**Predator™ Topical Pain Relief Cream OTC**

# DESCRIPTION

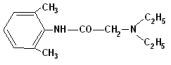
Lidocaine Hydrochloride Topical Cream USP 4% contains a local anesthetic agent and is administered topically. See INDICATIONS for specific uses.

Each mL contains:

Lidocaine Hydrochloride . . . . . 40 mg

**NOT FOR INJECTION OR ORAL ADMINISTRATION**

Lidocaine is a local anesthetic chemically designated as 2-(diethylamino)-N-(2,6-dimethyl-phenyl)-acetamide. It has the following structural formula:



SAMBRIA™ PHARMACEUTICALS

# 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.

## 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. Care should be taken to ensure no more than the recommended dose is used daily for more than seven (7) consecutive days without the recommendation of a licensed medical professional. In the event use beyond seven (7) consecutive days is required, it may be necessary to have regular blood tests to determine safe lidocaine plasma levels.

## 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.

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. 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 2.0 hours. Because of the rapid rate at which lidocaine is metabolized, any condition that affects liver function may alter lidocaine kinetics. The half-life may be prolonged two-fold or more in patients with liver dysfunction. Renal dysfunction does not affect lidocaine kinetics but may increase the accumulation of metabolites.

Factors such as acidosis and the use of CNS stimulants and depressants affect the CNS levels of lidocaine required to produce overt systemic effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma 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

Lidocaine Hydrochloride Topical Cream is indicated for use as a topical anesthetic.

# CONTRAINDICATIONS

Lidocaine is contraindicated in patients with a known hypersensitivity, either to local anesthetics of the amide type or to the components of the topical Cream. Lidocaine is also contraindicated in patients with severe hepatic or renal dysfunction. See WARNINGS, PRECAUTIONS and ADVERSE REACTIONS for additional information.

# 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. THIS PRODUCT IS NOT INTENDED FOR USE AS A TOPICAL ANESTHETIC ADMINISTERED TO MICOUS MEMBRANES.

Lidocaine Hydrochloride Topical Cream should be used with extreme caution if there is sepsis or severely traumatized mucosa in the area of application, since under such conditions there is the potential for rapid systemic absorption. Rapid concentrated systemic absorption may cause negative alterations in cardiac function.

# 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 and/or its metabolites. Tolerance to elevated blood levels 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.

Lidocaine Hydrochloride Topical Cream 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 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 administration.

## Information for Patients

This product is not to be administered orally (mouth) or in the ocular (eye) area. If used improperly by oral administration the patient should be aware that the production of topical anesthesia may impair swallowing and thus enhance the danger of aspiration. For this reason, any device (including hands and fingers) used to administer this product topically should be cleaned well before possible contact with eyes, intra-nasally or mouth. This is particularly important in children because of their frequency of hand-to-eye, hand-to-nostrils and hand-to-mouth contact. ***This product should be kept out of the reach of children under twelve (12) years of age.***

In the event of accidental oral administration, numbness of the tongue or buccal mucosa may increase the danger of unintentional biting trauma. Food and chewing gum should not be taken while or immediately after administering this product to avoid accidental oral application. Immediately contact a licensed healthcare professional in case of accidental oral, nasal or ocular administration.

***This product is not intended for oral (by mouth), nasal (in the nose), anal or ocular (in the eyes) use. This product is not intended for use on open wounds.***

Hands and fingers used to administer this product should not contact eyes or mouth unless washed with soap and water prior to contact.

## 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

## 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. This product is not recommended for use in pregnant human females.

## Labor and Delivery

Lidocaine is not contraindicated in labor and delivery. Should Lidocaine Hydrochloride Topical Cream be used concomitantly with other products containing lidocaine, the total dose being administered 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. This product is not recommended in use with nursing mothers unless under the direct supervision of a medical professional.

## Pediatric Use

Dosage in children should be reduced commensurate with age, body weight and physical conditions. See DOSAGE AND ADMINISTRATION. This product should not be used on children under 12 years of age unless directed by a licensed physician.

# 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 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 steps in the management of convulsions consist 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. Prior to use of local anesthetics, the clinician should be familiar with these anticonvulsant drugs. Supportive treatment of circulatory depression may require administration of intravenous fluids and, when appropriate, a vasopressor (e.g., ephedrine) as indicated by the clinical situation.

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 Lidocaine Hydrochloride Topical Cream 4% is used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind.

The dosage varies and depends upon the area to be anesthetized, vascularity of the tissues, individual tolerance and the technique of anesthesia. The lowest dosage needed to provide effective anesthesia should be administered. Dosages should be reduced for children and for elderly and debilitated patients. The maximum dose should not exceed 2.5 mg/kg (1.2 mg/lb.) of body weight. Although the incidence of adverse effects with Lidocaine Hydrochloride Topical Cream is rare, caution should be exercised particularly when employing large volumes, since the incidence of adverse effects is directly proportional to the total dose of local anesthetic agent administered.

The dosages recommended below are for normal healthy adults:

The suggested dosage of Lidocaine Hydrochloride Topical Cream is 0.5 to 1.5 mL (20 - 60 mg of lidocaine hydrochloride); i.e., 0.3-0.75 mg/kg or 0.6-0.375 mg/lb. of body weight.

Wash and disinfect affected area prior to application. Apply by rubbing a thin film of cream into affected area topically in a vigorous circular motion for 45 – 60 seconds until cream is completely absorbed into skin.

4% lidocaine cream should be used no more than once every 4 hours and twice daily for a period of seven (7) consecutive days. Licensed physician should be consulted before using more than the recommended dose or for longer than the recommended dosing period.

NOTE: The Cream may be applied with a sterile swab which is discarded after use and never reused under any circumstances. The affected area should be disinfected prior to topical administration.

## Maximum Recommended Dosages

## Normal Healthy Adults

The maximum total daily recommended dose of Lidocaine Hydrochloride Topical Cream should be such that the dose of lidocaine hydrochloride is kept below 300 mg, and in any case, should never exceed 4.5 mg/kg (2 mg/lb) of body weight.

## Children

It is difficult to recommend a maximum dose of any drug for children, since it would vary as a function of age and weight. For children of less than ten years who have a normal lean body mass and normal body development, the maximum dose may be determined by the application of one of the standard pediatric drug formulas (e.g., Clark's rule). For example, in a child of five years weighing 50 lbs., when calculated according to Clark's rule, the total daily dose of lidocaine should not exceed 75-100 mg. In any case, the maximum dose of Lidocaine Hydrochloride should not exceed 7 mg/kg (3.2 mg/lb) of body weight. When used without epinephrine, the amount of Lidocaine Hydrochloride administered should be such that the dose is kept below 300 mg, and in any case, should not exceed 4.5 mg/kg (2.0 mg/lb) of body weight.

# HOW SUPPLIED

Lidocaine Hydrochloride Topical Cream USP 4%

Jar containing one fluid ounce (28 grams)

Store at Controlled Room Temperature of 15°-30°C (59°-86°F).