydrochloride Oral Topical Solution, USP) is indicated to provide relief of pain and discomfort in connection with:

- Irritated or inflamed mucous membranes of the mouth and pharynx, e.g. lesions following tonsillectomy;
- Introduction of instruments and catheters into the respiratory and digestive tracts, e.g. bronchoscopy, esophagoscopy;
- Painful diseases of the upper gastrointestinal tract e.g. esophagitis.

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 (2 to <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. Use in this patient population should be limited to those situations where safer alternatives are not available or have been tried but failed (see WARNINGS AND PRECAUTIONS-Special Populations). Do not use to treat teething pain in infants and children.

CONTRAINDICATIONS

pms-LIDOCAINE VISCOUS 2% is contraindicated in:

- patients with a known history of hypersensitivity to local anesthetics of the amide type or to other components of the solution (see DOSAGE FORMS, COMPOSITION AND PACKAGING).
- patients with a known hypersensitivity to methylparaben and/or propylparaben (preservatives used in pms-LIDOCAINE VISCOUS 2%), or to their metabolite para amino benzoic acid (PABA).

Formulations of lidocaine containing parabens should also be avoided in patients with a history of allergic reactions to ester local anesthetics, which are metabolized to PABA.

WARNINGS AND PRECAUTIONS

Life-threatening and fatal events in infants and young children

Postmarketing cases of seizures, cardiopulmonary arrest, and death in patients under the age of 3 years have been reported with use of lidocaine hydrochloride solution due to accidental ingestion, or accidental overdose when it was not administered in strict adherence to the dosing and administration recommendations.

pms-LIDOCAINE VISCOUS 2% should not be administered to infants and children for teething pain. pms-LIDOCAINE VISCOUS 2% 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. Use in this patient population should be limited to those situations where safer alternatives are not available or have been tried but failed (see WARNINGS AND PRECAUTIONS, Special Populations).

General

EXCESSIVE DOSAGE, OR SHORT INTERVALS BETWEEN DOSES, CAN RESULT IN HIGH PLASMA LEVELS OF LIDOCAINE OR ITS METABOLITES AND SERIOUS ADVERSE EFFECTS.

PATIENTS SHOULD BE INSTRUCTED TO STRICTLY ADHERE TO THE RECOMMENDED DOSAGE. 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).

Absorption from the wound surfaces and 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.

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.

pms-LIDOCAINE VISCOUS 2% IS FOR ORAL TOPICAL USE ONLY AND MUST NOT BE USED FOR INJECTION.

pms-LIDOCAINE VISCOUS 2% 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.

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 patients 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.

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.

pms-LIDOCAINE VISCOUS 2% is ineffective when applied to intact skin.

Lidocaine has been shown to be porphyrinogenic in animal models. pms-LIDOCAINE VISCOUS 2% 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

pms-LIDOCAINE VISCOUS 2% 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.

pms-LIDOCAINE VISCOUS 2% should be used with caution in patients in severe shock.

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 monoethylglycinexylidide (MEGX, which has some CNS activity), and then further to metabolites glycinexylidide (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 pms-LIDOCAINE VISCOUS 2% 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

pms-LIDOCAINE VISCOUS 2% should be used with caution in persons with known drug sensitivities.

pms-LIDOCAINE VISCOUS 2% is contraindicated in patients with known hypersensitivities to local anesthetics of the amide type, to other components in the formulation, methylparaben and/or propylparaben (preservatives) and their metabolite para amino benzoic acid (PABA). The use of paraben-containing lidocaine preparations should also be avoided in patients who are allergic to ester local anesthetics (see CONTRAINDICATIONS).

Special Populations

Debilicated 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 pms-LIDOCAINE VISCOUS 2% 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: Postmarketing cases of seizures, cardiopulmonary arrest, and death in patients under the age of 3 years have been reported with use of lidocaine hydrochloride solution due to accidental ingestion, or accidental overdose when it was not administered in strict adherence to the dosing and administration recommendations.

pms-LIDOCAINE VISCOUS 2% should not be administered to infants and children for teething pain. pms-LIDOCAINE VISCOUS 2% 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. Use in this population should be limited to those situations where safer alternatives are not available or have been tried but failed.

To decrease the risk of serious adverse events with use of pms-LIDOCAINE VISCOUS 2% solution, instruct caregivers to strictly adhere to the prescribed dose and frequency of administration and store the prescription bottle safely out of reach of children.

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 (see DOSAGE AND ADMINISTRATION).

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 50 times the amount of 2,6-dimethylaniline to which a 50 kg subject would be exposed following the application of 20 g of lidocaine viscous 2% 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 20 g lidocaine viscous 2% 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, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. (See DOSAGE AND ADMINISTRATION, WARNINGS AND PRECAUTIONS, ACTION AND CLINICAL PHARMACOLOGY and OVERDOSAGE)

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, lightheadedness, 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.

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 instances, 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).

DRUG INTERACTIONS

Overview

Lidocaine is mainly metabolized in the liver by CYP1A2 and CYP3A4 to its two major metabolites, monoethylglycinexylidene (MEGX) and glycinexylidene (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 pms-LIDOCAINE VISCOUS 2% 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 pms-LIDOCAINE VISCOUS 2% 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

Local anesthetics and agents structurally related to amide-type local anesthetics

pms-LIDOCAINE VISCOUS 2% 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.

Antiarrhythmic 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 propranolol 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.

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 pms-LIDOCAINE VISCOUS 2% is used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind.

The degree of absorption from mucous membranes is variable but especially high from the bronchial tree. The degree of systemic absorption depends on whether the lidocaine viscous is swallowed or expectorated. It is therefore important to expectorate in order to avoid unnecessary absorption. After a swallowed single dose of 300 mg (15 mL) of lidocaine viscous, the resulting blood concentrations are low in adults.

Special Populations

Pediatric patients: pms-LIDOCAINE VISCOUS 2% should not be administered to sooth teething pain in infants and children, and should be used only as a last resort in children under the age of 2, when safer alternatives are not available or have been tried but failed. There is insufficient data to support the safety and efficacy of this product in this patient population at this time.

Care must be taken to ensure correct dosage in all pediatric patients as there have been cases of overdose due to inappropriate dosing.

pms-LIDOCAINE VISCOUS 2% should also 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.

Mode of Administration

pms-LIDOCAINE VISCOUS 2% IS FOR ORAL TOPICAL USE ONLY AND MUST NOT BE USED FOR INJECTION (see WARNINGS AND PRECAUTIONS).

Adults (18 years of age and older)

- For oral analgesia, the solution should be swished around in the mouth and spat out or swallowed slowly.
- For use in the pharynx, the solution should be gargled and may be swallowed.

Children 2 to <18 years of age

- The solution should not be swallowed. Children should swish or gargle the solution, then spit it out.

- For young children with difficulty spitting out the solution, the dose and solution must be accurately measured and applied, to the affected area only, with a cotton tip applicator.

Children <3 years of age

- If treatment with pms-LIDOCAINE VISCOUS 2% solution is considered necessary (i.e. other available options have failed), the solution must be accurately measured and applied, to the affected area only, with a cotton tip applicator.

Recommended Dose and Dosage Adjustment

Adults

For treatment of pain from irritated or inflamed mucous membranes of the mouth and throat, 5 mL to 10 mL of pms-LIDOCAINE VISCOUS 2% (100 mg - 200 mg lidocaine hydrochloride) is recommended, per dose. Wait at least 3 hours between doses. No more than six doses may be given in 24 hours. Total dosage of pms-LIDOCAINE VISCOUS 2% in 24 hours should not exceed 60 mL or 1200 mg lidocaine hydrochloride.

For topical anesthesia before introduction of instruments and catheters into the upper respiratory or digestive tracts, 10 mL - 15 mL of pms-LIDOCAINE VISCOUS 2% (200 mg - 300 mg lidocaine hydrochloride) is recommended. When combined with other lidocaine products (e.g. for bronchoscopy), the total dosage of lidocaine hydrochloride should not exceed 400 mg.

For diseases of the upper gastrointestinal tract, 5 mL - 15 mL of pms-LIDOCAINE VISCOUS 2% (100 mg - 300 mg of lidocaine hydrochloride) should be swallowed quickly in one gulp. Wait at least 3 hours between doses. Six doses may be given in 24 hours. Total dosage of pms-LIDOCAINE VISCOUS 2% in 24 hours should not exceed 60 mL or 1200 mg lidocaine hydrochloride.

Pediatric patients >12 years of age, or younger but weighing ≥50 kg

For children over 12 years of age, or children weighing 50 kg or more, for treatment of irritated or inflamed mucous membranes of the mouth and throat, a dose of 5 mL-10 mL of pms-LIDOCAINE VISCOUS 2% (100 mg - 200 mg lidocaine hydrochloride) is recommended. The dose should be adjusted commensurate with weight and physical condition. Wait at least 3 hours between doses. No more than four doses should be given during 24 hours.

Pediatric patients 2 – 12 years of age, or older and weighing <50kg

In patients 2 -12 years of age who weigh less than 50 kg, for treatment of irritated or inflamed mucous membranes of the mouth and throat, the dose should not exceed 4 mg/kg of lidocaine hydrochloride (0.2 mL/kg) and should be adjusted based on weight and physical condition. After swishing, pms-LIDOCAINE VISCOUS 2% should be spat out, not swallowed. If they have trouble spitting it out, it should be applied with a cotton tip applicator. Wait at least 3 hours between doses. No more than four doses should be given during 24 hours.

Children <3 years of age

If treatment with pms-LIDOCAINE VISCOUS 2% solution is considered necessary (i.e. as a last resort) for infants and children under 3 years of age, pms-LIDOCAINE VISCOUS 2% solution

must be accurately measured and applied to the affected area only with a cotton tip applicator (see WARNINGS AND PRECAUTIONS-Special Populations).

- The maximum dosage for the treatment of infants and children under 3 years of age is 4 mg/kg.
- Wait at least 3 hours between doses. No more than four doses should be given during 24 hours. At the present time there is not enough documentation to allow recommendations for a more prolonged use of viscous lidocaine in children under the age of 2.
- Do not use this product to treat teething pain in infants and children.

OVERDOSAGE

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, lightheadedness, 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.

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 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.

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

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

After application of pms-LIDOCAINE VISCOUS 2%, local anesthesia is achieved within 5 minutes. Duration of anesthesia is approximately 20 - 30 minutes. LIDOCAINE VISCOUS 2% 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 the systemic circulation rapidly, 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 subject to biotransformation in the liver. In 17 healthy male volunteers, when 15 mL of lidocaine hydrochloride solution (300 mg) was swallowed after repeated doses, the mean peak plasma concentration of lidocaine was 0.5 mcg/mL after the first dose and 0.8 mcg/mL after the last dose. When the dose was instead spat out, the mean peak concentration was 0.08 mcg/mL and individual maximum concentrations did not exceed 0.3 mcg/mL. Lidocaine and its metabolites concentrations were below 0.05 mcg/mL 12 hours after the last dose.

Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6.0 mcg free base per mL.

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 mcg 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 of lidocaine 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.

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.

STORAGE AND STABILITY

Store between 15°C and 30°C.

DOSAGE FORMS, COMPOSITION AND PACKAGING

pms-LIDOCAINE VISCOUS 2% is a red, viscous solution with an odour of cherries.

pms-LIDOCAINE VISCOUS 2% has a low surface tension which provides for an even film over the mucous membrane. Prolonged contact is possible due to its high viscosity.

Composition

pms-LIDOCAINE VISCOUS 2% contains 20 mg/mL of lidocaine hydrochloride as a medicinal ingredient and the following non medicinal ingredients: artificial cherry flavor, FD&C Red No.2, glycerin, methylparaben, propylene glycol, propylparaben, purified water, sodium saccharin, sodium carboxymethylcellulose. Citric acid and sodium citrate to adjust pH.

Packaging

pms-LIDOCAINE VISCOUS 2% is supplied in 50 mL and 100 mL HDPE bottles.

REFERENCES

1. Greenblatt D.J., Benjamin D.M., Willis C.R., Harmatz J.S., Zinny M.A. Lidocaine Plasma Concentrations Following Administration of Intraoral Lidocaine Solution. Arch Otolaryngol, 1985; 111: 298-300
2. XYLOCAINE VISCOUS 2% Prescribing Information, AstraZeneca Canada Inc., Date of revision: October 20, 2015, control number: 182650

PART III: CONSUMER INFORMATION**pms-LIDOCAINE VISCOUS 2%**

Lidocaine Hydrochloride Oral Topical Solution, USP

This leaflet is part III of a two-part "Prescribing Information" published when pms-LIDOCAINE VISCOUS 2% was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about pms-LIDOCAINE VISCOUS 2%. Contact your doctor or pharmacist if you have any questions about the drug.

Before using pms-LIDOCAINE VISCOUS 2%, read this leaflet carefully.

Please keep this leaflet to refer to until you have used up all your pms-LIDOCAINE VISCOUS 2%.

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:**

pms-LIDOCAINE VISCOUS 2% is used to produce a temporary loss of feeling or numbness of the area where it is applied in adults and children 2 years of age and older, and can be used:

- before certain types of examinations done by your doctor.

pms-LIDOCAINE VISCOUS 2% could also:

- relieve the pain and discomfort of a sore throat, such as after the tonsils are removed;
- provide relief in other painful diseases of the mouth, throat or esophagus;
- cause a loss of feeling in the throat area, before certain types of examinations are performed by your doctor.

WHAT IT DOES:

pms-LIDOCAINE VISCOUS 2% is the brand name for a topical anesthetic that contains the drug lidocaine. Oral topical anesthetics are used to produce a temporary loss of feeling or numbness on the area where they are applied.

pms-LIDOCAINE VISCOUS 2% should start to work within 5 minutes after you apply it. The effect usually lasts 20 to 30 minutes.

WHEN IT SHOULD NOT BE USED:

Do not use pms-LIDOCAINE VISCOUS 2% 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);
- are allergic to methylparaben and/or propylparaben (preservatives used in pms-LIDOCAINE VISCOUS 2%) or their metabolite para amino benzoic acid (PABA).

WHAT THE MEDICINAL INGREDIENT IS:

lidocaine hydrochloride 2%

NONMEDICINAL INGREDIENTS ARE:

artificial cherry flavor, FD&C Red No.2, glycerin, methylparaben, propylene glycol, propylparaben, purified water, sodium saccharin, sodium carboxymethylcellulose. Citric acid and sodium citrate to adjust pH.

Tell your doctor if you think you may be sensitive to any of the above ingredients.

WHAT DOSAGE FORMS IT COMES IN:

pms-LIDOCAINE VISCOUS 2%, 50 mL and 100 mL bottles.

WARNINGS AND PRECAUTIONS

pms-LIDOCAINE VISCOUS 2% should not be used to soothe teething pain in infants and children. Incorrect dosing can lead to serious side effects, including seizures, loss of consciousness, and death.

BEFORE you use pms-LIDOCAINE VISCOUS 2% tell your doctor or pharmacist:

- 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 pms-LIDOCAINE VISCOUS 2% or any other medicines ending with "caine";
- if you think you may be allergic or sensitive to any ingredients in pms-LIDOCAINE VISCOUS 2% (see above);
- if there is an infection, skin rash, cut or wound at or near the area you want to apply pms-LIDOCAINE VISCOUS 2%;
- if you have a skin condition that is severe or that covers a large area;
- if you have a 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 THIS 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 pharmacist 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 you are going to use high doses of pms-LIDOCAINE VISCOUS 2% for a long time;
- fluvoxamine, for depression, if you are going to use high doses of pms-LIDOCAINE VISCOUS 2% for a long time.

Usage of such medicines at the same time as pms-LIDOCAINE VISCOUS 2% may increase the risk of serious side effects.

PROPER USE OF THIS MEDICATION

This medication is for oral topical use only.

If this medicine is recommended by your doctor, be sure to follow the directions for use that have been given. If you are treating yourself, or your child, follow the directions below. It is important to follow the instructions on how much, how to apply and, where to apply pms-LIDOCAINE VISCOUS 2%. Check with your doctor or pharmacist if you have any questions about your directions, or how to calculate or measure the correct dose amounts.

The following are general guidelines for the maximum amount of pms-LIDOCAINE VISCOUS 2% that should be used without a doctor's advice. These guidelines apply only to otherwise healthy people. If you have a special skin condition or other condition that requires a doctor's supervision, ask your doctor about the maximum amount of pms-LIDOCAINE VISCOUS 2% that you should use.

Conditions where dose adjustments may be required:

- elderly patients
- 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)

USUAL DOSE:

Dose for Adults (18 Years of age and older)

- The usual effective dose for adults is 5 mL to 10 mL (1-2 measured teaspoons) at a time. Use the smallest amount needed to control your symptoms.
- Do not use this amount more than six times in a 24-hour period. Wait at least 3 hours between doses.
- The **total dose** for a 24-hour period should be no more than 60 mL. (12 measured teaspoons, or 4 measured tablespoons).
- Swish the appropriate amount around in your mouth to treat pain in the mouth area. To treat the throat, gargle the liquid in the back of the throat and swallow or spit the liquid out. Adults (but not children) may swallow the solution to treat the esophagus.

Dose for Children over 12 Years of Age, or younger and weighing 50 kg (110 lbs) or more

- The usual effective dose is 5 - 10 mL (1-2 measured teaspoons) at a time. Use the smallest amount needed to control the symptoms.
- Wait at least 3 hours between doses. No more than four doses should be given during a 24-hour period.
- After rinsing with the medication to treat the mouth, or gargling to treat the throat, children should not swallow the solution but spit it out.

Dose for Children 2-12 Years of Age, or older and weighing less than 50 kg (110 lbs)

- DO NOT use pms-LIDOCAINE VISCOUS 2% solution to soothe teething pain in infants or children, because serious side effects may occur.
- There may be special considerations for children under 3 years of age. DO NOT use pms-LIDOCAINE VISCOUS 2% for children in this age group without a doctor's supervision.
- The dose depends on the child's weight. Use the smallest amount possible to treat the pain. The dose should never be more than 10 mL (2 measured teaspoons) at a time.
- For each dose, use no more than 1 mL of pms-LIDOCAINE VISCOUS 2% solution per 5 kilogram (11 pounds) of the child's weight. For example, if the child weighs 25 kg (55 pounds), use a maximum of 5 mL (1 measured teaspoon) of pms-LIDOCAINE VISCOUS 2% solution per dose.
- Wait at least 3 hours between doses. No more than four doses should be given during a 24-hour period.
- Do not treat with pms-LIDOCAINE VISCOUS 2% for more than 24 hours in children under 2 years of age.
- Children should swish or gargle the solution and spit it out, not swallow it. For young children who might have trouble spitting it out, and children < 3 years of age, it should be applied with a cotton tip applicator, and only to the affected area.

Do not use more pms-LIDOCAINE VISCOUS 2%; or more often or for a longer period of time than either your doctor ordered or than these package directions recommend as this may cause unwanted side effects (see SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM).

To get the most effect from your dose of medicine:

- Shake the bottle well before using this medicine, so that you get an even dose each time you use it.
- Use only an accurate measuring device, such as a measured cup or a measured teaspoon to dose this medicine correctly.
- When used in the mouth or throat try to increase the length of time pms-LIDOCAINE VISCOUS 2% is in contact with the affected area. For example, if you are treating mouth sores, swish the liquid around in your mouth and then spit it out. For a sore throat, roll the

liquid around at the back of your throat or gargle. Adults (but not children) may swallow the medicine; children should always spit it out or have the dose applied with a cotton tipped applicator.

- Do not drink water or other liquids right after you use pms-LIDOCAINE VISCOUS 2%, as this will decrease the amount of relief you get from the medicine.
- Avoid contact with your eyes.

If you are treating yourself and your condition does not seem to improve within three to five days, check with your doctor about continuing to use pms-LIDOCAINE VISCOUS 2%.

OVERDOSE:

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

Early signs of overdosage are numbness of the lips and around the mouth, lightheadedness, dizziness and sometimes blurred vision. In the event of a serious overdosage, trembling, seizures, and subsequently unconsciousness may occur.

If not rapidly treated, serious overdosage can lead to death. If you think you or anyone else is experiencing any of the above signs, discontinue use and get emergency help right away.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like any medication, pms-LIDOCAINE VISCOUS 2% may cause side effects in some people.

Avoid eating or chewing gum when pms-LIDOCAINE VISCOUS 2% is used in the mouth or throat since numbness in these areas may interfere with swallowing and could potentially cause choking. Numbness of the tongue or gum 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, pms-LIDOCAINE VISCOUS 2% 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 pms-LIDOCAINE VISCOUS 2%, stop using it and check with your doctor or pharmacist as soon as possible.

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 assistance
		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

This is not a complete list of side effects. For any unexpected effects while taking pms-LIDOCAINE VISCOUS 2% contact your doctor or pharmacist.

pms-LIDOCAINE VISCOUS 2% 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 heartbeat, fainting, nervousness, unusual sweating, trembling or seizures.

The above are extremely rare and usually require large amounts of pms-LIDOCAINE VISCOUS 2% over a long period of time.

Consult your doctor immediately if any of these symptoms appear.

HOW TO STORE IT

Remember to keep **pms-LIDOCAINE VISCOUS 2% well out of the reach and sight of children** when you are not using it.

Keep pms-LIDOCAINE VISCOUS 2% between 15°C and 30°C. Do not keep pms-LIDOCAINE VISCOUS 2% in the bathroom medicine cabinet or other warm, moist places. Store in the original package.

Do not use pms-LIDOCAINE VISCOUS 2% after the expiry date marked on the package.

Reporting Side Effects

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

3 ways to report:

- Online at MedEffect™
(www.healthcanada.gc.ca/medeffect);
 - By calling 1-866-234-2345 (toll-free);
 - By completing a Consumer Side Effect Reporting Form and sending it by:
 - Fax to 1-866-678-6789 (toll-free), or
 - Mail to: Canada Vigilance Program
Health Canada, Postal Locator 0701E
Ottawa, ON
K1A 0K9
- Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect™ (www.healthcanada.gc.ca/medeffect).

NOTE: Contact your health professional if you need information about how to manage your side effects. 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 pms-LIDOCAINE VISCOUS 2%.

This document plus the full prescribing information, prepared for health professionals, can be obtained by contacting Pharmascience Inc. at 1-888-550-6060.

This leaflet was prepared by
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