



INTERNATIONAL MEDICATION SYSTEMS, LIMITED
 1886 SANTA ANITA AVENUE, SOUTH EL MONTE, CALIFORNIA 91733
 AREA CODE (800) 423-4136 FAX (626) 459-5255

MATERIAL SAFETY DATA SHEET

SECTION I. MATERIAL IDENTIFICATION			
Identity/Material Name: Lidocaine Hydrochloride Injection USP, 2%			
Stock Number: 3390			
NDC Number: 0548-3390-00			
Unit Size: 100 mg/ 5 mL (one single dose vial and a Luer-Jet™ vial injector)			
Manufacture's Name: International Medication Systems, Limited (IMS)		Telephone (800)423-4136	
Address: 1886 Santa Anita Avenue, South El Monte, California 91733		Fax: (626)459-5255	
SECTION II. HAZARDOUS INGREDIENTS/IDENTITY INFORMATION			
Ingredient Name:	Amount per mL:	Permissible Exposure Level:	
Lidocaine HCl USP	20 mg	Unknown	
Sodium Hydroxide NF	As needed to adjust pH	Unknown	
Sodium Chloride USP	6.0 mg	Unknown	
Water for Injection USP	QS Ad	N/A	
SECTION III. PHYSICAL/CHEMICAL DATA			
Boiling Point (°C):	Unknown	Melting Point (°C):	N/A
Viscosity:	Viscous	Vapor Pressure:	Unknown
Specific Gravity:	N/A	Percentage Volatile:	N/A
Vapor Density:	Unknown	Evaporation:	Water solvent will slowly evaporate
Solubility in Water: Miscible with water			
Appearance and Odor: Clear, slightly yellow, odorless solution.			
SECTION IV. FIRE AND EXPLOSION DATA			
Flash Point: Unknown	Flammable Limits: LEL	N/A	UEL N/A
Extinguishing Media: Water, carbon dioxide, dry chemical or foam.			
Special Fire Procedures: Unknown			
Approved By: <u>QA/Diana [Signature]</u>		Date Prepared: <u>5-15-01</u>	

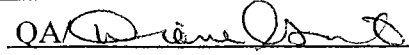
MATERIAL SAFETY DATA SHEET

SECTION V. REACTIVITY DATA

Stability:	Stable under ordinary conditions of use and storage.
Conditions to Avoid:	Temperature outside of 15°C to 30°C. Freezing.
Incompatibility (Materials to Avoid):	Lidocaine hydrochloride should be used with caution in patients with digitalis toxicity accompanied by atrioventricular block. Concomitant use of beta-blocking agents may reduce hepatic blood flow and thereby reduce lidocaine clearance. Lidocaine and tocainide are pharmacologically similar. The concomitant use of these two agents may cause an increased incidence of adverse reactions, including central nervous system adverse reactions, such as seizure.
Hazardous Decomposition Products:	Unknown

SECTION VI. HEALTH HAZARDS DATA

LD ₅₀	Oral: 459 (346 - 773) mg/kg (as the salt) in non-fasted female rats 214 (159 - 324) mg/kg (as the salt) in fasted female rats
Mutagenicity, Carcinogenicity, Pregnancy, Fertility, and Lactation:	Long term studies of lidocaine in animals to evaluate the carcinogenic and mutagenic potential or the effect on fertility have not been conducted. Pregnancy Category B. Reproduction studies have been performed in rats at doses up to 6.6 times the human dose and have revealed no significant findings. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only when clearly needed. The effects of lidocaine hydrochloride on the mother and the fetus, when used in the management of cardiac arrhythmias during labor and delivery, are not known. Lidocaine readily crosses the placental barrier. Since lidocaine is distributed into milk, the drug should be used with caution in nursing women. Limited data suggest that the amount of drug that potentially would be ingested by a breast-fed infant is small.
Effect and Treatment of Overdosage:	Overdosage of lidocaine hydrochloride usually results in signs of central nervous system or cardiovascular toxicity. Adverse experiences following the administration of lidocaine are similar in nature to those observed with other amide local anesthetic agents. Adverse experiences may result from high plasma levels caused by excessive dosage 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 reactions are excitatory and/or depressant, and may be characterized by light-headedness, 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 reactions may be very brief or may not occur at all,

Approved By: <u>OA </u>	Date Prepared: <u>5-15-01</u>
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MATERIAL SAFETY DATA SHEET

SECTION VI. HEALTH HAZARDS DATA (CONTINUED)

Effect and Treatment of Overdosage (Continued):

in which case, the first manifestation of toxicity may be drowsiness, merging into unconsciousness and respiratory arrest.

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

Allergic reactions as a result of sensitivity to lidocaine are extremely rare and, if they occur, should be managed by conventional means.

In order to manage possible adverse reactions, resuscitative equipment, oxygen and other resuscitative drugs should be immediately available when lidocaine hydrochloride injection is used.

Should convulsions or signs of respiratory depression and arrest develop, the patency of the airway and adequacy of ventilation must be assured immediately. Should convulsions persist despite ventilatory therapy with oxygen, small increments of anticonvulsive agents may be given intravenously. Examples of such agents include a benzodiazepine (e.g., diazepam), an ultrashort-acting barbiturate (e.g., thiopental or thiamylal), or a short-acting barbiturate (e.g., pentobarbital or secobarbital). If the patient is under general anesthesia, a short-acting muscle relaxant (e.g., succinylcholine) may be administered. Longer acting drugs should be used only when recurrent convulsions are evidenced.

Should circulatory depression occur, vasopressors may be used. Should cardiac arrest occur, standard CPR procedures should be instituted. Dialysis is of negligible value in the treatment of acute overdosage from lidocaine hydrochloride.

Eye Contact: Flush eyes immediately with copious amounts of water. Seek medical attention if deemed necessary.

Inhalation: Unknown

Accidental Ingestion: Seek physician's care.

Skin Irritation: Avoid direct skin contact. Wash affected skin surfaces immediately with mild soap and copious amounts of water.

Systemic: Lidocaine Hydrochloride Injection USP is a sterile, aqueous solution of lidocaine, an antiarrhythmic agent. It is intended for intravenous administration by either injection or continuous infusion. It is specifically indicated in the acute management of ventricular arrhythmias such as those occurring in relation to acute myocardial infarction, or during cardiac manipulation, such as cardiac surgery.

Studies of the effects of therapeutic concentrations of lidocaine on the electrophysiological properties of mammalian Purkinje fibers have shown that lidocaine attenuates phase 4 diastolic depolarization, decreases automaticity and causes a decrease or no change in excitability and membrane responsiveness. Action potential duration and effective refractory period of Purkinje fibers are decreased. While the ratio of effective refractory period of action potential duration is increased. Action potential duration and effective refractory period of

Approved By: QA [Signature] Date Prepared: 5-15-01

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SECTION VI. HEALTH HAZARDS DATA (CONTINUED)

Systemic:
(Continued)

ventricular muscle are also decreased. Effective refractory period of the AV node may increase, decrease or remain unchanged, and atrial effective refractory period is unchanged.

Lidocaine raises the ventricular fibrillation threshold. No significant interactions between lidocaine and the autonomic nervous system have been described and consequently lidocaine has little or effect on autonomic tone.

Clinical electrophysiological studies with lidocaine have demonstrated no change in sinus node recovery time or sinoatrial conduction time. AV nodal conduction time is unchanged or shortened, and His-Purkinje conduction time is unchanged.

At therapeutic doses, lidocaine has minimal hemodynamic effects in normal subjects and in patients with heart disease. Lidocaine has been shown to cause no, or minimal, decrease in ventricular contractility, cardiac output, arterial pressure or heart rate.

Lidocaine is rapidly metabolized by the liver, and less than 10% of a dose is excreted unchanged in the urine. Oxidative N-dealkylation, a major pathway of metabolism, results in the metabolites monoethylglycinexylidide and glycinexylidide. The pharmacological/toxicological activities of these metabolites are similar to, but less potent than, lidocaine. The primary metabolite in urine is a conjugate of 4-hydroxy-2,6,-dimethylaniline.

The elimination half-life of lidocaine following an intravenous bolus injection is typically 1.5 to 2 hours. There are data that indicate that the half-life may be 3 hours or longer following infusions of greater than 24 hours.

Because of the rapid rate at which lidocaine is metabolized, any condition that alters liver function, including changes in liver blood flow, which could result from severe congestive heart failure in shock, may alter lidocaine kinetics. The half-life may be two-fold or more, greater in patients with liver dysfunction. Renal dysfunction does not affect lidocaine kinetics, but may increase the accumulation of metabolites. Caution should be taken in the use of lidocaine hydrochloride in patients with severe liver or kidney disease because accumulation of the drug or metabolites may occur.

Therapeutic effects of lidocaine are generally associated with plasma levels at 6 to 25 $\mu\text{mole/L}$ (1.5 to 6 μg free base per mL). The blood to plasma distribution ratio is approximately 0.84. Objective adverse manifestations become increasingly apparent with increasing plasma levels above 6 μg free base per mL.

The plasma protein binding of lidocaine is dependent on drug concentration, and the fraction bound decreases with increasing concentration. At concentrations of 1 to 4 g free base per mL, 60 to 80 percent of lidocaine is protein bound. In addition to lidocaine concentration, the binding is dependent on the plasma concentration of the α -1-acid glycoprotein.

Lidocaine readily crosses the placental and blood-brain barriers. Dialysis has negligible effects on the kinetics of lidocaine.

Systemic toxicity may result in manifestations of central nervous system depression (sedation) or irritability (twitching), which may progress to frank convulsions accompanied by respiratory depression and/or arrest. Early recognition of premonitory signs, assurance of adequate oxygenation and, where necessary, establishment of artificial airway with ventilatory support are essential to management of this problem.

Approved By: OAR Diane De X

Date Prepared: 5-15-01

SECTION VI. HEALTH HAZARDS DATA (CONTINUED)

Systemic (Continued): Constant electrocardiographic monitoring is essential to the proper administration of lidocaine hydrochloride. Signs of excessive depression of cardiac electrical activity such as sinus node dysfunction, prolongation of the P-R interval and QRS complex or the appearance or aggravation of arrhythmias, should be followed by flow adjustment and, if necessary, prompt cessation of the intravenous infusion of this agent. Occasionally, acceleration of ventricular rate may occur when lidocaine hydrochloride is administered to patients with atrial flutter or fibrillation.

Lidocaine hydrochloride should be used with caution in the treatment of patients with hypovolemia, severe congestive heart failure, shock, and all forms of heart block. In patients with sinus bradycardia or incomplete heart block, the administration of lidocaine hydrochloride intravenously for the elimination of ventricular ectopic beats, without prior acceleration in heart rate (e.g., by atropine, isoproterenol or electric pacing), may promote more frequent and serious ventricular arrhythmias or complete heart block.

Dosage should be reduced for children and for debilitated and/or elderly patients, commensurate with their age and physical status. The safety of amide local anesthetic agents in patients with genetic predisposition to malignant hypothermia has not been fully assessed; therefore, lidocaine should be used with caution in such patients. In hospital environments where drugs known to be triggering agents for malignant hypothermia (fulminate hypermetabolism) are administered, it is suggested that a standard protocol for management should be available. It is not known whether lidocaine may trigger this reaction; however, large doses resulting in significant plasma concentrations, as may be achieved by intravenous infusion, pose potential risk to these individuals. Recognition of 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 triggering agent and institution of treatment including oxygen therapy, supportive measures and dantrolene.

Lidocaine hydrochloride is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type. Lidocaine hydrochloride should not be used in patients with Stokes-Adams syndrome, Wolff-Parkinson-White syndrome, or with severe degrees of sinoatrial, atrioventricular, or intraventricular block in the absence of an artificial pacemaker.

Although specific studies have not been conducted, lidocaine hydrochloride has been used clinically without evidence of abuse of this drug or of psychological or physical dependence as a result of its use.

SECTION VII. PRECAUTIONS FOR SAFE HANDLING AND USE


Precautions: Improper engaging may cause glass breakage and subsequent injury.

Steps to be Taken if Released or Spilled: Absorb onto paper. Wash spill site with copious amounts of water.

Waste Disposal: Approved chemical waste incineration or approved aqueous discharge to municipal or on-site wastewater treatment systems.

Approved By: QA/ Diane J. [Signature] Date Prepared: 5-15-01

MATERIAL SAFETY DATA SHEET

SECTION VIII. CONTROL MEASURES	
Respiratory Protection:	N/A
Ventilation:	Local ventilation adequate.
Skin Protection:	Adequate skin protection recommended including gloves.
Eye Protection:	Adequate eye protection recommended including safety glasses.
Approved By: QA/ 	Date Prepared: 5-15-01

Rx Only. Refer to package insert for additional information.

The information contained herein is believed to be complete and accurate. However, it is the user's responsibility to determine the suitability of the information for their particular purpose. International Medication Systems, Limited assumes no additional liability or responsibility resulting from the usage of, or reliance on this information.