

**A4017-25 SPINAL 25G WHITACRE - regional anesthesia kit**  
**Smiths Medical ASD, Inc.**

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**EPINEPHRINE injection, USP**

1:1000 (1 mg/mL)

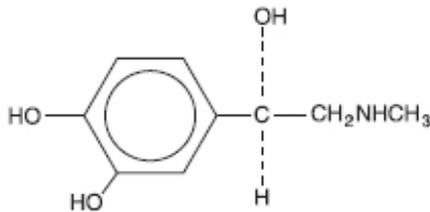
**Ampul**

**Protect from light until ready to use.**

**Rx only**

**Description**

Epinephrine Injection, USP 1:1000 is a sterile, nonpyrogenic solution. Each mL contains epinephrine 1 mg; sodium chloride 9 mg; sodium metabisulfite 0.9 mg added. May contain hydrochloric acid for pH adjustment. The solution contains no bacteriostat or antimicrobial agent. It is administered by the following routes: intravenous, intracardiac (left ventricular chamber), via endotracheal tube into the bronchial tree, subcutaneous or intramuscular. Epinephrine, USP is a sympathomimetic (adrenergic) agent designated chemically as 4-[1-hydroxy-2 (methylamino) ethyl]-1,2 benzenediol, a white, microcrystalline powder. It has the following structural formula:



Sodium Chloride, USP is chemically designated NaCl, a white, crystalline compound freely soluble in water.

**Clinical Pharmacology**

The actions of epinephrine resemble the effects of stimulation of adrenergic nerves. To a variable degree it acts on both alpha and beta receptor sites of sympathetic effector cells. Its most prominent actions are on the beta receptors of the heart, vascular and other smooth muscle. When given by rapid intravenous injection, it produces a rapid rise in blood pressure, mainly systolic, by (1) direct stimulation of cardiac muscle which increases the strength of ventricular contraction, (2) increasing the heart rate and (3) constriction of the arterioles in the skin, mucosa and splanchnic areas of the circulation. When given by slow intravenous injection epinephrine usually produces only a moderate rise in systolic and a fall in diastolic pressure. Although some increase in pulse pressure occurs, there is usually no great elevation in mean blood pressure. Accordingly, the compensatory reflex mechanisms that come into play with a pronounced increase in blood pressure do not antagonize the direct cardiac actions of epinephrine as much as with catecholamines that have a predominant action on alpha receptors.

Total peripheral resistance decreases by action of epinephrine on beta receptors of the skeletal muscle vasculature and blood flow is thereby enhanced. Usually this vasodilator effect of the drug on the circulation predominates so that the modest rise in systolic pressure which follows slow injection or absorption is mainly the result of direct cardiac stimulation and increase in cardiac output. In some instances peripheral resistance is not altered or may even rise owing to a greater ratio of alpha to beta activity in different vascular areas. Epinephrine relaxes the smooth muscles of the bronchi and iris and is a physiologic antagonist of histamine. The drug also produces an increase in blood sugar and glycogenolysis in the liver. Intravenous injection produces an immediate and intensified response. Following intravenous injection epinephrine disappears rapidly from the blood stream. Epinephrine is rapidly inactivated in the body and is degraded by enzymes in the liver and other tissues. The large portion of injection doses is excreted in the urine as inactivated compounds. The remainder is excreted

in the urine as unchanged or conjugated compounds.

## **Indications and Usage**

Epinephrine is used to relieve respiratory distress due to bronchospasm, to provide rapid relief of hypersensitivity reactions to drugs and other allergens, and to prolong the action of anesthetics. Its cardiac effects may be of use in restoring cardiac rhythm in cardiac arrest due to various causes, but it is not used in cardiac failure or in hemorrhagic, traumatic, or cardiogenic shock. Epinephrine is used as a hemostatic agent. It is also used in treating mucosal congestion of hay fever, rhinitis, and acute sinusitis; to relieve bronchial asthmatic paroxysms; in syncope due to complete heart block or carotid sinus hypersensitivity; for symptomatic relief of serum sickness, urticaria, angioneurotic edema; for resuscitation in cardiac arrest following anesthetic accidents; in simple (open angle) glaucoma; for relaxation of uterine musculature and to inhibit uterine contractions. Epinephrine Injection can be utilized to prolong the action of anesthetics used in local and regional anesthesia.

## **Contraindications**

Epinephrine is contraindicated in patients with known hypersensitivity to sympathomimetic amines, in patients with angle closure glaucoma, and patients in shock (nonanaphylactic). It should not be used in patients anesthetized with agents such as cyclopropane or halothane as these may sensitize the heart to the arrhythmic action of sympathomimetic drugs. Addition of epinephrine to local anesthetics for injection of certain areas (e.g., fingers, toes, ears, etc.) is contraindicated because of danger that vasoconstriction may result in sloughing of tissue.

Except as diluted for admixture with local anesthetics to reduce absorption and prolong action, epinephrine should not ordinarily be used in those cases where vasopressor drugs may be contraindicated, e.g., in thyrotoxicosis, diabetes, in obstetrics when maternal blood pressure is in excess of 130/80 and in hypertension and other cardiovascular disorders.

## **Warnings**

Inadvertently induced high arterial blood pressure may result in angina pectoris, aortic rupture or cerebral hemorrhage. Epinephrine may induce potentially serious cardiac arrhythmias in patients not suffering from heart disease and in patients with organic heart disease or who are receiving drugs that sensitize the myocardium. Parenterally administered epinephrine initially may produce constriction of renal blood vessels and decrease urine formation. Epinephrine Injection, USP is subject to oxidation and should be protected against exposure to light and stored in light-resistant containers. Epinephrine is the preferred treatment for serious allergic or other emergency situations even though this product contains sodium metabisulfite, a sulfite that may in other products cause allergic-type reactions including anaphylactic symptoms or life-threatening or less severe asthmatic episodes in certain susceptible persons. The alternatives to using epinephrine in a life-threatening situation may not be satisfactory. The presence of a sulfite in this product should not deter administration of the drug for treatment of serious allergic or other emergency situations.

## **Precautions**

Do not use the Injection if its color is pinkish or darker than slightly yellow or if it contains a precipitate. Do not administer unless solution is clear and container is intact. Discard unused portion. Although epinephrine can produce ventricular fibrillation, its actions in restoring electrical activity in asystole and in enhancing defibrillation of the fibrillating ventricle are well documented. The drug, however, should be used with caution in patients with ventricular fibrillation. Epinephrine should be used cautiously in patients with hyperthyroidism, hypertension and cardiac arrhythmias. All vasopressors should be used cautiously in patients taking monoamine oxidase (MAO) inhibitors. Epinephrine should not be administered concomitantly with other sympathomimetic drugs (such as isoproterenol) because of possible additive effects and increased toxicity. Combined effects may induce serious cardiac arrhythmias. They may be administered alternately when the preceding effect of other such drugs has subsided. Administration of epinephrine to patients receiving cyclopropane or halogenated hydrocarbon general anesthetics such as halothane which sensitize the

myocardium, may induce cardiac arrhythmia. (See CONTRAINDICATIONS.) When encountered, such arrhythmias may respond to administration of a beta-adrenergic blocking drug. Epinephrine also should be used cautiously with other drugs (e.g., digitalis glycosides) that sensitize the myocardium to the actions of

sympathomimetic agents. Diuretic agents may decrease vascular response to pressor drugs such as epinephrine. Epinephrine may antagonize the neuron blockade produced by guanethidine resulting in decreased antihypertensive effect and requiring increased dosage of the latter.

*Pregnancy Category C.* Animal reproduction studies have not been conducted with epinephrine. It is also not known whether epinephrine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Epinephrine should be given to a pregnant woman only if clearly needed.

*Labor and Delivery.* Parenteral administration of epinephrine if used to support blood pressure during low or other spinal anesthesia for delivery can cause acceleration of fetal heart rate and should not be used in obstetrics when maternal blood pressure exceeds 130/80. (See CONTRAINDICATIONS.)

### **Adverse Reactions**

Transient and minor side effects of anxiety, headache, fear and palpitations occur only with systemic therapeutic doses, especially in hyperthyroid individuals. Adverse effects such as cardiac arrhythmias and excessive rise in blood pressure may occur with systemic therapeutic doses or with inadvertent overdosage. Other adverse reactions include cerebral hemorrhage, hemiplegia, subarachnoid hemorrhage, anginal pain in patients with angina pectoris, anxiety, restlessness, headache, tremor, weakness, dizziness, pallor and respiratory difficulty. Such reactions are unlikely when epinephrine is diluted to 1:200,000 for injection with local anesthetic agents.

### **Overdosage**

Erroneous administration of large doses of epinephrine may lead to precordial distress, vomiting, headache, dyspnea, as well as unusually elevated blood pressure. (See WARNINGS.) Toxic effects of overdosage can be counteracted by injection of an alpha-adrenergic blocker and a betaadrenergic blocker. In the event of a sharp rise in blood pressure, rapid-acting vasodilators such as the nitrites, or alpha-adrenergic blocking agents can be given to counteract the marked pressor effect of large doses of epinephrine.

### **Dosage and Administration**

Subcutaneously or intramuscularly – 0.2 to 1 mL (mg). Start with a small dose and increase if required.

**Note:** The subcutaneous is the preferred route of administration. If given intramuscularly, injection into the buttocks should be avoided.

### **Hypersensitivity Reactions**

For bronchial asthma and certain allergic manifestations, e.g., angioedema, urticaria, serum sickness, anaphylactic shock, use epinephrine subcutaneously. The adult intravenous dose for hypersensitivity reactions or to relieve bronchospasm usually ranges from 0.1 to 0.25 mg injected slowly. Neonates may be given a dose of 0.01 mg per kg of body weight; for the infant 0.05 mg is an adequate initial dose and this may be repeated at 20 to 30 minute intervals in the management of asthma attacks.

### **Cardiac Resuscitation**

A dose of 0.5 mL (0.5 mg) diluted to 10 mL with sodium chloride injection can be administered intravenously or intracardially to restore myocardial contractility. Intracardiac injection should only be administered by personnel well trained in the technique, if there has not been sufficient time to establish an intravenous route. External cardiac massage should follow intracardial administration to permit the drug to enter coronary circulation. The drug should be used secondarily to unsuccessful attempts with physical or electromechanical methods.

### **Ophthalmologic Use**

Ophthalmologic use (for producing conjunctival decongestion, to control hemorrhage, produce mydriasis and reduce intraocular pressure) – use a concentration of 1:10,000 (0.1 mg/mL) to 1:1000 (1 mg/mL).

**Regional Anesthesia**

A final concentration of 1:200,000 of epinephrine injection is recommended for infiltration injection, nerve block, caudal or other epidural blocks. From 0.3 to 0.4 mg of epinephrine (0.3 to 0.4 mL of 1:1000 solution) may be mixed with spinal anesthetic agents. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. (See PRECAUTIONS.)

**How Supplied** Epinephrine Injection, USP 1:1000 (1 mg/mL) is supplied in a 1 mL ampul single-dose container (NDC 0409-7241-61).

Store at 20 to 25°C (68 to 77°F). [See USP Controlled Room Temperature.]

Protect from light.

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Printed in USA EN-1927

Hospira, Inc., Lake Forest, IL 60045 USA

**Epinephrine Pack Label**

1 DEC 2012

961203A

RL-2361 (11/07)



1 mL

NDC 0409-7241-61



**Epinephrine**  
**Injection, USP**  
**1:1000**  
**(1 mg/mL)**  
**SQ/IM**

Hospira, Inc., Lake Forest, IL   
60045 USA **Rx only** Hospira

**LIDOCAINE HYDROCHLORIDE (lidocaine hydrochloride anhydrous) injection, solution**  
**AQUEOUS SOLUTIONS FOR INFILTRATION**  
**AND NERVE BLOCK**

**Ampul**

**Plastic Multiple-dose Fliptop Vial**

**Glass Teartop Vial**

Rx only

**DESCRIPTION**

Lidocaine Hydrochloride Injection, USP is a sterile, nonpyrogenic solution of lidocaine hydrochloride in water for injection for parenteral administration in various concentrations with characteristics as follows:

<b>Concentration</b>	<b>0.5%</b>	<b>1%</b>	<b>1.5%</b>	<b>2%</b>
mg/mL lidocaine HCl (anhyd.)	5	10	15	20

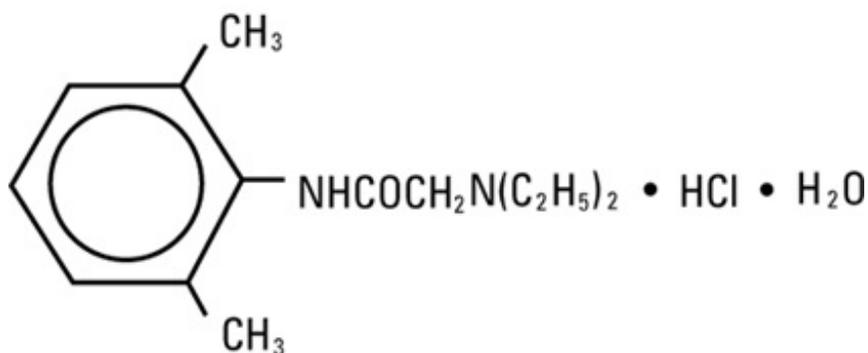
mg/mL sodium chloride      8      7      6.5      6

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Multiple-dose vials contain 0.1% of methylparaben added as preservative. May contain sodium hydroxide and/or hydrochloric acid for pH adjustment. The pH is 6.5 (5.0 to 7.0). See HOW SUPPLIED section for various sizes and strengths.

Lidocaine is a local anesthetic of the amide type.

Lidocaine Hydrochloride, USP is chemically designated 2-(diethylamino)-N-(2,6-dimethylphenyl)-acetamide monohydrochloride monohydrate, a white powder freely soluble in water. The molecular weight is 288.82. It has the following structural formula:



The semi-rigid vial used for the plastic vials is fabricated from a specially formulated polyolefin. It is a copolymer of ethylene and propylene. The safety of the plastic has been confirmed by tests in animals according to USP biological standards for plastic containers. The container requires no vapor barrier to maintain the proper drug concentration.

### 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. With central neural blockade these changes may be attributable to block of autonomic fibers, a direct depressant effect of the local anesthetic agent on various components of the cardiovascular system and/or the beta-adrenergic receptor stimulating action of epinephrine when present. The net effect is normally a modest hypotension when the recommended dosages are not exceeded.

**Pharmacokinetics and metabolism:** Information derived from diverse formulations, concentrations and usages reveals that lidocaine is completely absorbed following parenteral administration, its rate of absorption depending, for example, upon various factors such as the site of administration and the presence or absence of a vasoconstrictor agent. Except for intravascular administration, the highest blood levels are obtained following intercostal nerve block and the lowest after subcutaneous administration.

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

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

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 elimination half-life of lidocaine following an intravenous bolus injection 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 levels above 6.0 mcg free base per mL. In the rhesus monkey arterial blood levels of 18-21 mcg/mL have been shown to be threshold for convulsive activity.

## **INDICATIONS AND USAGE**

Lidocaine Hydrochloride Injection, USP is indicated for production of local or regional anesthesia by infiltration techniques such as percutaneous injection and intravenous regional anesthesia by peripheral nerve block techniques such as brachial plexus and intercostal and by central neural techniques such as lumbar and caudal epidural blocks, when the accepted procedures for these techniques as described in standard textbooks are observed.

## **CONTRAINDICATIONS**

Lidocaine is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type.

## **WARNINGS**

**LIDOCAINE HYDROCHLORIDE INJECTION, FOR INFILTRATION AND NERVE BLOCK, SHOULD BE EMPLOYED ONLY BY CLINICIANS WHO ARE WELL VERSED IN DIAGNOSIS AND MANAGEMENT OF DOSE-RELATED TOXICITY AND OTHER ACUTE EMERGENCIES THAT MIGHT ARISE FROM THE BLOCK TO BE EMPLOYED AND THEN ONLY AFTER ENSURING THE IMMEDIATE AVAILABILITY OF OXYGEN, OTHER RESUSCITATIVE DRUGS, CARDIOPULMONARY EQUIPMENT, AND THE PERSONNEL NEEDED FOR PROPER MANAGEMENT OF TOXIC REACTIONS AND RELATED EMERGENCIES (See also ADVERSE REACTIONS and PRECAUTIONS). DELAY IN PROPER MANAGEMENT OF DOSE-RELATED TOXICITY, UNDERVENTILATION FROM ANY CAUSE AND/OR ALTERED SENSITIVITY MAY LEAD TO THE DEVELOPMENT OF ACIDOSIS, CARDIAC ARREST AND, POSSIBLY, DEATH.**

Intra-articular infusions of local anesthetics following arthroscopic and other surgical procedures is an unapproved use, and there have been post-marketing reports of chondrolysis in patients receiving such infusions. The majority of reported cases of chondrolysis have involved the shoulder joint; cases of gleno-humeral chondrolysis have been described in pediatric and adult patients following intra-articular infusions of local anesthetics with and without epinephrine for periods of 48 to 72 hours. There is insufficient information to determine whether shorter infusion periods are not associated with these findings. The time of onset of symptoms, such as joint pain, stiffness and loss of motion can be variable, but may begin as early as the 2nd month after surgery. Currently, there is no effective treatment for chondrolysis; patients who experienced chondrolysis have required additional diagnostic and therapeutic procedures and some required arthroplasty or shoulder replacement.

To avoid intravascular injection, aspiration should be performed before the local anesthetic solution is injected. The needle must be repositioned until no return of blood can be elicited by aspiration. Note, however, that the absence of blood in the syringe does not guarantee that intravascular injection has

been avoided.

Local anesthetic solutions containing antimicrobial preservatives (e.g., methylparaben) should not be used for epidural or spinal anesthesia because the safety of these agents has not been established with regard to intrathecal injection, either intentional or accidental.

### **PRECAUTIONS**General:

The safety and effectiveness of lidocaine depend on proper dosage, correct technique, adequate precautions, and readiness for emergencies. Standard textbooks should be consulted for specific techniques and precautions for various regional anesthetic procedures.

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. Syringe aspirations should also be performed before and during each supplemental injection when using indwelling catheter techniques. During the administration of epidural anesthesia, it is recommended that a test dose be administered initially and that the patient be monitored for central nervous system toxicity and cardiovascular toxicity, as well as for signs of unintended intrathecal administration before proceeding. When clinical conditions permit, consideration should be given to employing local anesthetic solutions that contain epinephrine for the test dose because circulatory changes compatible with epinephrine may also serve as a warning sign of unintended intravascular injection. An intravascular injection is still possible even if aspirations for blood are negative. 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 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 condition. Lidocaine should also be used with caution in patients with severe shock or heart block. Lumbar and caudal epidural anesthesia should be used with extreme caution in persons with the following conditions: existing neurological disease, spinal deformities, septicemia and severe hypertension.

Local anesthetic solutions containing a vasoconstrictor should be used cautiously and in carefully circumscribed quantities in areas of the body supplied by end arteries or having otherwise compromised blood supply. Patients with peripheral vascular disease and those with hypertensive vascular disease may exhibit exaggerated vasoconstrictor response. Ischemic injury or necrosis may result. Preparations containing a vasoconstrictor should be used with caution in patients during or following the administration of potent general anesthetic agents, since cardiac arrhythmias may occur under such conditions.

Careful and constant monitoring of cardiovascular and respiratory (adequacy of ventilation) vital signs and the patient's state of consciousness should be accomplished after each local anesthetic injection. It should be kept in mind at such times that restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors, depression or drowsiness may be early warning signs of central nervous system toxicity.

Since amide-type local anesthetics are metabolized by the liver, lidocaine should be used with caution in patients with hepatic disease. Patients with severe hepatic disease, because of their inability to metabolize local anesthetics normally, are at greater risk of developing toxic plasma concentrations. Lidocaine should also be used with caution in patients with impaired cardiovascular function since they may be less able to compensate for functional changes associated with the prolongation of A-V conduction produced by these drugs. 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 the management of malignant hyperthermia 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).

Proper tourniquet technique, as described in publications and standard textbooks, is essential in the performance of intravenous regional anesthesia. Solutions containing epinephrine or other vasoconstrictors should not be used for this technique.

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

**Use in the Head and Neck Area:** Small doses of local anesthetics injected into the head and neck area, including retrobulbar, dental and stellate ganglion blocks, may produce adverse reactions similar to systemic toxicity seen with unintentional intravascular injections of larger doses. Confusion, convulsions, respiratory depression and/or respiratory arrest and cardiovascular stimulation or depression have been reported. These reactions may be due to intra-arterial injections of the local anesthetic with retrograde flow to the cerebral circulation. Patients receiving these blocks should have their circulation and respiration monitored and be constantly observed. Resuscitative equipment and personnel for treating adverse reactions should be immediately available. Dosage recommendations should not be exceeded. (See DOSAGE AND ADMINISTRATION).

Information for Patients:

When appropriate, patients should be informed in advance that they may experience temporary loss of sensation and motor activity, usually in the lower half of the body following proper administration of epidural anesthesia.

Clinically Significant Drug Interactions:

The administration of local anesthetic solutions containing epinephrine or norepinephrine to patients receiving monoamine oxidase inhibitors or tricyclic antidepressants may produce severe prolonged hypertension.

Phenothiazines and butyrophenones may reduce or reverse the pressor effect of epinephrine.

Concurrent use of these agents should generally be avoided. In situations when concurrent therapy is necessary, careful patient monitoring is essential.

Concurrent administration of vasopressor drugs (for the treatment of hypotension related to obstetric blocks) and ergot-type oxytocic drugs may cause severe persistent hypertension or cerebrovascular accidents.

Drug Laboratory Test Interactions:

The intramuscular injection of lidocaine may result in an increase in creatine phosphokinase levels. Thus, the use of this enzyme determination without isoenzyme separation as a diagnostic test for the presence of acute myocardial infarction may be compromised by the intramuscular injection of lidocaine.

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.

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:

Local anesthetics rapidly cross the placenta and when used for epidural, paracervical, pudendal or

caudal block anesthesia, can cause varying degrees of maternal, fetal and neonatal toxicity (See CLINICAL PHARMACOLOGY—**Pharmacokinetics**). The potential for toxicity depends upon the procedure performed, the type and amount of drug used, and the technique of drug administration. Adverse reactions in the parturient, fetus and neonate involve alterations of the central nervous system peripheral vascular tone and cardiac function.

Maternal hypotension has resulted from regional anesthesia. Local anesthetics produce vasodilation by blocking sympathetic nerves. Elevating the patient's legs and positioning her on her left side will help prevent decreases in blood pressure. The fetal heart rate also should be monitored continuously, and electronic fetal monitoring is highly advisable.

Epidural, spinal, paracervical, or pudendal anesthesia may alter the forces of parturition through changes in uterine contractility or maternal expulsive efforts. In one study, paracervical block anesthesia was associated with a decrease in the mean duration of first stage labor and facilitation of cervical dilation. However, spinal and epidural anesthesia have also been reported to prolong the second stage of labor by removing the parturient's reflex urge to bear down or by interfering with motor function. The use of obstetrical anesthesia may increase the need for forceps assistance.

The use of some local anesthetic drug products during labor and delivery may be followed by diminished muscle strength and tone for the first day or two of life. The long-term significance of these observations is unknown. Fetal bradycardia may occur in 20 to 30 percent of patients receiving paracervical nerve block anesthesia with the amide-type local anesthetics and may be associated with fetal acidosis. Fetal heart rate should always be monitored during paracervical anesthesia. The physician should weigh the possible advantages against risks when considering paracervical block in prematurity, toxemia of pregnancy and fetal distress. Careful adherence to recommended dosage is of the utmost importance in obstetrical paracervical block. Failure to achieve adequate analgesia with recommended doses should arouse suspicion of intravascular or fetal intracranial injection. Cases compatible with unintended fetal intracranial injection of local anesthetic solution have been reported following intended paracervical or pudendal block or both. Babies so affected present with unexplained neonatal depression at birth, which correlates with high local anesthetic serum levels, and often manifest seizures within six hours. Prompt use of supportive measures combined with forced urinary excretion of the local anesthetic has been used successfully to manage this complication.

Case reports of maternal convulsions and cardiovascular collapse following use of some local anesthetics for paracervical block in early pregnancy (as anesthesia for elective abortion) suggest that systemic absorption under these circumstances may be rapid. The recommended maximum dose of each drug should not be exceeded. Injection should be made slowly and with frequent aspiration. Allow a 5-minute interval between sides.

**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:**

Dosages in pediatric patients should be reduced, commensurate with age, body weight and physical condition. See DOSAGE AND ADMINISTRATION.

## **ADVERSE REACTIONS**

**Systemic:** 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, rapid absorption or inadvertent intravascular injection, 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 local anesthetic agents or to the methylparaben used as a preservative in multiple dose vials. 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.

**Neurologic:** The incidences of adverse reactions associated with the use of local anesthetics may be related to the total dose of local anesthetic administered and are also dependent upon the particular drug used, the route of administration and the physical status of the patient. In a prospective review of 10,440 patients who received lidocaine for spinal anesthesia, the incidences of adverse reactions were reported to be about 3 percent each for positional headaches, hypotension and backache; 2 percent for shivering; and less than 1 percent each for peripheral nerve symptoms, nausea, respiratory inadequacy and double vision. Many of these observations may be related to local anesthetic techniques, with or without a contribution from the local anesthetic.

In the practice of caudal or lumbar epidural block, occasional unintentional penetration of the subarachnoid space by the catheter may occur. Subsequent adverse effects may depend partially on the amount of drug administered subdurally.

These may include spinal block of varying magnitude (including total spinal block), hypotension secondary to spinal block, loss of bladder and bowel control, and loss of perineal sensation and sexual function. Persistent motor, sensory and/or autonomic (sphincter control) deficit of some lower spinal segments with slow recovery (several months) or incomplete recovery have been reported in rare instances when caudal or lumbar epidural block has been attempted. Backache and headache have also been noted following use of these anesthetic procedures.

There have been reported cases of permanent injury to extraocular muscles requiring surgical repair following retrobulbar administration.

## **OVERDOSAGE**

Acute emergencies from local anesthetics are generally related to high plasma levels encountered during therapeutic use of local anesthetics or to unintended subarachnoid injection of local anesthetic solution (see ADVERSE REACTIONS, WARNINGS and PRECAUTIONS).

**Management of Local Anesthetic Emergencies:** The first consideration is prevention, best accomplished by careful monitoring of cardiovascular and respiratory vital signs and the patient's state of consciousness after each local anesthetic injection. At the first sign of change, oxygen should be administered.

The first step in the management of convulsions, as well as underventilation or apnea due to unintended subarachnoid injection of drug solution, 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. Underventilation or apnea due to unintentional subarachnoid injection of local anesthetic solution may produce these same signs and also lead to cardiac arrest if ventilatory support is not instituted. If cardiac arrest should occur standard cardiopulmonary resuscitative measures should be instituted.

Endotracheal intubation, employing drugs and techniques familiar to the clinician, may be indicated, after initial administration of oxygen by mask, if difficulty is encountered in the maintenance of a patent airway or if prolonged ventilatory support (assisted or controlled) is indicated.

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

The oral LD<sub>50</sub> of lidocaine HCl in non-fasted female rats is 459 (346–773) mg/kg (as the salt) and 214 (159–324) mg/kg (as the salt) in fasted female rats.

## **DOSAGE AND ADMINISTRATION**

Table 1 (Recommended Dosages) summarizes the recommended volumes and concentrations of Lidocaine Hydrochloride Injection, USP for various types of anesthetic procedures. The dosages suggested in this table are for normal healthy adults and refer to the use of epinephrine-free solutions. When larger volumes are required only solutions containing epinephrine should be used, except in those cases where vasopressor drugs may be contraindicated.

There have been adverse event reports of chondrolysis in patients receiving intra-articular infusions of local anesthetics following arthroscopic and other surgical procedures. Lidocaine is not approved for this use (see WARNINGS and DOSAGE AND ADMINISTRATION).

These recommended doses serve only as a guide to the amount of anesthetic required for most routine procedures. The actual volumes and concentrations to be used depend on a number of factors such as type and extent of surgical procedure, depth of anesthesia and degree of muscular relaxation required, duration of anesthesia required, and the physical condition of the patient. In all cases the lowest concentration and smallest dose that will produce the desired result should be given. Dosages should be reduced for children and for elderly and debilitated patients and patients with cardiac and/or liver disease.

The onset of anesthesia, the duration of anesthesia and the degree of muscular relaxation are proportional to the volume and concentration (i.e., total dose) of local anesthetic used. Thus, an increase in volume and concentration of Lidocaine Hydrochloride Injection will decrease the onset of anesthesia, prolong the duration of anesthesia, provide a greater degree of muscular relaxation and increase the segmental spread of anesthesia. However, increasing the volume and concentration of Lidocaine Hydrochloride Injection may result in a more profound fall in blood pressure when used in epidural anesthesia. Although the incidence of side effects with lidocaine is quite low, caution should be exercised when employing large volumes and concentrations, since the incidence of side effects is directly proportional to the total dose of local anesthetic agent injected.

For intravenous regional anesthesia, only the 50 mL single-dose vial containing 0.5% Lidocaine Hydrochloride Injection, USP should be used.

### **Epidural Anesthesia**

For epidural anesthesia, only the following available specific products of Lidocaine Hydrochloride Injection by Hospira are recommended:

- 1%. . . . . 30 mL single-dose teartop vials
- 1.5%. . . . . 20 mL single-dose ampuls

2%..... 10 mL single-dose ampuls

Although these solutions are intended specifically for epidural anesthesia, they may also be used for infiltration and peripheral nerve block provided they are employed as single dose units. These solutions contain no bacteriostatic agent. In epidural anesthesia, the dosage varies with the number of dermatomes to be anesthetized (generally 2–3 mL of the indicated concentration per dermatome).

**Caudal and Lumbar Epidural Block:** As a precaution against the adverse experiences sometimes observed following unintentional penetration of the subarachnoid space, a test dose such as 2–3 mL of 1.5% lidocaine hydrochloride should be administered at least 5 minutes prior to injecting the total volume required for a lumbar or caudal epidural block. The test dose should be repeated if the patient is moved in a manner that may have displaced the catheter. Epinephrine, if contained in the test dose (10–15 mcg have been suggested), may serve as a warning of unintentional intravascular injection. If injected into a blood vessel, this amount of epinephrine is likely to produce a transient "epinephrine response" within 45 seconds, consisting of an increase in heart rate and systolic blood pressure, circumoral pallor, palpitations and nervousness in the unsedated patient. The sedated patient may exhibit only a pulse rate increase of 20 or more beats per minute for 15 or more seconds. Patients on beta-blockers may not manifest changes in heart rate, but blood pressure monitoring can detect an evanescent rise in systolic blood pressure. Adequate time should be allowed for onset of anesthesia after administration of each test dose. The rapid injection of a large volume of Lidocaine Hydrochloride Injection through the catheter should be avoided, and, when feasible, fractional doses should be administered.

In the event of the known injection of a large volume of local anesthetic solutions into the subarachnoid space, after suitable resuscitation and if the catheter is in place, consider attempting the recovery of drug by draining a moderate amount of cerebrospinal fluid (such as 10 mL) through the epidural catheter.

### Maximum Recommended Dosages

**NOTE: The products accompanying this insert do not contain epinephrine.**

**Adults:** For normal healthy adults, the individual maximum recommended dose of lidocaine HCl with epinephrine should not exceed 7 mg/kg (3.5 mg/lb) of body weight and in general it is recommended that the maximum total dose not exceed 500 mg. When used without epinephrine, the maximum individual dose should not exceed 4.5 mg/kg (2 mg/lb) of body weight and in general it is recommended that the maximum total dose does not exceed 300 mg. For continuous epidural or caudal anesthesia, the maximum recommended dosage should not be administered at intervals of less than 90 minutes. When continuous lumbar or caudal epidural anesthesia is used for non-obstetrical procedures, more drug may be administered if required to produce adequate anesthesia.

The maximum recommended dose per 90 minute period of lidocaine hydrochloride for paracervical block in obstetrical patients and non-obstetrical patients is 200 mg total. One-half of the total dose is usually administered to each side. Inject slowly five minutes between sides. (See also discussion of paracervical block in PRECAUTIONS).

For intravenous regional anesthesia, the dose administered should not exceed 4 mg/kg in adults.

**Children:** It is difficult to recommend a maximum dose of any drug for children, since this varies as a function of age and weight. For children over 3 years of age who have a normal lean body mass and normal body development, the maximum dose is determined by the child's age and weight. For example, in a child of 5 years weighing 50 lbs., the dose of lidocaine HCl should not exceed 75 — 100 mg (1.5 — 2 mg/lb). The use of even more dilute solutions (i.e., 0.25 — 0.5%) and total dosages not to exceed 3 mg/kg (1.4 mg/lb) are recommended for induction of intravenous regional anesthesia in children.

In order to guard against systemic toxicity, the lowest effective concentration and lowest effective dose should be used at all times. In some cases it will be necessary to dilute available concentrations with 0.9% sodium chloride injection in order to obtain the required final concentration.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever the solution and container permit. Solutions that are discolored and/or contain particulate matter should not be used.

**Table 1**  
**Recommended Dosages of Lidocaine Hydrochloride Injection, USP for Various Anesthetic Procedures in Normal Healthy Adults**

Procedure	Lidocaine Hydrochloride Injection, USP (without Epinephrine)	
	Conc. (%)	Vol. (mL) Total Dose (mg)
Infiltration		
Percutaneous	0.5 or 1.0	1–60 5–300
Intravenous Regional	0.5	10–60 50–300
Peripheral Nerve Blocks, e.g.		
Brachial	1.5	15–20 225–300
Dental	2.0	1–5 20–100
Intercostal	1.0	3 30
Paravertebral	1.0	3–5 30–50
Pudendal (each side)	1.0	10 100
Paracervical Obstetrical Analgesia (each side)	1.0	10 100
Sympathetic Nerve Blocks, e.g.		
Cervical (stellate ganglion)	1.0	5 50
Lumbar	1.0	5–10 50–100
Central Neural Blocks		
Epidural*		
Thoracic	1.0	20–30 200–300
Lumbar		
Analgesia	1.0	25–30 250–300
Anesthesia	1.5	15–20 225–300
	2.0	10–15 200–300
Caudal		
Obstetrical Analgesia	1.0	20–30 200–300
Surgical Anesthesia	1.5	15–20 225–300

\*Dose determined by number of dermatomes to be anesthetized (2 to 3 mL/dermatome).

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THE ABOVE SUGGESTED CONCENTRATIONS AND VOLUMES SERVE ONLY AS A GUIDE. OTHER VOLUMES AND CONCENTRATIONS MAY BE USED PROVIDED THE TOTAL MAXIMUM RECOMMENDED DOSE IS NOT EXCEEDED.

**Sterilization, Storage and Technical Procedures:** Disinfecting agents containing heavy metals, which cause release of respective ions (mercury, zinc, copper, etc.) should not be used for skin or mucous membrane disinfection as they have been related to incidence of swelling and edema. When chemical disinfection of multi-dose vials is desired, either isopropyl alcohol (91%) or 70% ethyl alcohol is recommended. Many commercially available brands of rubbing alcohol, as well as solutions of ethyl alcohol not of USP grade, contain denaturants which are injurious to rubber and, therefore, are not to be used. It is recommended that chemical disinfection be accomplished by wiping the vial stopper thoroughly with cotton or gauze that has been moistened with the recommended alcohol just prior to use.

### HOW SUPPLIED

Lidocaine Hydrochloride Injection, USP is supplied as follows:

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NDC	Container	Concentration	Size	Total (mg)
<b>Single-dose:</b>				
0409-4278-01	Glass Teartop Vial	0.5% (5 mg/mL)	50 mL	250
0409-4713-01	Glass Ampul	1% (10 mg/mL)	2 mL (bulk – 400 units)	20
0409-4713-02	Glass Ampul	1% (10 mg/mL)	5 mL	50
0409-4713-05	Glass Ampul	1% (10 mg/mL)	5 mL (bulk – 400 units)	50
0409-4713-20	Glass Ampul	1% (10 mg/mL)	20 mL	200
0409-4713-32	Glass Ampul	1% (10 mg/mL)	2 mL	20
0409-4713-62	Glass Ampul	1% (10 mg/mL)	2 mL (bulk – 800 units)	20
0409-4713-65	Glass Ampul	1% (10 mg/mL)	5 mL (bulk – 800 units)	50
0409-4279-02	Glass Teartop Vial	1% (10 mg/mL)	30 mL	300
0409-4270-01	Sterile Glass Teartop Vial	1% (10 mg/mL)	30 mL	300
0409-4776-01	Glass Ampul	1.5% (15 mg/mL)	20 mL	300
0409-4056-01	Sterile Glass Ampul	1.5% (15 mg/mL)	20 mL	300
0409-4282-01	Glass Ampul	2% (20 mg/mL)	2 mL	40
0409-4282-02	Glass Ampul	2% (20 mg/mL)	10 mL	200
<b>Multiple-dose:</b>				
0409-4275-01	Plastic Fliptop Vial	0.5% (5 mg/mL)	50 mL	250
0409-4276-01	Plastic Fliptop Vial	1% (10 mg/mL)	20 mL	200
0409-4276-02	Plastic Fliptop Vial	1% (10 mg/mL)	50 mL	500
0409-4277-01	Plastic Fliptop Vial	2% (20 mg/mL)	20 mL	400
0409-4277-02	Plastic Fliptop Vial	2% (20 mg/mL)	50 mL	1000

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Single-dose products are preservative-free.

Store at 20 to 25°C (68 to 77°F). [See USP Controlled Room Temperature.]

Lidocaine Hydrochloride Injection, USP solutions packaged in ampuls and glass teartop vials may be autoclaved one time only. Autoclave at 15 pounds pressure, 121°C (250°F) for 15 minutes. **DO NOT AUTOCLAVE PRODUCT IN PLASTIC VIALS.**

Revised: February, 2010

Printed in USA

EN-2421

Hospira, Inc., Lake Forest, IL 60045 USA

**Lidocaine Pack Label**

EXP 1 SEP 2013

LOT 931153A

RL-1467 (9/05)



5 mL

NDC 0409-4713-65

**Preservative-Free**

<b>1%</b>	<b>LIDOCAINE HCl</b> Injection, USP <b>10 mg/mL</b>
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**Rx** only

**HOSPIRA, INC.**



1	1 in 1 PACKAGE, COMBINATION	
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### Quantity of Parts

Part #	Package Quantity	Total Product Quantity
Part 1	1 AMPULE	1 mL
Part 2	1 AMPULE	5 mL

### Part 1 of 2

#### EPINEPHRINE

epinephrine injection, solution

### Product Information

Item Code (Source)	NDC:0409-7241
Route of Administration	EPIDURAL, INTRASPINAL, INTRATHECAL

### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
EPINEPHRINE (UNII: YKH834O4BH) (EPINEPHRINE - UNII:YKH834O4BH)	EPINEPHRINE	1 mg in 1 mL

### Inactive Ingredients

Ingredient Name	Strength
SODIUM CHLORIDE (UNII: 451W47IQ8X)	9 mg in 1 mL
SODIUM METABISULFITE (UNII: 4VON5FNS3C)	

### Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0409-7241-61	1 mL in 1 AMPULE		

### Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
unapproved drug other		05/03/2010	

### Part 2 of 2

#### LIDOCAINE HYDROCHLORIDE

lidocaine hydrochloride anhydrous injection, solution

**Product Information**

<b>Item Code (Source)</b>	NDC:0409-4713
<b>Route of Administration</b>	INFILTRATION, SUBCUTANEOUS

**Active Ingredient/Active Moiety**

<b>Ingredient Name</b>	<b>Basis of Strength</b>	<b>Strength</b>
<b>LIDOCAINE HYDROCHLORIDE ANHYDROUS</b> (UNII: EC2CNF7XFP) (Lidocaine - UNII:98PI200987)	LIDOCAINE HYDROCHLORIDE ANHYDROUS	10 mg in 1 mL

**Inactive Ingredients**

<b>Ingredient Name</b>	<b>Strength</b>
<b>Sodium Chloride</b> (UNII: 451W47IQ8X)	7 mg in 1 mL
<b>Water</b> (UNII: 059QF0KO0R)	
<b>Sodium Hydroxide</b> (UNII: 55X04QC32I)	
<b>Hydrochloric Acid</b> (UNII: QTT17582CB)	

**Packaging**

#	<b>Item Code</b>	<b>Package Description</b>	<b>Marketing Start Date</b>	<b>Marketing End Date</b>
1	NDC:0409-4713-65	5 mL in 1 AMPULE		

**Marketing Information**

<b>Marketing Category</b>	<b>Application Number or Monograph Citation</b>	<b>Marketing Start Date</b>	<b>Marketing End Date</b>
ANDA	ANDA080408	03/30/2010	

**Marketing Information**

<b>Marketing Category</b>	<b>Application Number or Monograph Citation</b>	<b>Marketing Start Date</b>	<b>Marketing End Date</b>
premarket notification	K965017	09/28/2012	

**Labeler** - Smiths Medical ASD, Inc. (137835299)**Establishment**

<b>Name</b>	<b>Address</b>	<b>ID/FEI</b>	<b>Business Operations</b>
Smiths Medical ASD, Inc.		137835299	relabel, manufacture

**Establishment**

<b>Name</b>	<b>Address</b>	<b>ID/FEI</b>	<b>Business Operations</b>
Hospira, Inc.		030606222	manufacture

