DESCRIPTION:
Xylocaine (lidocaine HCl) Injections are sterile, nonpyrogenic, aqueous solutions of lidocaine HCl, containing 1 mg methylparaben as an antiseptic preservative. Xylocaine with Paraben Free (MPF) is an isotonic solution containing sodium chloride. Xylocaine solutions contain lidocaine HCl, which is chemically designated as acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl)-monohydrochloride and has the molecular wt. 270.8. Lidocaine HCl (C8H9NO2 • HCl) has the following structural formula:

CH3
H
O
N
CH2
H

Epinephrine is (1) -3, 4-Dihydroxy-a-(methylamino) methyl benzylic alcohol and has the molecular wt. 183.21. Epinephrine (C9H13NO3) has the following structural formula:

CH3
H
O
N
CH2
H

Dosage forms listed as Xylocaine-MPF indicate single dose solutions that are Methyl Paraben Free (MPF).

Xylocaine MPF is a sterile, nonpyrogenic, isotonic solution containing sodium chloride. Xylocaine in multiple dose vials: Each mL also contains 1 mg methylparaben as an antiseptic preservative. The pH of these solutions is adjusted to approximately 6.5 (5.0 to 7.0), with sodium hydroxide and/or hydrochloric acid.

Xylocaine MPF with Epinephrine is a sterile, nonpyrogenic, isotonic solution containing sodium chloride. Each mL contains lidocaine hydrochloride and epinephrine, with 0.5 mg sodium metabisulfite, a sulfite that may cause sensitivity in some individuals. The pH of these solutions is adjusted to approximately 4.5 (3.3 to 5.5) with sodium hydroxide and/or hydrochloric acid. Filled under nitrogen.

CLINICAL PHARMACOLOGY:
Mechanism of Action
Lidocaine HCl stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses thereby effecting local anesthetic action.

Pharmacokinetics and Metabolism
Information derived from diverse formulations, concentrations and usages reveals that lidocaine HCl 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 intravenous administration, the highest blood levels are obtained following intracostal nerve block and the lowest after subcutaneous administration.

The plasma binding of lidocaine HCl 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 HCl is protein bound. Binding is also dependent on the plasma concentration of the alpha-1-acid glycoprotein.

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

Lidocaine HCl 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 monoethylglycinexilidide and glycinexilidide.

The pharmacological/toxicological actions of these metabolites are similar to, but less potent than, those of lidocaine HCl. Approximately 90% of lidocaine HCl 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-dimethylamino.

The elimination half-life of lidocaine HCl following an intravenous bolus injection is typically 1.5 to 2 hours. Because of the rapid rate at which lidocaine HCl is metabolized, any condition that affects liver function may alter lidocaine HCl kinetics. The half-life may be prolonged two-fold or more in patients with liver dysfunction. Renal dysfunction does not affect lidocaine HCl 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 HCl required to produce overt systemic effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6 mcg free base per mL. In the rhesus monkey arterial blood levels of 18 to 21 mcg/mL have been shown to be threshold for convulsive activity.

INDICATIONS AND USAGE:
Xylocaine (lidocaine HCl) Injections are 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 HCl is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type.

WARNINGS:
XYLOCANE INJECTIONS 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 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 RESULT IN THE DEVELOPMENT OF ACIDOSIS, CARDIAC ARREST AND, POSSIBLY, DEATH.

Intra-arterial 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-arterial 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 associated with these findings. The time of onset of symptoms, such as joint pain, stiffness and loss of motion can be variable, but may be 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 shoul-der replacement.

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

Local anesthetic solutions containing anti- microbial preservatives (eg, 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.

Xylocaine with epinephrine solutions contain sodium metabisulfite, a sulfite that may cause
allergic-type reactions including anaphylactic symptoms and life-threatening or less severe allergic reactions which may occur in certain susceptible people. The overall prevalence of sulfa-like sensitivity in the general population is unknown and probably low. Sulfisoxazole is seen more frequently in asthmatic than in non-asthmatic people.

PRECAUTIONS:

General
The safety and effectiveness of lidocaine HCl injection, USP, Xylocaine® Rx only isotonic solution containing sodium chloride. Xylocaine MPF is a sterile, nonpyrogenic, aqueous solutions that contain are excreted by the kidneys. Biotransformation. At concentrations of 1 to 4 mcg of free factors such as the site of administration and parenteral administration, its rate of absorp-

Lidocaine HCl (C14H22N2 is protein bound. Binding is also dependent on liver, and metabolites and unchanged drug is protein bound. Binding is also dependent on

In the Head and Neck Area
Small doses of local anesthetics injected into the head and neck include dental and peripheral den
tal and stellate ganglion blocks, may produce adverse reactions and systemic toxicity, seen with unintentional intravascular injections of larger doses. Confusion, convulsions, respira
tory depression and/or respiratory arrest, and cardiovascular stimulation or depression have been reported. These reactions may be due to intra-arterial injection of the local anesthetic with retrograde flow to the cerebral circulation. Patients receiving these blocks should have their cardiovascular system continuously monitored and be constantly observed. Resuscitative equip

Information for Patients
When appropriate 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 anesthe

Clinically Significant Drug Interactions
The administration of local anesthetic solutions containing epinephrine or a vasoepinephrine to patients receiving monoamine oxidase inhibitors or tricyclic antidepressants may produce severe, prolonged hypertensive and tachycardic episodes. Phenothiazines and butyrophenones may reduce or reverse the pressor effect of epinephrine. Concurrent use of these agents should gener

Drug/Laboratory Test Interactions
The intramuscular injection of lidocaine HCl may result in an increase in creatine phosphokinase levels. However, this enzyme determination, without isozyme separation, as a diagnostic sign of myocardial infarction may be compromised by the intramuscular injection of lidocaine HCl. Studies of lidocaine HCl in animals to evaluate the carinoic 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 that are 10 times the human dose and have revealed no evidence of harm to the fetus caused by lidocaine HCl. There are, however, no adequate and well-controlled studies in pregnant women. Animal reproduction studies are not always predictive of human response. General considerations should be given to this factor before administering lidocaine HCl 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 therapeutic levels for local, pudendal or caudal block anesthesia, can cause varying degrees of maternal, fetal and neonatal toxicity (see CLINICAL PHARMACOLOGY, Pharma
cinetics and Metabolism). The potential for toxicity depends upon the procedure performed, the technique used, the type 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 transient maternal hypotension. 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 recommended.

Epidual, spinal, paracervical, or pudendal anesthesia may alter the forces of parturition through changes in uterine contractility and maternal efforts. In some cases, 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 and paracervical block anesthesia may be associated with fetal acidosis. Fetal heart rate should always be monitored during regional anesthesia. The physician should weigh the possible advantages against risks when considering a paracervical block in the presence of toxemia of pregnancy, and fetal distress. Careful adherence to recommended dosage is of the utmost importance in obstetric local anesthetic blocks. Failure to achieve adequate analge

Asthma is more common in asthmatic than in non-asthmatic people. Pregnancy (as elective abort

It is not known whether this drug is excreted in human milk. Caution is advised when lidocaine HCl is administered to a nurs

Pediatric Use
Doses in children should be reduced, commensurate with age, body weight and physical condition, see DOSAGE AND ADMINISTRATION.

ADVERSE REACTIONS:

Systemic
Adverse experiences following the administra
tion of lidocaine HCl are similar in nature to those observed with other amide local anes

Central Nervous System
CNS manifestations are excitation and/or depression and may include lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tingling, blurred or double vision, loss of sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest. The excitation manifestations may be very brief or may not occur at all, in which case the first manifesta

tion of toxicity may be drowsiness merging into unconsciousness and respiratory arrest.
Drowsiness following the administration of lidocaine HCl 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, in severe cases, cardiogenic collapse, which may lead to cardiac arrest.

**Allergic**

Allergic reactions are characterized by cutaneous lesions, urticaria, edema or anaphylactoid reaction. The incidence of these reactions may occur as a result of sensitivity either to local anesthetic agents or to the methyprylon employed as an adjunct intravenously. Allergic reactions as a result of sensitivity to lidocaine HCl are rare, but when they occur, they can 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 HCl for spinal anesthesia, the incidences of adverse reactions were reported to be about 3 percent each for positional headaches, hypotension and vomiting, 2 percent for shivering, and less than 1 percent each for peripheral nerve symptoms, nausea, respiratory inadequacy and drowsiness. Of these observations, one may be related to local anesthetic techniques, with or without a contribution from the local anesthetic.

In large volumes of lumbosacral block, occasional unintentional penetration of the subarachnoid space by the catheter may occur. Such unintentional 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, disturbances of skin sensation and sexual function. Persistent motor, sensory and/or autonomic (sphincter control) deficits of the lower spinal segments with slow recovery (several months) or incomplete recovery have been reported in rare instances when spinal 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 extravascular muscles requiring surgical repair following retrobulbar administration.

**Oversedation:**

Acute overdosage from local anesthetics are generally related to high plasma levels encountered during therapeutic use of local anesthetics for spinal or 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 and constant 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 administration of oxygen, at 3 to 4 L/min, as well as ventilation or apnea due to undetected subarachnoid injection of drug solution must be considered. Immediate attention to the maintenance of a patent airway or if prolonged and effective resuscitative measures should be instituted. Endotracheal intubation, employing drugs and techniques available to the clinician should be indicated, after initial administration of oxygen by mask, if difficulty is encountered in the maintenance of respiration and if prolonged ventilatory support is required (assisted or controlled) is indicated.

**Dialysis of Negligible Value**

Dialysis is of negligible value in the treatment of acute overdosage with lidocaine HCl. The oral LD50 of lidocaine HCl in non-fasted female rats is 459 (346 to 773) mg/kg (as the salt) and 214 (159 to 324) mg/kg (as the salt) in fasted female rats.

**Dosage and Administration:**

**Table 1 (Recommended Dosages) summarizes the recommended volumes and concentrations of Xylocaine Injection for various types of anesthetic procedures. The dosages listed 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 following intrarticular infusions of local anesthetics following arthroscopic and other surgical procedures.

**Dosages should be reduced for children and for adults with cardiac and/or liver disease.**

**Central Neural Blocks**

<table>
<thead>
<tr>
<th>Procedure Conc (%)</th>
<th>Vol (mL)</th>
<th>Total Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental</td>
<td>2</td>
<td>1 to 5</td>
</tr>
<tr>
<td>Intercostal</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Brachial</td>
<td>1.5</td>
<td>15 to 20</td>
</tr>
<tr>
<td><strong>Lumbar</strong></td>
<td>1</td>
<td>5 to 10</td>
</tr>
<tr>
<td><strong>Paravertebral</strong></td>
<td>1</td>
<td>3 to 5</td>
</tr>
<tr>
<td><strong>Paravertebral</strong></td>
<td>1</td>
<td>5 to 10</td>
</tr>
<tr>
<td><strong>Dorsal</strong></td>
<td>1</td>
<td>3 to 5</td>
</tr>
</tbody>
</table>

**Epidural Anesthesia**

For epidural anesthesia, the following dosage forms of Xylocaine Injection are recommended:

- 1.0% without ephinephrine: 10 mL Polymap DuFi®
- 1.0% without ephinephrine: 30 mL single dose solutions
- 1.5% without ephinephrine: 10 mL Polymap DuFi®
- 2.0% without ephinephrine: 20 mL single dose solutions
- 1.5% with ephinephrine: 30 mL ampules, 30 mL single dose solutions
- 2.0% with ephinephrine: 20 mL ampules, 20 mL single dose solutions
- 2.25% with ephinephrine: 10 mL single dose solutions

Although these solutions are intended specifically for epidural use, they may 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 to 3 mL of the indicated concentration per dermatome).

**Caudal and Lumbar Epidural Block**

An acute reaction against the event is sometimes observed following unintentional penetration of the subarachnoid space, a test dose of 2 to 3 mL of a solution not containing epinephrine should be administered at least 5 minutes prior to injecting the total volume for each caudal or lumbar epidural test. The test dose should be repeated if the patient is moved in a manner that may have dispersed the local anesthetic.

Ephinephrine, if contained in the test dose (10 to 15 mcg have been suggested), may serve as a warning of unintentional intravascular injection. If injected into a blood vessel, this amount of ephinephrine is likely to produce a transient "epinephrine response" with or without concomitant signs of an increase in heart rate and systolic blood pressure, circulatory 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 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 local anesthetic through the catheter is to be avoided, and, when feasible, fractional doses should be administered.

In the event of the known injection of a large volume of local anesthetic solution into the subarachnoid space, the anesthetist should check whether the catheter is in place, consider attempting the recovery of drug remaining, and, if possible, achieve hemostasis.

**Maximum Recommended Dosages:**

**Adults**

For normal healthy adults, the individual maximum recommended dose of lidocaine HCl with ephinephrine should not exceed 7 mg/kg (3.5 mg/lb) of body weight, and in general it is recommended that the maximum total dose for spinal block should not exceed 500 mg. When used without ephinephrine the maximum individual dose should not exceed 4 mg/kg (2 mg/lb) of body weight. 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 local anesthetic 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 HCl using paracervical block in obstetrical patients and non-obstetrical patients is 200 mg total. One half of the total dose is usually injected at the beginning of 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 body size and metabolic factors as well as age and weight. For children over 3 years of age who have a normal lean body mass and normal body development, the maximum total dosages for children is determined by the child’s age and weight. In general, in a child of 50 kg, the maximum total dosage of lidocaine HCl should not exceed 75 to 100 mg (1.5 to 2 mg/lb). The use of more dilute solutions (ie, 0.5%) should result in total maximum 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 total dose should be used. 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.

NOTE: Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever the solution and container permit. The injection site is not to be used if its color is pinkish or darker than slightly yellow or if it contains a precipitate.
Infiltration
  Percutaneous  0.5 or 1  1 to 60  5 to 300
  Intravenous regional  0.5  10 to 60  50 to 300
Peripheral Nerve Blocks, eg, Brachial  1.5  15 to 20  225 to 300
  Dental  2  1 to 5  20 to 100
  Intercostal  1  3  30
  Paravertebral  1  3 to 5  30 to 50
  Pudendal (each side)  1  10  100
Paracervical
  Obstetrical analgesia (each side)  1  10  100
Sympathetic Nerve Blocks, eg, Cervical (stellate ganglion)  1  5  50
  Lumbar  1  5 to 10  50 to 100
Central Neural Blocks
  Epidural*
    Thoracic  1  20 to 30  200 to 300
    Lumbar  1  25 to 30  250 to 300
    Analgesia  1.5  15 to 20  225 to 300
    Anesthesia  2  10 to 15  200 to 300
Caudal
  Obstetrical analgesia  1  20 to 30  200 to 300
  Surgical anesthesia  1.5  15 to 20  225 to 300

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

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 incidents of swelling and edema. When chemical disinfection of multi-dose vials is desired, either isopropyl alcohol (91%) or ethyl alcohol (70%) 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.

Dosage forms listed as Xylocaine-MPF indicate single dose solutions that are Methyl Paraben Free (MPF).

How supplied:

<table>
<thead>
<tr>
<th>Xylocaine (lidocaine HCl) Concentration</th>
<th>Xylocaine-MPF</th>
<th>Xylocaine</th>
</tr>
</thead>
<tbody>
<tr>
<td>*</td>
<td>Ampules (mL)</td>
<td>Polyamp DuoFit ( ^\text{\textregistered} \text{\textregistered} ) (mL)</td>
</tr>
<tr>
<td>0.5%</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>0.5% 1:200,000</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>1%</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>1% 1:100,000</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>1% 1:200,000</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>1.5%</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>1.5% 1:200,000</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>2%</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>2% 1:100,000</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>2% 1:200,000</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

All solutions should be stored at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Protect from light.

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