May 30, 2006

Dockets Management Branch (HFA-305)
Food and Drug Administration
5600 Fishers Lane, Room /4-62
Rockville, MD 20857

CITIZEN PETITION

The undersigned submits this Petition pursuant to Section 505 of the Federal Food, Drug and Cosmetic Act and 21 CFR §314.55 (d) (2), §314.93 and §10.30 of the Food and Drug Administration's regulations, to request the Commissioner of Food and Drugs to make a determination that a certain non-aerosol spray oral anesthetic drug product is suitable for filing under an abbreviated new drug application (ANDA).

A. Action Requested

Petitioner requests that the Commissioner of Food and Drugs make a determination that an abbreviated new drug application (ANDA) is suitable for a non-aerosol oral anesthetic spray delivering 12 mg lidocaine hydrochloride per metered dose (equivalent to 10 mg lidocaine base).

B. Statement Of Grounds

The Drug Price Competition and Patent Term Restoration Act of 1984 ("The Hatch - Waxman Act") extends eligibility for the submission of ANDAs to certain drug products identical to those approved via new drug applications, as identified in the Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") published by the Food and Drug Administration. Where the proposed drug product differs from the "reference listed drug" in one or more respects, a person may petition the Agency, under section 505(j)(2)(c) of the Act, for a determination that the proposed drug product is suitable to be submitted as an ANDA.

The reference listed drug product that forms the basis for this petition is an oral anesthetic aerosol spray delivering 10 mg of the active pharmaceutical ingredient lidocaine per metered dose. (NDA 14-394 10% Xylocaine® (lidocaine) Oral Spray; AstraZeneca.) Exhibit A contains search results from the Discontinued section of the Orange Book showing the reference listed drug. To the best of Petitioner's knowledge, applicable U.S. patents that claim the drug substance, lidocaine, or the drug product have expired.

2006P-0230 CP1

Odan Laboratories Ltd. | Laboratoires Odan Ltée
325 ave. Stillview Ave., Pointe-Claire, QC, Canada H9R 2Y6 | TEL.: (514) 428-1628, 1-800-387-9342 | FAX: (514) 428-9783, 1-800-FAX-ODAN
www.odanlab.com

The proposed drug product, Lidodan® (Lidocaine HCl) 12% Oral Non-Aerosol Spray, differs from the listed product only in regard to active ingredient salt and dosage form (Lidocaine HCl non-aerosol spray solution instead of lidocaine 10% aerosol spray solution) and is identical with respect to strength[1], route of administration and conditions of use. Petitioner intends to request a waiver of evidence of *in vivo* bioequivalence for the proposed drug product pursuant to 21 CFR 320.22 (b) (3) in that it:
(i) Is a solution;
(ii) Contains the active drug moiety, lidocaine, in the same concentration as the reference listed drug product; and
(iii) Contains no inactive ingredient or other change in formulation from the reference listed drug product that may significantly affect systemic or local availability.

The availability of a non-aerosol oral spray would provide a valuable dosage form alternative to the health care community and patients, particularly since the aerosol oral spray has been discontinued and is no longer available.

Based on the foregoing, Petitioner believes that a 12% lidocaine hydrochloride non-aerosol oral spray warrants a finding of ANDA suitability, and that the Commissioner should grant permission for the filing of an ANDA for 12% lidocaine hydrochloride non-aerosol oral spray.

C. Environmental Impact

Petitioner hereby claims a categorical exclusion from the requirement of an Environmental Assessment (EA) statement. The approval of this petition will result in an abbreviated new drug application (ANDA) for a drug product that will be excluded from the requirement of an Environmental Assessment statement, pursuant to 2 1 CFR §25.31(a).

D. Economic Impact

In accordance with 21 CFR §10.30(b), information on economic impact will be submitted only if requested by the Commissioner following review of this petition.

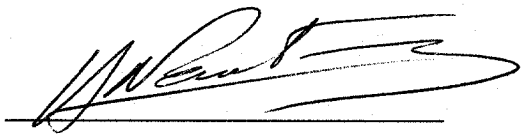
[1] 12% lidocaine HCl is equivalent to 10% of the active moiety, lidocaine base)

E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this Petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,

ODAN LABORATORIES, INC.



Herbert Nemteanu, B.Sc., MBA
Regulatory Affairs

Enclosures:
Exhibit A: Proprietary Name Search Results from "OB-Disc" table for query on "xylocaine."
Exhibit B: Draft package insert labeling for the proposed drug product.
Exhibit C: Copy of 10% Xylocaine®(lidocaine) Oral Spray insert
Exhibit D: Side- by-side insert comparison

Proprietary Name Search Results from "OB_Disc" table for query on "xylocaine."

Appl No	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
013334	DEXAMETHASONE SODIUM PHOSPHATE; LIDOCAINE HYDROCHLORIDE	INJECTABLE; INJECTION	EQ 4MG PHOSPHATE/ML;10MG/ML	DECADRON W/ XYLOCAINE	MERCK
010418	EPINEPHRINE; LIDOCAINE HYDROCHLORIDE	INJECTABLE; INJECTION	0.005MG/ML;1%	XYLOCAINE W/ EPINEPHRINE	ASTRAZENECA
010418	EPINEPHRINE; LIDOCAINE HYDROCHLORIDE	INJECTABLE; INJECTION	0.005MG/ML;1.5%	XYLOCAINE W/ EPINEPHRINE	ASTRAZENECA
010418	EPINEPHRINE; LIDOCAINE HYDROCHLORIDE	INJECTABLE; INJECTION	0.005MG/ML;2%	XYLOCAINE W/ EPINEPHRINE	ASTRAZENECA
006488	EPINEPHRINE; LIDOCAINE HYDROCHLORIDE	INJECTABLE; INJECTION	0.01MG/ML;2%	XYLOCAINE W/ EPINEPHRINE	ASTRAZENECA
006488	EPINEPHRINE; LIDOCAINE HYDROCHLORIDE	INJECTABLE; INJECTION	0.02MG/ML;2%	XYLOCAINE W/ EPINEPHRINE	ASTRAZENECA
014394	LIDOCAINE	AEROSOL; ORAL	10%	XYLOCAINE	ASTRAZENECA
008048	LIDOCAINE	OINTMENT; TOPICAL	5%	XYLOCAINE	ASTRAZENECA
014127	LIDOCAINE	SOLUTION; TOPICAL	5%	XYLOCAINE	ASTRAZENECA
013077	LIDOCAINE	SUPPOSITORY; RECTAL	100MG	XYLOCAINE	ASTRAZENECA
010418	LIDOCAINE HYDROCHLORIDE	INJECTABLE; INJECTION	1%	XYLOCAINE	ASTRAZENECA
010418	LIDOCAINE HYDROCHLORIDE	INJECTABLE; INJECTION	1.5%	XYLOCAINE	ASTRAZENECA
006488	LIDOCAINE HYDROCHLORIDE	INJECTABLE; INJECTION	2%	XYLOCAINE	ASTRAZENECA

010418	LIDOCAINE HYDROCHLORIDE	INJECTABLE; INJECTION	2%	XYLOCAINE	ASTRAZENECA
016297	LIDOCAINE HYDROCHLORIDE	INJECTABLE; SPINAL	1.5%	XYLOCAINE 1.5% W/ DEXTROSE 7.5%	ASTRAZENECA
010496	LIDOCAINE HYDROCHLORIDE	INJECTABLE; SPINAL	5%	XYLOCAINE 5% W/ GLUCOSE 7.5%	ASTRAZENECA

Return to Electronic Orange Book Home Page

FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Generic Drug Product Information & Patent Information - **Daily**
Orange Book Data Updated Through February, 2006
Patent and Generic Drug Product Data Last Updated: March 17, 2006

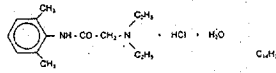
Lidodan™ (Lidocaine Hydrochloride) Non-Aerosol Oral Spray

12 mg Lidocaine Hydrochloride / metered dose (Equivalent to Lidocaine 10 mg)
Topical Anesthetic Spray For Use In The Oral Cavity

DESCRIPTION

LIDODAN™ (Lidocaine Hydrochloride) Non-Aerosol Oral Spray contains a local anesthetic agent and is administered topically in the oral cavity. See INDICATIONS for specific uses.

LIDODAN Non-Aerosol Oral Spray contains lidocaine HCl, which is chemically designated as acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl)-, monohydrochloride, monohydrate and has the following structural formula:



$C_{14}H_{22}N_2O \cdot HCl \cdot H_2O$ 288.81

Composition of LIDODAN Non-Aerosol Oral Spray:
Each actuation of the metered dose valve delivers a solution containing 12 mg of lidocaine hydrochloride (equivalent to 10 mg lidocaine base), purified water USP, sodium hydroxide and / or hydrochloric acid to adjust pH 5.0-7.0.

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 the local anesthetic action.

Onset and Duration of Action
LIDODAN (Lidocaine HCl) Non-Aerosol Oral Spray acts on intact mucous membranes to produce local anesthesia. Anesthesia occurs usually within 1-2 minutes and persists for approximately 10-15 minutes.

Hemodynamics:
Excessive blood levels may cause changes in cardiac output, total peripheral resistance, and mean arterial pressure. These changes may be attributable to a direct depressant effect of the local anesthetic agent on various components of the cardiovascular system.

Pharmacokinetics and Metabolism

Lidocaine may be absorbed following topical administration to mucous membranes, its rate of absorption and percent of dose absorbed depending 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 occurs most rapidly after intratracheal administration. Lidocaine is well-absorbed from the gastrointestinal tract, but little intact drug appears in the circulation because of biotransformation in the liver.

Lidocaine is metabolized rapidly by the liver, and metabolites and unchanged drug are excreted by the kidney. Biotransformation includes oxidative N-dealkylation, ring hydroxylation, cleavage of the amide linkage, and conjugation. N-dealkylation, a major pathway of biotransformation, yields the metabolites monoethylglycinexylidide and glycinexylidide. The pharmacological / toxicological actions of these metabolites are similar to, but less potent than, those of lidocaine. Approximately 90% of lidocaine administered is excreted in the form of various metabolites, and less than 10% is excreted unchanged. The primary metabolite in urine is a conjugate of 4-hydroxy-2, 6-dimethylaniline.

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.

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

Studies of lidocaine metabolism following intravenous bolus injections have shown that the elimination half-life of this agent is typically 1.5 to 2 hours. Because of the rapid rate at which lidocaine is metabolized, any condition that affects liver function may alter lidocaine kinetics. The half-life may be prolonged two-fold or more in patients with liver dysfunction. Renal dysfunction does not affect lidocaine kinetics but may increase the accumulation of metabolites.

Factors such as acidosis and the use of CNS stimulants and depressants affect the CNS levels of lidocaine required to produce overt systemic effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6.0 µg free base per mL. In the rhesus monkey arterial blood levels of 18-21 µg / mL have been shown to be threshold for convulsive activity.

INDICATIONS AND USAGE

LIDODAN (Lidocaine HCl) Non-Aerosol Oral Spray is indicated for the production of topical anesthesia of the accessible mucous membranes of the mouth and oropharynx.

CONTRAINDICATIONS

LIDODAN (Lidocaine HCl) Non-Aerosol Oral Spray is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type or to other components of LIDODAN Non-Aerosol Oral Spray.

WARNINGS

IN ORDER TO MANAGE POSSIBLE ADVERSE REACTIONS, RESUSCITATIVE EQUIPMENT, OXYGEN AND OTHER RESUSCITATIVE DRUGS MUST BE IMMEDIATELY AVAILABLE WHEN LOCAL ANESTHETIC AGENTS, SUCH AS LIDOCAINE, ARE ADMINISTERED TO MUCOUS MEMBRANES.

LIDODAN (Lidocaine HCl) Non-Aerosol Oral Spray should be used with extreme caution if there is sepsis or extremely traumatized mucosa in the area of application, since under such conditions there is the potential for rapid systemic absorption.

PRECAUTIONS

General: The safety and efficacy of lidocaine depend on proper dosage, correct technique, adequate precautions, and readiness for emergencies. Resuscitative equipment, oxygen, and other resuscitative drugs should be available for immediate use. (See WARNINGS and ADVERSE REACTIONS). The lowest dosage that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. Repeated doses of lidocaine may cause significant increases in blood levels with each repeated dose because of slow accumulation of the drug or its metabolites. Tolerance varies with the status of the patient. Debilitated, elderly patients, acutely ill patients, and children should be given reduced doses commensurate with their age and physical status. Lidocaine should also be used with caution in patients with severe shock or heart block.

LIDODAN (Lidocaine HCl) Non-Aerosol Oral Spray should be used with caution in patients with known drug sensitivities. Patients allergic to para-aminobenzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine.

Many drugs used during the conduct of anesthesia are considered potential triggering agents for familial malignant hyperthermia. Since it not known whether amide-type local anesthetics may trigger this reaction, and since the need for supplemental general anesthesia cannot be predicted in advance, it is suggested that a standard protocol for management should be available. Early unexplained signs of tachycardia, tachypnea, labile blood pressure and metabolic acidosis may precede temperature elevation. Successful outcome is dependent on early diagnosis, prompt discontinuance of the suspect triggering agent(s) and institution of treatment, including oxygen therapy, indicated supportive measures and dantrolene (consult dantrolene sodium intravenous package insert before using).

Information for Patients: 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. For this reason, food should not be ingested for 60 minutes following use of local anesthetic preparations in the mouth or throat area. This is particularly important in children because of their frequency of eating.

Numbness of the tongue or buccal mucosa may enhance the danger of unintentional biting trauma. Food and chewing gum should not be taken while the mouth or throat area is anesthetized.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Studies of lidocaine in animals to evaluate the carcinogenic and mutagenic potential or the effect on fertility have not been conducted.

Use in Pregnancy: Teratogenic Effects: Pregnancy Category B. Reproduction studies have been performed in rats at doses up to 6.6 times the human dose and have revealed no evidence of harm to the fetus caused by lidocaine. There are, however, no adequate and well-controlled studies in pregnant women. Animal reproduction studies are not always predictive of human response. General consideration should be given to this fact before administering lidocaine to women of childbearing potential, especially during early pregnancy when maximum organogenesis takes place.

Labor and Delivery: Lidocaine is not contraindicated in labor and delivery. Should LIDODAN (Lidocaine HCl) Non-Aerosol Oral Spray be used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind.

Nursing Mothers: Lidocaine is excreted in breast milk in small amounts. Caution should be exercised when lidocaine is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children below the age of 12 years have not been established.

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 excessive dosage or rapid absorption, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. 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 lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred or double vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest. The excitatory manifestations 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 blood level of the drug and may occur as a consequence of rapid absorption.

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

Allergic: Allergic reactions are characterized by cutaneous lesions, urticaria, edema or anaphylactoid reactions. Allergic reactions may occur as a result of sensitivity either to the local anesthetic agent or to other ingredients in the formulation. Allergic reactions as a result of sensitivity to lidocaine are extremely rare and, if they occur, should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.

OVERDOSAGE

Acute emergencies from local anesthetics are generally related to high plasma levels encountered during therapeutic use of local anesthetics (See ADVERSE REACTIONS, WARNINGS and PRECAUTIONS.)

Management of Local Anesthetic Emergencies: 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 convulsions 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. Immediately after the institution of these ventilatory measures, the adequacy of the circulation should be evaluated, keeping in mind that drugs used to treat convulsions sometimes depress the circulation when administered intravenously. Should convulsions persist despite adequate respiratory support, and if the status of the circulation permits, small increments of an ultra-short acting barbiturate (such as thiopental or thiamylal) or a benzodiazepine (such as diazepam) may be administered intravenously. The clinician should be familiar, prior to use of local anesthetics, with these anticonvulsant drugs. Supportive treatment of circulatory depression may require administration of intravenous fluids and, when appropriate, a vasopressor as directed by the clinical situation (e.g., ephedrine).

If not treated immediately, both convulsions and cardiovascular depression can result in hypoxia, acidosis, bradycardia, arrhythmias and cardiac arrest. If cardiac arrest should occur, standard cardiopulmonary resuscitative measures should be instituted.

Dialysis is of negligible value in the treatment of acute overdosage with lidocaine.

The intravenous LD50 of lidocaine HCl in female mice is 26 (21-31) mg / kg and the subcutaneous LD50 is 264 (203-304) mg / kg.

DOSAGE AND ADMINISTRATION

When LIDODAN (lidocaine HCl) Non-Aerosol Oral Spray is used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind.

Two metered doses per quadrant are recommended as the upper limit and, under no circumstances should one exceed three metered doses per quadrant of oral mucosa over a one-half hour period to produce the desired anesthetic effect. Experience in children is inadequate to recommend a pediatric dose at this time.

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 reprimed but the air in the nozzle must be voided before a full dose is delivered. This usually requires two actuations.

HOW SUPPLIED

LIDODAN Non-Aerosol Oral Spray is available in a 30 mL bottle spray with a metered dose valve.

NDC 61344-108-43 / NDC 61344-118-63: A 30 mL bottle provides a total amount of 3.0 g (w/w) of the active ingredient lidocaine (3.6 g of lidocaine hydrochloride). Each actuation of the metered dose valve delivers 10 mg of lidocaine (12 mg lidocaine HCl).

Avoid contact with the eyes. Inhalation and swallowing should be avoided.

Keep out of the reach of children.

Use only as directed; intentional misuse by deliberately concentrating and inhaling the contents can be harmful or fatal.

STORE AT CONTROLLED ROOM TEMPERATURE 15°-30°C (59°-86°F).

PROTECT FROM FREEZING.

Clean stainless steel nozzles may be steam-sterilized at 250°F (121°C) for 15 minutes.

Single Pak: One 30 mL bottle with 1 x 20 cm (8") stainless steel nozzle. (NDC 61344-108-43)
Three Pak: Three 30 mL bottles. (NDC 61344-118-63)
Nozzle Pak: Stainless steel: 2 x 20 cm (8") stainless steel reusable nozzles.
Nozzle Pak: Plastic: 24 x 20 cm plastic disposable nozzles.
Nozzle Pak: Plastic: 96 x 20 cm plastic disposable nozzles.

Odan Laboratories Ltd.
Montreal, QC, Canada H9R 2Y6

1-800-387-9342 www.odanlabs.com

ODAN

10% Xylocaine® Oral Spray

(lidocaine)

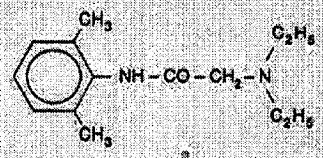
Flavored Topical Anesthetic Aerosol For Use In The Oral Cavity

WARNING — CONTENTS UNDER PRESSURE

DESCRIPTION

Xylocaine (lidocaine) 10% Oral Spray contains a local anesthetic agent and is administered topically in the oral cavity. See INDICATIONS for specific uses.

Xylocaine 10% Oral Spray contains lidocaine, which is chemically designated as acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl)-, and has the following structural formula:



Composition of Xylocaine (lidocaine) 10% Oral Spray:

Each actuation of the metered dose valve delivers a solution containing lidocaine, 10 mg, cetylpyridinium chloride, absolute alcohol, saccharin, flavor, and polyethylene glycol.

And as propellants: trichlorofluoromethane/dichlorodifluoromethane (65%/35%).

WARNING: Contains trichlorofluoromethane and dichlorodifluoromethane, substances which harm public health and environment by destroying ozone in the upper atmosphere.

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.

Onset and Duration of Action: Xylocaine (lidocaine) 10% Oral Spray acts on intact mucous membranes to produce local anesthesia. Anesthesia occurs usually within 1–2 minutes and persists for approximately 10–15 minutes.

Hemodynamics: Excessive blood levels may cause changes in cardiac output, total peripheral resistance, and mean arterial pressure. These changes may be attributable to a direct depressant effect of the local anesthetic agent on various components of the cardiovascular system.

Pharmacokinetics and Metabolism: Lidocaine may be absorbed following topical administration to mucous membranes, its rate of absorption and percent of dose absorbed depending 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 occurs most rapidly after intratracheal administration. Lidocaine is well-absorbed from the gastrointestinal tract, but little intact drug appears in the circulation because of biotransformation in the liver.

Lidocaine is metabolized rapidly by the liver, and metabolites and unchanged drug are excreted by the kidney. Biotransformation includes oxidative N-dealkylation, ring hydroxylation, cleavage of the amide linkage, and conjugation. N-dealkylation, a major pathway of biotransformation, yields the metabolites monoethylglycinexylidide and glycinexylidide. The pharmacological/toxicological actions of these metabolites are similar to, but less potent than, those of lidocaine. Approximately 90% of lidocaine administered is excreted in the form of various metabolites, and less than 10% is excreted unchanged. The primary metabolite in urine is a conjugate of 4-hydroxy-2, 6-dimethylaniline.

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.

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

Studies of lidocaine metabolism following intravenous bolus injections have shown that the elimination half-life of this agent is typically 1.5 to 2 hours. Because of the rapid rate at which lidocaine is metabolized, any condition that affects liver function may alter lidocaine kinetics. The half-life may be prolonged two-fold or more in patients with liver dysfunction. Renal dysfunction does not affect lidocaine kinetics but may increase the accumulation of metabolites.

Factors such as acidosis and the use of CNS stimulants and depressants affect the CNS levels of lidocaine required to produce overt systemic effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6 µg free base per mL. In the rhesus monkey arterial blood levels of 18–21 µg/mL have been shown to be threshold for convulsive activity.

INDICATIONS AND USAGE

Xylocaine (lidocaine) 10% Oral Spray is indicated for the production of topical anesthesia of the accessible mucous membranes of the mouth and oropharynx.

CONTRAINDICATIONS

Lidocaine is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type or to other components of Xylocaine 10% Oral Spray.

WARNINGS

IN ORDER TO MANAGE POSSIBLE ADVERSE REACTIONS, RESUSCITATIVE EQUIPMENT, OXYGEN AND OTHER RESUSCITATIVE DRUGS MUST BE IMMEDIATELY AVAILABLE WHEN LOCAL ANESTHETIC AGENTS, SUCH AS LIDOCAINE, ARE ADMINISTERED TO MUCOUS MEMBRANES.

Xylocaine 10% Oral Spray should be used with extreme caution if there is sepsis or extremely traumatized mucosa in the area of application, since under such conditions there is the potential for rapid systemic absorption.

PRECAUTIONS

General: The safety and effectiveness of lidocaine depend on proper dosage, correct technique, adequate precautions, and readiness for emergencies. Resuscitative equipment, oxygen, and other resuscitative drugs should be available for immediate use. (See WARNINGS and ADVERSE REACTIONS.) The lowest dosage that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. Repeated doses of lidocaine may cause significant increases in blood levels with each repeated dose because of slow accumulation of the drug or its metabolites. Tolerance varies with the status of the patient. Debilitated, elderly patients, acutely ill patients, and children should be given reduced doses commensurate with their age and physical status. Lidocaine should also be used with caution in patients with severe shock or heart block.

Xylocaine 10% Oral Spray should be used with caution in patients with known drug sensitivities. Patients allergic to para-amino-benzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine.

Many drugs used during the conduct of anesthesia are considered potential triggering agents for familial malignant hyperthermia. Since it is not known whether amide-type local anesthetics may trigger this reaction and since the need for supplemental general anesthesia cannot be predicted in advance, it is suggested that a standard protocol for management should be available. Early unexplained signs

of tachycardia, tachypnea, labile blood pressure and metabolic acidosis may precede temperature elevation. Successful outcome is dependent on early diagnosis, prompt discontinuance of the suspect triggering agent(s) and institution of treatment, including oxygen therapy, indicated supportive measures and dantrolene (consult dantrolene sodium intravenous package insert before using).

Information for Patients: 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. For this reason, food should not be ingested for 60 minutes following use of local anesthetic preparations in the mouth or throat area. This is particularly important in children because of their frequency of eating.

Numbness of the tongue or buccal mucosa may enhance the danger of unintentional biting trauma. Food and chewing gum should not be taken while the mouth or throat area is anesthetized.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Studies of lidocaine in animals to evaluate the carcinogenic and mutagenic potential or the effect on fertility have not been conducted.

Use in Pregnancy: Teratogenic Effects. Pregnancy Category B. Reproduction studies have been performed in rats at doses up to 6.6 times the human dose and have revealed no evidence of harm to the fetus caused by lidocaine. There are, however, no adequate and well-controlled studies in pregnant women. Animal reproduction studies are not always predictive of human response. General consideration should be given to this fact before administering lidocaine to women of childbearing potential, especially during early pregnancy when maximum organogenesis takes place.

Labor and Delivery: Lidocaine is not contraindicated in labor and delivery. Should Xylocaine 10% Oral Spray be used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when lidocaine is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children below the age of 12 years have not been established.

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 excessive dosage or rapid absorption, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. 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 lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred or double vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest. The excitatory manifestations 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 blood level of the drug and may occur as a consequence of rapid absorption.

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

Allergic: Allergic reactions are characterized by cutaneous lesions, urticaria, edema or anaphylactoid reactions. Allergic reactions may occur as a result of sensitivity either to the local anesthetic agent or to other ingredients in the formulation. Allergic reactions as a result of sensitivity to lidocaine are extremely rare and, if they occur, should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.

OVERDOSAGE

Acute emergencies from local anesthetics are generally related to high plasma levels encountered during therapeutic use of local anesthetics. (See ADVERSE REACTIONS, WARNINGS, and PRECAUTIONS.)

Management of Local Anesthetic Emergencies: 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 convulsions 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. Immediately after the institution of these ventilatory measures, the adequacy of the circulation should be evaluated, keeping in mind that drugs used to treat convulsions sometimes depress the circulation when administered intravenously. Should convulsions persist despite adequate respiratory support, and if the status of the circulation permits, small increments of an ultra-short acting barbiturate (such as thiopental or thiamylal) or a benzodiazepine (such as diazepam) may be administered intravenously. The clinician should be familiar, prior to use of local anesthetics, with these anticonvulsant drugs. Supportive treatment of circulatory depression may require administration of intravenous fluids and, when appropriate, a vasopressor as directed by the clinical situation (e.g., ephedrine).

If not treated immediately, both convulsions and cardiovascular depression can result in hypoxia, acidosis, bradycardia, arrhythmias and cardiac arrest. If cardiac arrest should occur, standard cardiopulmonary resuscitative measures should be instituted.

Dialysis is of negligible value in the treatment of acute overdosage with lidocaine.

The intravenous LD_{50} of lidocaine HCl in female mice is 26 (21–31) mg/kg and the subcutaneous LD_{50} is 264 (203–304) mg/kg.

DOSAGE AND ADMINISTRATION

When Xylocaine 10% Oral Spray is used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind.

Two metered doses per quadrant are recommended as the upper limit and, *under no circumstances* should one exceed three metered doses per quadrant of oral mucosa over a one-half hour period to produce the desired anesthetic effect. Experience in children is inadequate to recommend a pediatric dose at this time.

HOW SUPPLIED

NDC 0186-0356-01: A 26.8 mL aerosol container provides a total amount of 3.3 g (w/w) of the active ingredient lidocaine. Each actuation of the metered dose valve delivers 10 mg of lidocaine.

Contents under pressure. Do not puncture or incinerate container. Do not expose to heat or store at temperatures above 120°F. Avoid contact with the eyes. Inhalation and swallowing should be avoided.

Keep out of the reach of children.

Use only as directed; intentional misuse by deliberately concentrating and inhaling the contents can be harmful or fatal.

STORE AT CONTROLLED ROOM TEMPERATURE 15°–30°C (59°–86°F).

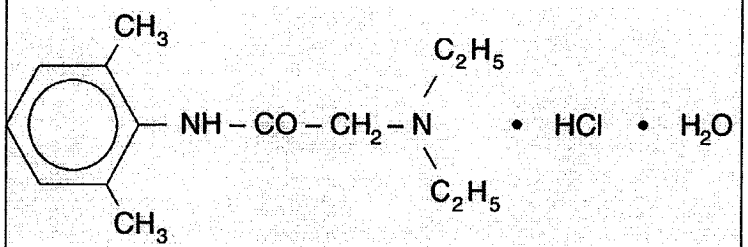
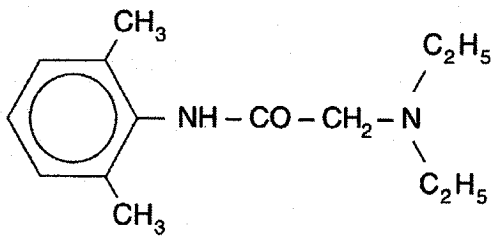
Manufactured by Armstrong Laboratories, Inc., West Roxbury, MA 02132.

Manufactured for

ASTRA®

Astra USA, Inc.
Westborough, MA 01581

021731R31 11/93 (31)

COMPARATIVE TABLE OF INSERT TEXTS		
Lidodan™ (Lidocaine Hydrochloride) Non-Aerosol Oral Spray	**10% Xylocaine® Oral Spray**	**Differences for LIDODAN**
Lidodan™ (Lidocaine Hydrochloride) Non-Aerosol Oral Spray 12 mg Lidocaine Hydrochloride/metered dose (Equivalent to Lidocaine 10 mg) Topical Anesthetic Spray For Use In The Oral Cavity	**10% Xylocaine® Oral Spray** (lidocaine) **WARNING - CONTENTS UNDER PRESSURE** Flavored Topical Anesthetic Aerosol For Use In The Oral Cavity	Lidocaine Salt vs. Base. Contents not under pressure. No flavor added.
DESCRIPTION LIDODAN™ (Lidocaine Hydrochloride) Non-Aerosol Oral Spray contains a local anesthetic agent and is administered topically in the oral cavity. See INDICATIONS for specific uses. LIDODAN Non-Aerosol Oral Spray contains lidocaine HCl, which is chemically designated as acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl)-, monohydrochloride, monohydrate and has the following structural formula:  $C_{14}H_{22}N_2O \cdot HCl \cdot H_2O$ 288.81 Composition of LIDODAN Non-Aerosol Oral Spray: Each actuation of the metered dose valve delivers a solution containing 12 mg of lidocaine hydrochloride (equivalent to 10 mg lidocaine base), purified water USP, sodium hydroxide and/or hydrochloric acid to adjust pH 5.0-7.0.	**DESCRIPTION** Xylocaine (lidocaine) 10% Oral Spray contains a local anesthetic agent and is administered topically in the oral cavity. See INDICATIONS for specific uses. Xylocaine 10% Oral Spray contains lidocaine, which is chemically designated as acetamide, 2 (diethylamino)-N-(2,6-dimethylphenyl)-, and has the following structural formula:  Composition of Xylocaine (lidocaine) 10% Oral Spray: Each actuation of the metered dose valve delivers a solution containing lidocaine, 10 mg, cetylpyridinium chloride, absolute alcohol; saccharin, flavor, and polyethylene glycol.	Contains amount of Lidocaine Hydrochloride, equivalent to Lidocaine base. Differences in excipients. Contains no Alcohol, Flavor, sweetener or PEG.

	And as propellants: trichlorofluoromethane / dichlorodifluoromethane (65%/35%). **WARNING:** Contains trichlorofluoromethane and dichlorodifluoromethane, substances which harm public health and environment, by destroying ozone in the upper atmosphere.	Contains no propellants (CFC or others).
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 the local anesthetic action. **Onset and Duration of Action:** LIDODAN (Lidocaine HCl) Non-Aerosol Oral Spray acts on intact mucous membranes to produce local anesthesia. Anesthesia occurs usually within 1-2 minutes and persists for approximately 10-15 minutes. **Hemodynamics:** Excessive blood levels may cause changes in cardiac output, total peripheral resistance, and mean arterial pressure. These changes may be attributable to a direct depressant effect of the local anesthetic agent on various components of the cardiovascular system. **Pharmacokinetics and Metabolism:** Lidocaine may be absorbed following topical administration to mucous membranes, its rate of absorption and percent of dose absorbed depending 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 occurs most rapidly after intratracheal administration. Lidocaine is well-absorbed from the gastrointestinal tract, but little intact drug appears in the circulation because of biotransformation in the liver. Lidocaine is metabolized rapidly by the liver, and metabolites and unchanged drug are excreted by the kidney. Biotransformation includes oxidative N-dealkylation, ring hydroxylation, cleavage of the amide linkage, and conjugation. N-dealkylation, a major pathway of biotransformation, yields the metabolites monoethylglycinexylidide and glycinexylidide. The pharmacological/toxicological actions of these metabolites are similar to, but less potent than, those of lidocaine. Approximately 90% of lidocaine administered is excreted in the form of various metabolites, and less than 10% is excreted unchanged. The	**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. **Onset and Duration of Action:** Xylocaine (lidocaine) 10% Oral Spray acts on intact mucous membranes to produce local anesthesia. Anesthesia occurs usually within 1-2 minutes and persists for approximately 10-15 minutes. **Hemodynamics:** Excessive blood levels may cause changes in cardiac output, total peripheral resistance, and mean arterial pressure. These changes may be attributable to a direct depressant effect of the local anesthetic agent on various components of the cardiovascular system. **Pharmacokinetics and Metabolism:** Lidocaine may be absorbed following topical administration to mucous membranes, its rate of absorption and percent of dose absorbed depending 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 occurs most rapidly after intratracheal administration. Lidocaine is well-absorbed from the gastrointestinal tract, but little intact drug appears in the circulation because of biotransformation in the liver. Lidocaine is metabolized rapidly by the liver, and metabolites and unchanged drug are excreted by the kidney. Biotransformation includes oxidative N-dealkylation, ring hydroxylation, cleavage of the amide linkage, and conjugation. N-dealkylation, a major pathway of biotransformation, yields the metabolites monoethylglycinexylidide and glycinexylidide. The pharmacological/toxicological actions of these metabolites are similar to, but less potent than, those of lidocaine. Approximately 90% of lidocaine administered is excreted in the form of various metabolites, and less than 10% is excreted unchanged. The	

primary metabolite in urine is a conjugate of 4-hydroxy-2, 6-dimethylaniline. 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. Lidocaine crosses the blood-brain and placental barriers, presumably by passive diffusion. Studies of lidocaine metabolism following intravenous bolus injections have shown that the elimination half-life of this agent is typically 1.5 to 2 hours. Because of the rapid rate at which lidocaine is metabolized, any condition that affects liver function may alter lidocaine kinetics. The half-life may be prolonged two-fold or more in patients with liver dysfunction. Renal dysfunction does not affect lidocaine kinetics but may increase the accumulation of metabolites. Factors such as acidosis and the use of CNS stimulants and depressants affect the CNS levels of lidocaine required to produce overt systemic effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6.0 µg free base per mL. In the rhesus monkey arterial blood levels of 18-21 µg/mL have been shown to be threshold for convulsive activity.	primary metabolite in urine is a conjugate of 4-hydroxy-2, 6-dimethylaniline. 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. Lidocaine crosses the blood-brain and placental barriers, presumably by passive diffusion. Studies of lidocaine metabolism following intravenous bolus injections have shown that the elimination half-life of this agent is typically 1.5 to 2 hours. Because of the rapid rate at which lidocaine is metabolized, any condition that affects liver function may alter lidocaine kinetics. The half-life may be prolonged two-fold or more in patients with liver dysfunction. Renal dysfunction does not affect lidocaine kinetics but may increase the accumulation of metabolites. Factors such as acidosis and the use of CNS stimulants and depressants affect the CNS levels of lidocaine required to produce overt systemic effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6 µg free base per mL. In the rhesus monkey arterial blood levels of 18-21 µg/mL have been shown to be threshold for convulsive activity.	
INDICATIONS AND USAGE LIDODAN (Lidocaine HCl) Non-Aerosol Oral Spray is indicated for the production of topical anesthesia of the accessible mucous membranes of the mouth and oropharynx.	**INDICATIONS AND USAGE** Xylocaine (lidocaine) 10% Oral Spray is indicated for the production of topical anesthesia of the accessible mucous membranes of the mouth and oropharynx.	
CONTRAINDICATIONS LIDODAN (Lidocaine HCl) Non-Aerosol Oral Spray is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type or to other components of LIDODAN Non-Aerosol Oral Spray.	**CONTRAINDICATIONS** Lidocaine is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type or to other components of Xylocaine 10% Oral Spray.	

WARNINGS IN ORDER TO MANAGE POSSIBLE ADVERSE REACTIONS, RESUSCITATIVE EQUIPMENT, OXYGEN AND OTHER RESUSCITATIVE DRUGS MUST BE IMMEDIATELY AVAILABLE WHEN LOCAL ANESTHETIC AGENTS, SUCH AS LIDOCAINE, ARE ADMINISTERED TO MUCOUS MEMBRANES. LIDODAN (Lidocaine HCl) Non-Aerosol Oral Spray should be used with extreme caution if there is sepsis or extremely traumatized mucosa in the area of application, since under such conditions there is the potential for rapid systemic absorption.	**WARNINGS** IN ORDER TO MANAGE POSSIBLE ADVERSE REACTIONS, RESUSCITATIVE EQUIPMENT, OXYGEN AND OTHER RESUSCITATIVE DRUGS MUST BE IMMEDIATELY AVAILABLE WHEN LOCAL ANESTHETIC AGENTS, SUCH AS LIDOCAINE, ARE ADMINISTERED TO MUCOUS MEMBRANES. Xylocaine 10% Oral Spray should be used with extreme caution if there is sepsis or extremely traumatized mucosa in the area of application, since under such conditions there is the potential for rapid systemic absorption.	
PRECAUTIONS **General:** The safety and efficacy of lidocaine depend on proper dosage, correct technique, adequate precautions, and readiness for emergencies. Resuscitative equipment, oxygen, and other resuscitative drugs should be available for immediate use. (See WARNINGS and ADVERSE REACTIONS). The lowest dosage that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. Repeated doses of lidocaine may cause significant increases in blood levels with each repeated dose because of slow accumulation of the drug or its metabolites. Tolerance varies with the status of the patient. Debilitated, elderly patients, acutely ill patients, and children should be given reduced doses commensurate with their age and physical status. Lidocaine should also be used with caution in patients with severe shock or heart block. LIDODAN (Lidocaine HCl) Non-Aerosol Oral Spray should be used with caution in patients with known drug sensitivities. Patients allergic to para-aminobenzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine. Many drugs used during the conduct of anesthesia are considered potential triggering agents for familial malignant hyperthermia. Since it not known whether amide-type local anesthetics may trigger this reaction, and since the need for supplemental general anesthesia cannot be predicted in advance, it is suggested that a standard protocol for management should be available. Early unexplained signs of tachycardia, tachypnea, labile blood	**PRECAUTIONS** **General:** The safety and efficacy of lidocaine depend on proper dosage, correct technique, adequate precautions, and readiness for emergencies. Resuscitative equipment, oxygen, and other resuscitative drugs should be available for immediate use. (See WARNINGS and ADVERSE REACTIONS). The lowest dosage that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. Repeated doses of lidocaine may cause significant increases in blood levels with each repeated dose because of slow accumulation of the drug or its metabolites. Tolerance varies with the status of the patient. Debilitated, elderly patients, acutely ill patients, and children should be given reduced doses commensurate with their age and physical status. Lidocaine should also be used with caution in patients with severe shock or heart block. Xylocaine 10% Oral Spray should be used with caution in patients with known drug sensitivities. Patients allergic to para-amino-benzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine. Many drugs used during the conduct of anesthesia are considered potential triggering agents for familial malignant hyperthermia. Since it not known whether amide-type local anesthetics may trigger this reaction, and since the need for supplemental general anesthesia cannot be predicted in advance, it is suggested that a standard protocol for management should be available. Early unexplained signs of tachycardia, tachypnea, labile blood pressure and metabolic acidosis may precede temperature elevation.	

pressure and metabolic acidosis may precede temperature elevation. Successful outcome is dependent on early diagnosis, prompt discontinuance of the suspect triggering agent(s) and institution of treatment, including oxygen therapy, indicated supportive measures and dantrolene (consult dantrolene sodium intravenous package insert before using). **Information for Patients:** 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. For this reason, food should not be ingested for 60 minutes following use of local anesthetic preparations in the mouth or throat area. This is particularly important in children because of their frequency of eating. Numbness of the tongue or buccal mucosa may enhance the danger of unintentional biting trauma. Food and chewing gum should not be taken while the mouth or throat area is anesthetized. **Carcinogenesis, Mutagenesis, Impairment of Fertility:** Studies of lidocaine in animals to evaluate the carcinogenic and mutagenic potential or the effect on fertility have not been conducted. **Use in Pregnancy:** Teratogenic Effects. Pregnancy Category B. Reproduction studies have been performed in rats at doses up to 6.6 times the human dose and have revealed no evidence of harm to the fetus caused by lidocaine. There are, however, no adequate and well-controlled studies in pregnant women. Animal reproduction studies are not always predictive of human response. General consideration should be given to this fact before administering lidocaine to women of childbearing potential, especially during early pregnancy when maximum organogenesis takes place. **Labor and Delivery:** Lidocaine is not contraindicated in labor and delivery. Should LIDODAN (Lidocaine HCl) Non-Aerosol Oral Spray be used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind. **Nursing Mothers:** Lidocaine is excreted in breast milk in small amounts. Caution should be exercised when lidocaine is administered to a nursing woman. **Pediatric Use:** Safety and effectiveness in children below the age	Successful outcome is dependent on early diagnosis, prompt discontinuance of the suspect triggering agent(s) and institution of treatment, including oxygen therapy, indicated supportive measures and dantrolene (consult dantrolene sodium intravenous package insert before using). **Information for Patients:** 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. For this reason, food should not be ingested for 60 minutes following use of local anesthetic preparations in the mouth or throat area. This is particularly important in children because of their frequency of eating. Numbness of the tongue or buccal mucosa may enhance the danger of unintentional biting trauma. Food and chewing gum should not be taken while the mouth or throat area is anesthetized. **Carcinogenesis, Mutagenesis, Impairment of Fertility:** Studies of lidocaine in animals to evaluate the carcinogenic and mutagenic potential or the effect on fertility have not been conducted. **Use in Pregnancy:** Teratogenic Effects. Pregnancy Category B. Reproduction studies have been performed in rats at doses up to 6.6 times the human dose and have revealed no evidence of harm to the fetus caused by lidocaine. There are, however, no adequate and well-controlled studies in pregnant women. Animal reproduction studies are not always predictive of human response. General consideration should be given to this fact before administering lidocaine to women of childbearing potential, especially during early pregnancy when maximum organogenesis takes place. **Labor and Delivery:** Lidocaine is not contraindicated in labor and delivery. Should Xylocaine 10% Oral Spray be used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind. **Nursing Mothers:** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when lidocaine is administered to a nursing woman. **Pediatric Use:** Safety and effectiveness in children below the age	Update medical information

of 12 years have not been established.	of 12 years have not been established.	
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 excessive dosage or rapid absorption, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. 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 lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred or double vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest. The excitatory manifestations 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 blood level of the drug and may occur as a consequence of rapid absorption. **Cardiovascular System:** Cardiovascular manifestations are usually depressant and are characterized by bradycardia, hypotension, and cardiovascular collapse, which may lead to cardiac arrest. **Allergic:** Allergic reactions are characterized by cutaneous lesions, urticaria, edema or anaphylactoid reactions. Allergic reactions may occur as a result of sensitivity either to the local anesthetic agent or to other ingredients in the formulation. Allergic reactions as a result of sensitivity to lidocaine are extremely rare and, if they occur, should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.	**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 excessive dosage or rapid absorption, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. 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 lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred or double vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest. The excitatory manifestations 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 blood level of the drug and may occur as a consequence of rapid absorption. **Cardiovascular System:** Cardiovascular manifestations are usually depressant and are characterized by bradycardia, hypotension, and cardiovascular collapse, which may lead to cardiac arrest. **Allergic:** Allergic reactions are characterized by cutaneous lesions, urticaria, edema or anaphylactoid reactions. Allergic reactions may occur as a result of sensitivity either to the local anesthetic agent or to other ingredients in the formulation. Allergic reactions as a result of sensitivity to lidocaine are extremely rare and, if they occur, should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.	

OVERDOSAGE Acute emergencies from local anesthetics are generally related to high plasma levels encountered during therapeutic use of local anesthetics (See ADVERSE REACTIONS, WARNINGS and PRECAUTIONS.) **Management of Local Anesthetic Emergencies:** 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 convulsions 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. Immediately after the institution of these ventilatory measures, the adequacy of the circulation should be evaluated, keeping in mind that drugs used to treat convulsions sometimes depress the circulation when administered intravenously. Should convulsions persist despite adequate respiratory support, and if the status of the circulation permits, small increments of an ultra-short acting barbiturate (such as thiopental or thiamylal) or a benzodiazepine (such as diazepam) may be administered intravenously. The clinician should be familiar, prior to use of local anesthetics, with these anticonvulsant drugs. Supportive treatment of circulatory depression may require administration of intravenous fluids and, when appropriate, a vasopressor as directed by the clinical situation (e.g., ephedrine). If not treated immediately, both convulsions and cardiovascular depression can result in hypoxia, acidosis, bradycardia, arrhythmias and cardiac arrest. If cardiac arrest should occur, standard cardiopulmonary resuscitative measures should be instituted. Dialysis is of negligible value in the treatment of acute overdosage with lidocaine. The intravenous LD_{50} of lidocaine HCl in female mice is 26 (21-31) mg/kg and the subcutaneous LD_{50} is 264 (203-304) mg/kg.	**OVERDOSAGE** Acute emergencies from local anesthetics are generally related to high plasma levels encountered during therapeutic use of local anesthetics. (See ADVERSE REACTIONS, WARNINGS and PRECAUTIONS.) **Management of Local Anesthetic Emergencies:** 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 convulsions 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. Immediately after the institution of these ventilatory measures, the adequacy of the circulation should be evaluated, keeping in mind that drugs used to treat convulsions sometimes depress the circulation when administered intravenously. Should convulsions persist despite adequate respiratory support, and if the status of the circulation permits, small increments of an ultra-short acting barbiturate (such as thiopental or thiamylal) or a benzodiazepine (such as diazepam) may be administered intravenously. The clinician should be familiar, prior to use of local anesthetics, with these anticonvulsant drugs. Supportive treatment of circulatory depression may require administration of intravenous fluids and, when appropriate, a vasopressor as directed by the clinical situation (e.g., ephedrine). If not treated immediately, both convulsions and cardiovascular depression can result in hypoxia, acidosis, bradycardia, arrhythmias and cardiac arrest. If cardiac arrest should occur, standard cardiopulmonary resuscitative measures should be instituted. Dialysis is of negligible value in the treatment of acute overdosage with lidocaine. The intravenous LD_{50} of lidocaine HCl in female mice is 26 (21-31) mg/kg and the subcutaneous LD_{50} is 264 (203-304) mg/kg.	

DOSAGE AND ADMINISTRATION When LIDODAN (Lidocaine HCl) Non-Aerosol Oral Spray is used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind. Two metered doses per quadrant are recommended as the upper limit and, *under no circumstances* should one exceed three metered doses per quadrant of oral mucosa over a one-half hour period to produce the desired anesthetic effect. Experience in children is inadequate to recommend a pediatric dose at this time. 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 reprimed but the air in the nozzle must be voided before a full dose is delivered. This usually requires two actuations.	**DOSAGE AND ADMINISTRATION** When Xylocaine 10% Oral Spray is used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind. Two metered doses per quadrant are recommended as the upper limit and, *under no circumstances* should one exceed three metered doses per quadrant of oral mucosa over a one-half hour period to produce the desired anesthetic effect. Experience in children is inadequate to recommend a pediatric dose at this time.	Pump priming instructions specific to Lidodan.

HOW SUPPLIED LIDODAN Non-Aerosol Oral Spray is available in a 30 mL bottle spray with a metered dose valve. NDC 61344-108-43 / NDC 61344-118-63: A 30 mL bottle provides a total amount of 3.0 g (w/w) of the active ingredient lidocaine (3.6 g of lidocaine hydrochloride). Each actuation of the metered dose valve delivers 10 mg of lidocaine (12 mg lidocaine HCl). Avoid contact with the eyes. Inhalation and swallowing should be avoided. Keep out of the reach of children. Use only as directed; intentional misuse by deliberately concentrating and inhaling the contents can be harmful or fatal. STORE AT CONTROLLED ROOM TEMPERATURE 15°-30°C (59°-86°F). PROTECT FROM FREEZING. Clean stainless steel nozzles may be steam-sterilized at 250°F (121°C) for 15 minutes. Single Pak: One 30 mL bottle with 1 x 20 cm (8") stainless steel nozzle. (NDC 61344-108-43) Three Pak: Three 30 mL bottles. (NDC 61344-118-63) Nozzle Pak: Stainless steel: 2 x 20 cm (8") stainless steel reusable nozzles. Nozzle Pak: Plastic: 24 x 20 cm plastic disposable nozzles. Nozzle Pak: Plastic: 96 x 20 cm plastic disposable nozzles. Odan Laboratories Ltd. Montreal, QC, Canada H9R 2Y6	**HOW SUPPLIED** NDC 0186-0356-01: A 26.8 mL aerosol container provides a total amount of 3.3 g (w/w) of the active ingredient lidocaine. Each actuation of the metered dose valve delivers 10 mg of lidocaine. Contents under pressure. Do not puncture or incinerate container. Do not expose to heat or store at temperatures above 120°F. Avoid contact with the eyes. Inhalation and swallowing should be avoided. Keep out of the reach of children. Use only as directed; intentional misuse by deliberately concentrating and inhaling the contents can be harmful or fatal. STORE AT CONTROLLED ROOM TEMPERATURE 15°-30°C (59°-86°F). Manufactured by Armstrong Laboratories, Inc., West Roxbury, MA 02132. Manufactured for ASTRA USA, Inc. Westborough, MA 01581	Change in manufacturer. Differences due to lidocaine moiety. Lidodan contents not under pressure. Protect from freezing. Additional info on cleaning stainless steel nozzles. Differences in manufacturer