HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LIDOCAINE HYDROCHLORIDE INJECTION, USP safely and effectively. See full prescribing information for LIDOCAINE HYDROCHLORIDE INJECTION, USP.

LIDOCAINE HYDROCHLORIDE INJECTION, USP, aqueous solutions for infiltration and nerve block
Initial U.S. Approval: 1948

---------- INDICATIONS AND USAGE----------
Lidocaine Hydrochloride Injection contains lidocaine, an amide local anesthetic. Lidocaine Hydrochloride Injection is indicated in adult and pediatric patients for the production of local or regional anesthesia or analgesia for surgery, dental, and oral surgery procedures, diagnostic and therapeutic procedures, and for obstetrical procedures. For each type of block indicated to produce local or regional anesthesia or analgesia, specific concentrations and presentations are recommended. (1, 2.2)

----------DOSAGE AND ADMINISTRATION----------
See Full Prescribing Information for recommended dosages and administration information for adult and pediatric patients. (2)

---------- DOSAGE FORMS AND STRENGTHS----------
- Lidocaine Hydrochloride Injection, single-dose vials: 0.5%, 1% (3)
- Lidocaine Hydrochloride Injection, single-dose ampuls: 1%, 1.5%, 2% (3)
- Lidocaine Hydrochloride Injection, multiple-dose vials: 0.5%, 1%, 2% (3)

----------CONTRAINDICATIONS---------- ------
- Known hypersensitivity to any local anesthetic agent of the amide-type or to other components of Lidocaine Hydrochloride Injection. (4)

----------WARNINGS AND PRECAUTIONS---------- ---
- Dose-Related Toxicity: Monitor cardiovascular and respiratory vital signs and patient's state of consciousness after injection of Lidocaine Hydrochloride Injection. (5.1)
- Methemoglobinemia: Cases of methemoglobinemia have been reported in association with local anesthetics use. See full prescribing information for more details on managing these risks. (5.2)
- Chondrolysis with Intra-Articular Infusion: Avoid intra-articular infusions as there have been post-marketing reports of chondrolysis in patients receiving such infusion. (5.4)
- Risk of Systemic Toxicities with Unintended Intravascular or Intrathecal Injection: Unintended intravascular or intrathecal injection may be associated with systemic toxicities, including CNS or cardiorespiratory depression and coma, progression ultimately to respiratory arrest. Aspirate for blood or cerebrospinal fluid (where applicable) prior to each dose and consider using a test dose of a lidocaine solution containing epinephrine. (5.7)

---------- ADVERSE REACTIONS---------- --------
Most common adverse reactions are as follows:
- Central Nervous System: 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. (6)
- Cardiovascular System: Bradycardia, hypotension, and cardiovascular collapse. (6)
- Allergic: Cutaneous lesions, urticaria, edema or anaphylactoid reactions. (6)
- Neurologic: Positional headaches, hypotension and backache. (6)
- Hematologic: Methemoglobinemia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- Local Anesthetics: The toxic effects of local anesthetics are additive. Monitor for neurologic and cardiovascular effects when additional local anesthetics are administered. (7.1)
- Monoamine Oxidase Inhibitors and Tricyclic Antidepressants: Administration of lidocaine solutions containing epinephrine to patients receiving monoamine oxidase inhibitors or tricyclic antidepressants may produce severe, prolonged hypertension. Concurrent use of these agents should generally be avoided. (5.5, 7.2)
- Ergot-type Oxytocic drugs: Concurrent administration of lidocaine solutions containing epinephrine and ergot-type oxytocic drugs may cause severe, persistent hypertension or cerebrovascular accidents. (5.5, 7.3)
- Nonselective Beta-Adrenergic Antagonists: Administration of lidocaine solutions containing epinephrine in patients receiving nonselective beta-adrenergic antagonist may cause severe hypertension and bradycardia. Concurrent use of these agents should generally be avoided. (5.5, 7.4)
- Drugs Associated with Methemoglobinemia: Patients are at increased risk of developing methemoglobinemia when concurrently exposed to nitrates, nitrites, local anesthetics, antineoplastic agents, antibiotics, antimalarials, anticonvulsants and other drugs. (7.5)
- Potent Inhalation Anesthetics: Serious dose-related cardiac arrhythmias may occur if lidocaine solutions containing epinephrine are used in patients during or following the administration of potent inhalation anesthetics. (5.11, 7.6)

---------- USE IN SPECIFIC POPULATIONS---------- --
- Geriatric Use: Elderly patients should be given reduced doses commensurate with their age and physical condition. (8.5)
- Hepatic Impairment: Consider reduced dosing and increased monitoring for local anesthetic systemic toxicity in patients with hepatic impairment. (8.6)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 1/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
- 2.1 Important Dosage and Administration Information
- 2.2 Recommended Concentrations and Dosages of Lidocaine Hydrochloride Injection in Adults
- 2.3 Use in Epidural Anesthesia
- 2.4 Test Dose for Epidural Blocks
- 2.5 Intravenous Regional Anesthesia (Bier Block)
- 2.6 Maximum Recommended Dosage

3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
- 5.1 Dose-Related Toxicity
- 5.2 Methemoglobinemia
- 5.3 Antimicrobial Preservatives in Multiple-Dose Vials
- 5.4 Chondrolysis with Intra-Articular Infusion
- 5.5 Risk of Adverse Reactions Due to Drug Interactions with Lidocaine Solutions Containing Epinephrine
- 5.6 Anaphylactic Reactions
- 5.7 Risk of Systemic Toxicities with Unintended Intravascular or Intrathecal Injection
- 5.8 Risk of Toxicity in Patients with Hepatic Impairment
- 5.9 Risk of Use in Patients with Impaired Cardiovascular Function
- 5.10 Risk of Ischemic Injury or Necrosis in Body Areas with Limited Blood Supply
- 5.11 Risk of Cardiac Arrhythmias with Concomitant Use of Potent Inhalation Anesthetics
- 5.12 Risk of Adverse Reactions with Use in the Head and Neck Area
- 5.13 Familial Malignant Hyperthermia
- 5.14 Risk of Respiratory Arrest with Use in Ophthalmic Surgery
- 5.15 Risk of Inadvertent Trauma to Tongue, Lips, and Buccal Mucosa in Dental Applications
- 5.16 Drug/Laboratory Test Interactions

6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
- 7.1 Local Anesthetics
- 7.2 Monoamine Oxidase Inhibitors and Tricyclic Antidepressants
- 7.3 Ergot-Type Oxytocic Drugs
- 7.4 Nonselective Beta-Adrenergic Antagonists
- 7.5 Drugs Associated with Methemoglobinemia
- 7.6 Potent Inhalation Anesthetics

8 USE IN SPECIFIC POPULATIONS
- 8.1 Pregnancy
- 8.2 Lactation
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Hepatic Impairment

10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY
- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Lidocaine Hydrochloride Injection is indicated in adult and pediatric patients for the production of local or regional anesthesia or analgesia for surgery, dental, and oral surgery procedures, diagnostic and therapeutic procedures, and for obstetrical procedures. Specific concentrations and presentations of Lidocaine Hydrochloride Injection are recommended for each type of block indicated to produce local or regional anesthesia or analgesia *[see Dosage and Administration (2.2)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage and Administration Information

- Lidocaine Hydrochloride Injection is not recommended for intrathecal use.
- Avoid use of Lidocaine Hydrochloride Injection solutions containing antimicrobial preservatives (i.e., multiple-dose vials) for epidural or caudal anesthesia *[see Warnings and Precautions (5.3)]*.
- Discard unused portions of solution not containing preservatives, i.e., those supplied in single-dose vials, following initial use.
- Visually inspect this product for particulate matter and discoloration prior to administration whenever solution and container permit. Lidocaine Hydrochloride Injection is a clear solution. Do not administer solutions which are discolored or contain particulate matter.
- Mixing or the prior or intercurrent use of any other local anesthetic with Lidocaine Hydrochloride Injection is not recommended because of insufficient data on the clinical use of such mixtures.

<u>Administration Precautions</u>

- Lidocaine Hydrochloride Injection is to be administered in carefully adjusted dosages by or under the supervision of experienced clinicians who are well versed in the diagnosis and management of dose-related toxicity and other acute emergencies which might arise from the block to be employed.
- Use Lidocaine Hydrochloride Injection only if the following are immediately available: oxygen, cardiopulmonary resuscitative equipment and drugs, and the personnel resources needed for proper management of toxic reactions and related emergencies *[see Warnings and Precautions (5.1), Adverse Reactions (6), Overdosage (10)]*.
- The toxic effects of local anesthetics are additive. Monitor for neurologic and cardiovascular effects related to local anesthetic systemic toxicity when additional local anesthetics are administered with Lidocaine Hydrochloride Injection *[see Warnings and Precautions (5.1), Drug Interactions (7.1), Overdosage (10)]*.
- Aspirate for blood or cerebrospinal fluid (where applicable) prior to injecting Lidocaine Hydrochloride Injection, both the initial dose and all subsequent doses, to avoid intravascular or intrathecal injection. However, a negative aspiration for blood or cerebrospinal fluid does not ensure against an intravascular or intrathecal injection *[see Warnings and Precautions (5.7)]*.
- Avoid rapid injection of a large volume of Lidocaine Hydrochloride Injection and use fractional (incremental) doses when feasible.
- During major regional nerve blocks, such as those of the brachial plexus or lower extremity, the patient should have an indwelling intravenous catheter to assure adequate intravenous access. The lowest dosage of Lidocaine Hydrochloride Injection that results in effective anesthesia should be used to avoid high plasma levels and serious adverse reactions.
- Perform careful and constant monitoring of cardiovascular and respiratory (adequacy of oxygenation and ventilation) vital signs and the patient's level of consciousness after each local anesthetic injection.

- Use lidocaine solutions containing epinephrine in carefully restricted quantities in areas of the body supplied by end arteries or having otherwise compromised blood supply such as digits, nose, external ear, or penis *[see Warnings and Precautions (5.10)]*.

2.2 Recommended Concentrations and Dosages of Lidocaine Hydrochloride Injection in Adults

The dosage of Lidocaine Hydrochloride Injection administered varies with the anesthetic procedure, the area to be anesthetized, the vascularity of the tissues, the number of neuronal segments to be blocked, the depth of anesthesia and degree of muscle relaxation required, the duration of anesthesia desired, individual tolerance, and the physical condition of the patient. Administer the smallest dosage and concentration required to produce the desired result.

The types of block and recommended Lidocaine Hydrochloride Injection concentrations are shown in Table 1. The dosages suggested in this table are for normal healthy adults and refer to the use of epinephrine-free solutions. Consider administration of solutions containing epinephrine when large volumes are required.

Table 1: Recommended Dosages in Adults

Procedure	Lidocaine Hydrochloride Injection (without Epinephrine)		
	Conc. (%)	**Vol. (mL)**	**Total Dose (mg)**
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, e.g.,			
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, e.g.,			
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			
Analgesia	1	25 to 30	250 to 300
Anesthesia	1.5	15 to 20	225 to 300
	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).

** Dose should not exceed 4 mg/kg.

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 *[see Dosage and Administration (2.5)]*.

These recommended doses serve only as a guide to the amount of local anesthetic required for most indicated 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. The maximum dosage limit within the recommended dosage range must be individualized in each case after evaluating the size and physical status of the patient, as well as the anticipated rate of systemic absorption from a particular injection site.

2.3 Use in Epidural Anesthesia

During the administration of epidural anesthesia, it is recommended that a test dose of a lidocaine solution containing epinephrine be administered initially and the effects monitored before the full dose is given. When using a "continuous" catheter technique, test doses should be given prior to both the initial and all supplemental doses, because a catheter in the epidural space can migrate into a blood vessel or through the dura *[see Dosage and Administration (2.4)]*.

During epidural administration, administer Lidocaine Hydrochloride Injection 1% (10 mg/mL), 1.5% (15 mg/mL, and 2% (20 mg/mL) solutions in incremental doses of 3 mL to 5 mL with sufficient time between doses to detect toxic manifestations of unintentional intravascular or intrathecal injection. Administer injections slowly, with frequent aspirations before and during the injection to avoid intravascular injection. Perform syringe aspirations before and during each supplemental injection in continuous (intermittent) catheter techniques. Repeat doses of Lidocaine Hydrochloride Injection should be preceded by a test dose containing epinephrine if not clinically contraindicated. Use only the single-dose vials for caudal or epidural anesthesia; avoid use of the multiple-dose vials for these procedures, which contain a preservative *[see Dosage and Administration (2.1, 2.4), Warnings and Precautions (5.7)]*.

2.4 Test Dose for Epidural Blocks

In the event of the known injection of a large volume of local anesthetic solution 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.

A lidocaine solution containing epinephrine is recommended for use as a test dose prior to caudal and lumbar epidural blocks when clinical conditions permit. This test dose may serve as a warning of unintended intravascular or intrathecal injection. Closely monitor for early clinical signs of toxicity following each test dose *[see Warnings and Precautions (5.7)]*. Allot adequate time for onset of spinal block to detect possible intrathecal injection. An intravascular or intrathecal injection is still possible even if results of the test dose are negative. The test dose itself may produce a systemic toxic reaction, high spinal, or cardiovascular effects from the epinephrine *[see Warnings and Precautions (5.1), Overdosage (10)]*.

2.5 Intravenous Regional Anesthesia (Bier Block)

For intravenous regional anesthesia, use only the 50 mL single-dose vial containing Lidocaine Hydrochloride Injection 0.5%. Lidocaine solutions containing epinephrine or other vasoconstrictors should not be used for this technique. Proper use of the double tourniquet technique is essential in the performance of intravenous regional anesthesia.

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

2.6 Maximum Recommended Dosage

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

Adults

The maximum individual dose of lidocaine hydrochloride should not exceed 4.5 mg/kg 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, a higher total dose 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 Pregnancy (8.1)]*.

Pediatric Patients

A maximum dose of Lidocaine Hydrochloride Injection for children varies based on age and weight. For children over 3 years of age with 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 approximately 23 kg, the dose of lidocaine hydrochloride should not exceed approximately 75 mg to 100 mg (3.3 mg/kg to 4.4 mg/kg). The use of dilute solutions (i.e., 0.25% to 0.5%) and total dosages not to exceed 3 mg/kg are recommended for induction of intravenous regional anesthesia in children.

The lowest effective concentration and lowest effective dose should be used. Dilution of available concentrations with 0.9% sodium chloride injection may be required to obtain the required final concentration.

3 DOSAGE FORMS AND STRENGTHS

Lidocaine Hydrochloride Injection, USP is a clear solution available as:

- 0.5% (250 mg per 50 mL) (5 mg per mL), 50 mL single-dose teartop vials
- 1% (20 mg per 2 mL) (10 mg per mL), 2 mL single-dose ampuls
- 1% (50 mg per 5 mL) (10 mg per mL), 5 mL single-dose ampuls
- 1% (300 mg per 30 mL) (10 mg per mL), 30 mL single-dose teartop vials
- 1.5% (300 mg per 20 mL) (15 mg per mL), 20 mL single-dose ampuls
- 2% (40 mg per 2 mL) (20 mg per mL), 2 mL single-dose ampuls
- 2% (200 mg per 10 mL) (20 mg per mL), 10 mL single-dose ampuls

- 0.5% (250 mg per 50 mL) (5 mg per mL), 50 mL multiple-dose fliptop vials
- 1% (200 mg per 20 mL) (10 mg per mL), 20 mL multiple-dose fliptop vials
- 1% (500 mg per 50 mL) (10 mg per mL), 50 mL multiple-dose fliptop vials
- 2% (400 mg per 20 mL) (20 mg per mL), 20 mL multiple-dose fliptop vials
- 2% (1000 mg per 50 mL) (20 mg per mL), 50 mL multiple-dose fliptop vials

4 CONTRAINDICATIONS

Lidocaine Hydrochloride Injection is contraindicated in patients with a known hypersensitivity to lidocaine or to any local anesthetics of the amide-type or to other components of Lidocaine Hydrochloride Injection.

5 WARNINGS AND PRECAUTIONS

5.1 Dose-Related Toxicity

The safety and effectiveness of Lidocaine Hydrochloride Injection depends on proper dosage, correct technique, adequate precautions, and readiness for emergencies. Careful and constant monitoring of cardiovascular and respiratory (adequacy of ventilation) vital signs and the patient's state of consciousness should be performed after injection of Lidocaine Hydrochloride Injection solutions.

Possible early warning signs of central nervous system (CNS) toxicity are restlessness, anxiety, incoherent speech, lightheadedness, numbness and tingling of the mouth and lips, metallic taste, tinnitus, dizziness, blurred vision, tremors, twitching, CNS depression, or drowsiness. 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.

During major regional nerve blocks, such as those of the brachial plexus or lower extremity, the patient should have an indwelling intravenous catheter to assure adequate intravenous access. Use the lowest dosage of Lidocaine Hydrochloride Injection that results in effective anesthesia to avoid high plasma levels and serious adverse effects. Avoid rapid injection of a large volume of Lidocaine Hydrochloride Injection solution and administer fractional (incremental) doses when feasible.

Injection of repeated doses of Lidocaine Hydrochloride Injection may cause significant increases in plasma levels with each repeated dose due to slow accumulation of the drug or its metabolites, or to slow metabolic degradation. Tolerance to elevated blood levels varies with the status of the patient. Debilitated, elderly patients and acutely ill patients should be given reduced doses commensurate with their age and physical status.

5.2 Methemoglobinemia

Cases of methemoglobinemia have been reported in association with local anesthetic use. Although all patients are at risk for methemoglobinemia, patients with glucose-6-phosphate dehydrogenase deficiency, congenital or idiopathic methemoglobinemia, cardiac or pulmonary compromise, infants under 6 months of age, and concurrent exposure to oxidizing agents or their metabolites are more susceptible to developing clinical manifestations of the condition *[see Drug Interactions (7.5)]*. If local anesthetics must be used in these patients, close monitoring for symptoms and signs of methemoglobinemia is recommended.

Signs of methemoglobinemia may occur immediately or may be delayed some hours after exposure and are characterized by a cyanotic skin discoloration and abnormal coloration of the blood. Methemoglobin levels may continue to rise; therefore, immediate treatment is required to avert more serious central nervous system and cardiovascular adverse effects, including seizures, coma, arrhythmias, and death. Discontinue Lidocaine Hydrochloride Injection and any other oxidizing agents. Depending on the severity of the symptoms, patients may respond to supportive care, i.e., oxygen therapy, hydration. More severe symptoms may require treatment with methylene blue, exchange transfusion, or hyperbaric oxygen.

5.3 Antimicrobial Preservatives in Multiple-Dose Vials

Avoid use of Lidocaine Hydrochloride Injection solutions containing antimicrobial preservatives (i.e., those supplied in multiple-dose vials) for epidural or caudal anesthesia because safety has not been established with such use.

5.4 Chondrolysis with Intra-Articular Infusion

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.

5.5 Risk of Adverse Reactions Due to Drug Interactions with Lidocaine Solutions Containing Epinephrine

Risk of Severe, Persistent Hypertension Due to Drug Interactions Between Lidocaine Solutions Containing Epinephrine and Monoamine Oxidase Inhibitors and Tricyclic Antidepressants

Administration of lidocaine solutions containing epinephrine in patients receiving monoamine oxidase inhibitors (MAOI), or tricyclic antidepressants may result in severe, prolonged hypertension. Concurrent use of these agents should generally be avoided. In situations when concurrent therapy is necessary, careful monitoring of the patient's hemodynamic status is essential *[see Drug Interactions (7.2)]*.

Risk of Severe, Persistent Hypertension or Cerebrovascular Accidents Due to Drug Interactions Between Lidocaine Solutions Containing Epinephrine and Ergot-Type Oxytocic Drugs

Concurrent administration of lidocaine solutions containing epinephrine and ergot-type oxytocic drugs may cause severe, persistent hypertension or cerebrovascular accidents. Avoid use of lidocaine solutions containing epinephrine concomitantly with ergot-type oxytocic drugs *[see Drug Interactions (7.3)]*.

Risk of Hypertension and Bradycardia Due to Drug Interactions Between Lidocaine Solutions Containing Epinephrine and Nonselective Beta-Adrenergic Antagonists

Administration of lidocaine solutions containing epinephrine in patients receiving nonselective beta-adrenergic antagonists may cause severe hypertension and bradycardia. Concurrent use of these agents should generally be avoided. In situations when concurrent therapy is necessary, careful monitoring of the patient's blood pressure and heart rate is essential *[see Drug Interactions (7.4)]*.

5.6 Anaphylactic Reactions

Anaphylactic reactions may occur following administration of lidocaine hydrochloride *[see Adverse Reactions (6)]*. Lidocaine hydrochloride 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 hydrochloride.

5.7 Risk of Systemic Toxicities with Unintended Intravascular or Intrathecal Injection

Unintended intravascular or intrathecal injection of Lidocaine Hydrochloride Injection may be associated with systemic toxicities, including CNS or cardiorespiratory depression and coma, progressing ultimately to respiratory arrest. Unintentional intrathecal injection during the intended performance of caudal or lumbar epidural block or nerve blocks near the vertebral column has resulted in underventilation or apnea ("Total or High Spinal"). A high spinal has been characterized by paralysis of the legs, loss of consciousness, respiratory paralysis, and bradycardia *[see Adverse Reactions (6)]*.

Aspirate for blood or cerebrospinal fluid (where applicable) before injecting Lidocaine Hydrochloride Injection, both the initial dose and all subsequent doses, to avoid intravascular or intrathecal injection. However, a negative aspiration for blood or cerebrospinal fluid does not ensure against an intravascular or intrathecal injection.

Use of Test Dose with Epidural Anesthesia

To serve as a warning of unintended intravascular or intrathecal injection, a lidocaine solution containing epinephrine may be used for a test dose prior to administration of the full dose in caudal and lumbar epidural blocks *[see Dosage and Administration (2.4)]*. An intravascular or intrathecal injection is still possible even if results of the test dose are negative.

Signs/symptoms of unintended intravascular or intrathecal injection of the test dose and monitoring recommendations are described below.

- Unintended intravascular injection: Likely to produce a transient “epinephrine response” within 45 seconds, consisting of an increase in heart rate and/or 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. Therefore, following the test dose, the heart rate should be monitored for increases. Patients on beta-blockers may not manifest changes in heart rate, but blood pressure monitoring can detect a transient rise in systolic blood pressure.

- Unintended intrathecal injection: Evidenced within a few minutes by signs of spinal block (e.g., decreased sensation of the buttocks, paresis of the legs, or, in the sedated patient, absent knee jerk).

The test dose itself may produce a systemic toxic reaction, high spinal or epinephrine-induced cardiovascular effects *[see Overdosage (10)]*.

5.8 Risk of Toxicity in Patients with Hepatic Impairment

Because amide local anesthetics such as lidocaine are metabolized by the liver, consider reduced dosing and increased monitoring for lidocaine systemic toxicity in patients with moderate to severe hepatic impairment who are treated with Lidocaine Hydrochloride Injection, especially with repeat doses *[see Use in Specific Populations (8.6)]*.

5.9 Risk of Use in Patients with Impaired Cardiovascular Function

Lidocaine Hydrochloride Injection should also be given in reduced doses 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. Monitor patients closely for blood pressure, heart rate, and ECG changes.

5.10 Risk of Ischemic Injury or Necrosis in Body Areas with Limited Blood Supply

Use lidocaine solutions containing epinephrine in carefully restricted quantities in areas of the body supplied by end arteries or having otherwise compromised blood supply, such as digits, nose, external ear, or penis. Patients with peripheral vascular disease and those with hypertensive vascular disease may exhibit exaggerated vasoconstrictor response. Ischemic injury or necrosis may result.

5.11 Risk of Cardiac Arrhythmias with Concomitant Use of Potent Inhalation Anesthetics

Serious dose-related cardiac arrhythmias may occur if preparations containing a vasoconstrictor such as epinephrine are used in patients during or following the administration of potent inhalation anesthetics *[see Drug Interactions (7.6)]*. In deciding whether to concurrently use lidocaine solutions containing epinephrine with potent inhalation anesthetics in the same patient, the combined action of both agents upon the myocardium, the concentration and volume of vasoconstrictor used, and the time since injection, when applicable, should be taken into account.

5.12 Risk of Adverse Reactions with Use in the Head and Neck Area

Small doses of local anesthetics (e.g., Lidocaine Hydrochloride Injection) 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. The injection procedures require the utmost care. Confusion, convulsions, respiratory 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. They may also be due to puncture of the dural sheath of the optic nerve during retrobulbar block with diffusion of any local anesthetic along the subdural space to the midbrain. Monitor circulation and respiration and constantly observe patients receiving Lidocaine Hydrochloride Injection blocks. Resuscitative equipment and drugs, and personnel for treating adverse reactions should be immediately available. Dosage recommendations should not be exceeded *[see Dosage and Administration (2.2)]*.

5.13 Familial Malignant Hyperthermia

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).

5.14 Risk of Respiratory Arrest with Use in Ophthalmic Surgery

Clinicians who perform retrobulbar blocks should be aware that there have been reports of respiratory arrest following local anesthetic injection. Prior to retrobulbar block (e.g., with Lidocaine Hydrochloride Injection), as with all other regional procedures, resuscitative equipment and drugs, and personnel to manage respiratory arrest or depression, convulsions, and cardiac stimulation or depression should be immediately available *[see Warnings and Precautions (5.12)]*. As with other anesthetic procedures, patients should be constantly monitored following ophthalmic blocks for signs of these adverse reactions, which may occur following relatively low total doses.

5.15 Risk of Inadvertent Trauma to Tongue, Lips, and Buccal Mucosa in Dental Applications

Because of the long duration of anesthesia, when Lidocaine Hydrochloride Injection is used for dental injections, warn patients about the possibility of inadvertent trauma to tongue, lips, and buccal mucosa and advise them not to chew solid foods until sensation returns *[see Patient Counseling Information (17)]*.

5.16 Drug/Laboratory Test Interactions

The intramuscular injection of lidocaine hydrochloride 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 hydrochloride.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions have been reported and described in the Warnings and Precautions section of the labeling:

- Dose-Related Toxicity *[see Warnings and Precautions (5.1)]*
- Methemoglobinemia *[see Warnings and Precautions (5.2)]*
- Chondrolysis with Intra-Articular Infusion *[see Warnings and Precautions (5.4)]*
- Severe, Persistent Hypertension, Cerebrovascular Accidents, and Bradycardia Due to Drug Interactions *[see Warnings and Precautions (5.5)]*
- Allergic-Type Reactions *[see Warnings and Precautions (5.6)]*
- Systemic Toxicities with Unintended Intravascular or Intrathecal Injection *[see Warnings and Precautions (5.7)]*
- Respiratory Arrest Following Retrobulbar Block *[see Warnings and Precautions (5.14)]*

The following adverse reactions from voluntary reports or clinical studies have been reported with lidocaine or lidocaine and epinephrine. Because many of these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Adverse reactions to Lidocaine Hydrochloride Injection are characteristic of those associated with other amide-type local anesthetics. A major cause of adverse reactions to this group of drugs is excessive plasma levels, which may be due to overdosage, unintentional intravascular injection, or slow metabolic degradation.

The most commonly encountered acute adverse reactions that demand immediate counter measures were related to the CNS and the cardiovascular system. These adverse reactions were generally dose-related and due to high plasma levels which may have resulted from overdosage, rapid absorption from the injection site, diminished tolerance, or from unintentional intravascular injection of the local anesthetic solution. In addition to systemic

dose-related toxicity, unintentional intrathecal injection of drug during the intended performance of caudal or lumbar epidural block or nerve blocks near the vertebral column (especially in the head and neck region) has resulted in underventilation or apnea ("Total or High Spinal"). Also, hypertension due to loss of sympathetic tone and respiratory paralysis or underventilation due to cephalad extension of the motor level of anesthesia have occurred. This has led to secondary cardiac arrest when untreated.

When used for dental injections, paresthesia of the lips, tongue, and oral tissues have been reported. Persistent paresthesia lasting weeks to months and, in some instances, lasting greater than one year, have also been reported.

Nervous System Disorders

Adverse reactions were characterized by excitation and/or depression of the central nervous system and included 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 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 hydrochloride 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.

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.

In the practice of caudal or lumbar epidural block, unintentional penetration of the subarachnoid space by the catheter or needle has occurred. Subsequent adverse effects may have depended partially on the amount of drug administered intrathecally and the physiological and physical effects of a dural puncture. A high spinal has been characterized by paralysis of the legs, loss of consciousness, respiratory paralysis, and bradycardia.

Neurologic effects following epidural or caudal anesthesia have included spinal block of varying magnitude (including high or total spinal block); hypotension secondary to spinal block; urinary retention; fecal and urinary incontinence; loss of perineal sensation and sexual function; persistent anesthesia, paresthesia, weakness, paralysis of the lower extremities and loss of sphincter control, all of which had slow, incomplete, or no recovery; headache; backache; septic meningitis; meningismus; slowing of labor; increased incidence of forceps delivery; and cranial nerve palsies due to traction on nerves from loss of cerebrospinal fluid.

Neurologic effects following other procedures or routes of administration have included persistent anesthesia, paresthesia, weakness, paralysis, all with slow, incomplete, or no recovery.

Convulsions: Incidence varied with the procedure used and the total dose administered. In a survey of studies of epidural anesthesia, overt toxicity progressing to convulsions occurred in approximately 0.1% of local anesthetic administrations. The incidences of adverse neurologic 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.

Cardiac Disorders

High doses or unintentional intravascular injection have led to high plasma levels and related depression of the myocardium, decreased cardiac output, heartblock, hypotension, bradycardia, ventricular arrhythmias, including ventricular tachycardia and ventricular fibrillation, and cardiac arrest *[see Warnings and Precautions (5.9)]*.

Immune System Disorders

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 the multiple-dose vials *[see Warnings and Precautions (5.6)]*.

There have been no reports of cross sensitivity between lidocaine hydrochloride and procainamide or between lidocaine hydrochloride and quinidine.

Hematologic

Methemoglobinemia *[See Warnings and Precautions (5.2)]*.

7 DRUG INTERACTIONS

7.1 Local Anesthetics

The toxic effects of local anesthetics are additive. If coadministration of other local anesthetics with Lidocaine Hydrochloride Injection cannot be avoided, monitor patients for neurologic and cardiovascular effects related to local anesthetic systemic toxicity *[see Warnings and Precautions (5.1)]*.

7.2 Monoamine Oxidase Inhibitors and Tricyclic Antidepressants

The administration of lidocaine solutions containing epinephrine to patients receiving monoamine oxidase inhibitors or tricyclic antidepressants may produce severe, prolonged hypertension. Concurrent use of these agents should generally be avoided. In situations when concurrent therapy is necessary, careful monitoring of the patient’s hemodynamic status is essential *[see Warnings and Precautions (5.5)]*.

7.3 Ergot-Type Oxytocic Drugs

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. Avoid use of lidocaine solutions containing epinephrine concomitantly with ergot-type oxytocic drugs *[see Warnings and Precautions (5.5)]*.

7.4 Nonselective Beta-Adrenergic Antagonists

Administration of lidocaine solutions containing epinephrine in patients receiving nonselective beta-adrenergic antagonists may cause severe hypertension and bradycardia. Concurrent use of these agents should generally be avoided. In situations when concurrent therapy is necessary, careful monitoring of the patient's blood pressure and heart rate is essential *[see Warnings and Precautions (5.5)]*.

7.5 Drugs Associated with Methemoglobinemia

Patients that are administered local anesthetics may be at increased risk of developing methemoglobinemia when concurrently exposed to the following oxidizing agents:

Class	Examples
Nitrates/Nitrites	nitroglycerin, nitroprusside, nitric oxide, nitrous oxide
Local anesthetics	articaine, benzocaine, bupivacaine, lidocaine, mepivacaine, prilocaine, procaine, ropivacaine, tetracaine
Antineoplastic agents	cyclophosphamide, flutamide, rasburicase, ifosfamide, hydroxyurea
Antibiotics	dapsone, sulfonamides, nitrofurantoin, para-aminosalicylic acid
Antimalarials	chloroquine, primaquine
Anticonvulsants	phenytoin, sodium valproate, phenobarbital
Other drugs	acetaminophen, metoclopramide, quinine, sulfasalazine

7.6 Potent Inhalation Anesthetics

Serious dose-related cardiac arrhythmias may occur if lidocaine solutions containing epinephrine are used in patients during or following the administration of potent inhalation anesthetics *[see Warnings and Precautions (5.11)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available published data and decades of clinical use with lidocaine hydrochloride in pregnant women have not identified any drug-associated risk for major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Local anesthetics may cause varying degrees of toxicity to the mother and fetus and adverse reactions include alterations of the central nervous system, peripheral vascular tone and cardiac function *(see Clinical Considerations)*.

In a published animal reproduction study, pregnant rats administered lidocaine by continuous subcutaneous infusion at a dose approximately 9.6 times the maximum recommended human dose (MRHD) of 500 mg of lidocaine hydrochloride during the period of organogenesis resulted in lower fetal body weights *[*see *Data]*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defects, loss, or other adverse outcomes. In the United States general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Maternal Adverse Reactions

Maternal hypotension has resulted from regional anesthesia. Local anesthetics produce vasodilation by blocking sympathetic nerves. Therefore, during treatment of systemic toxicity, maternal hypotension or fetal bradycardia following regional block, the parturient should be maintained in the left lateral decubitus position if possible or manual displacement of the uterus off the great vessels be accomplished. Elevating the patient's legs will also help prevent decreases in blood pressure. The fetal heart rate also should be monitored continuously, and electronic fetal monitoring is highly advisable.

Labor or 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 (12.3)]*. The incidence and degree of toxicity depend 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. However, dosage recommendations for spinal anesthesia are much lower than dosage recommendations for other major blocks.

Spinal anesthesia may alter the forces of parturition through changes in uterine contractility or maternal expulsive efforts. Spinal anesthesia has 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.

Data

Animal Data

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 hydrochloride.

In a published study, lidocaine administered to pregnant rats by continuous subcutaneous infusion during the period of organogenesis at 100, 250, and 500 mg/kg/day, did not produce any structural abnormalities, but did result in lower fetal weights at 500 mg/kg/day dose (approximately 9.6 times the maximum recommended human dose [MRHD] of 500 mg lidocaine on a mg/m^2 basis) in the absence of maternal toxicity.

8.2 Lactation

Risk Summary

Published data report the presence of lidocaine and its metabolites in human milk in low amounts, along with poor oral bioavailability. There are no data on the effect of lidocaine on the breastfed infant or the effect on milk production. The developmental and health benefits of breastfeeding should be considered along with the

mother's clinical need for Lidocaine Hydrochloride Injection and any potential adverse effects on the breastfed child from Lidocaine Hydrochloride Injection or from the underlying maternal condition.

8.4 Pediatric Use

Dosages in children should be reduced, commensurate with age, body weight and physical condition *[see Dosage and Administration (2.6)]*.

8.5 Geriatric Use

Elderly patients should be given reduced doses commensurate with their age and physical condition *[see Dosage and Administration (2.6)]*.

8.6 Hepatic Impairment

Amide-type local anesthetics such as lidocaine are metabolized by the liver. Patients with severe hepatic impairment, because of their inability to metabolize local anesthetics normally, are at greater risk of developing toxic plasma concentrations and potentially local anesthetic systemic toxicity. Therefore, consider reduced dosing and increased monitoring for local anesthetic systemic toxicity in patients with hepatic impairment treated with Lidocaine Hydrochloride Injection, especially with repeat doses *[see Warnings and Precautions (5.8)]*.

10 OVERDOSAGE

Clinical Presentation

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 Warnings and Precautions (5.1), Adverse Reactions (6)]*.

Management

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 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, a benzodiazepine (such as diazepam) may be administered intravenously. The clinician should be familiar, prior to the 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.

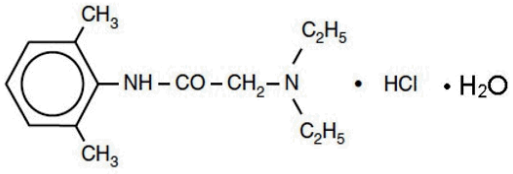
Endotracheal intubation, employing drugs and techniques familiar to the clinician, may be indicated, after initial administration of oxygen by mask, if difficulty is encountered in the maintenance of a patent airway or if prolonged ventilatory support (assisted or controlled) is indicated.

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

11 DESCRIPTION

Lidocaine Hydrochloride Injection, USP contains lidocaine hydrochloride, an amide local anesthetic, as the active pharmaceutical ingredient. The route of administration for Lidocaine Hydrochloride Injection is by injection, for infiltration, nerve block, epidural and caudal use. Multiple-dose vials contain methylparaben and they should not be used for caudal and lumbar epidural blocks.

Lidocaine hydrochloride is chemically designated as acetamide, 2-(diethylamino)-N-(2,6-dimethylphenyl), monohydrochloride monohydrate and has the molecular weight is of 288.8 g/mol. Lidocaine hydrochloride molecular formula is $C_{14}H_{22}N_2O•HCl•H_2O$, and has the following structural formula:



Lidocaine Hydrochloride Injection, USP is a sterile, nonpyrogenic, isotonic, clear solution containing lidocaine hydrochloride and sodium chloride in water for injection for parenteral administration in various concentrations with characteristics as follows:

Concentration	**0.5%**	**1%**	**1.5%**	**2%**
mg/mL lidocaine hydrochloride (anhydrous)	5	10	15	20
mg/mL sodium chloride	8	7	6.5	6

Multiple-dose vials contain 0.1% of methylparaben added as an antiseptic 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/Storage and Handling (16)]* for various sizes and strengths.

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.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Lidocaine hydrochloride stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses thereby effecting local anesthetic action.

12.2 Pharmacodynamics

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.

Factors such as acidosis and the use of CNS stimulants and depressants affect the CNS levels of lidocaine hydrochloride required to produce overt systemic effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6 mcg free base per mL.

12.3 Pharmacokinetics

Systemic plasma levels of lidocaine following Lidocaine Hydrochloride Injection do not correlate with local efficacy.

Absorption

Information derived from diverse formulations, concentrations and usages reveals that lidocaine hydrochloride 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.

Distribution

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

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

Elimination

The elimination half-life of lidocaine hydrochloride following an intravenous bolus injection is typically 1.5 to 2 hours.

Metabolism

Lidocaine hydrochloride is metabolized rapidly by the liver, and 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 hydrochloride.

Excretion

Approximately 90% of lidocaine hydrochloride administered is excreted in the form of various metabolites, and less than 10% is excreted unchanged by the kidneys. The primary metabolite in urine is a conjugate of 4-hydroxy-2,6-dimethylaniline.

Specific Populations

Patients with Hepatic Impairment

Because of the rapid rate at which lidocaine hydrochloride is metabolized, any condition that affects liver function may alter lidocaine hydrochloride kinetics. The half-life may be prolonged two-fold or more in patients with liver dysfunction.

Patients with Renal Impairment

Renal dysfunction does not affect lidocaine hydrochloride kinetics but may increase the accumulation of metabolites.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Studies of lidocaine hydrochloride in animals to evaluate the carcinogenic potential have not been conducted.

Mutagenesis

Studies of lidocaine hydrochloride in animals to evaluate the mutagenic potential have not been conducted.

Impairment of Fertility

In a published study, female Sprague-Dawley rats were treated subcutaneously with lidocaine via osmotic pumps starting two weeks prior to mating, and reproductive effects were assessed. Rats dosed up to the high dose of 500 mg/kg/day (approximately 45 times the MRDD on a mg/m^2 basis) showed no effects on copulatory rate, pregnancy rate, numbers of corpora lutea, or implantations.

16 HOW SUPPLIED/STORAGE AND HANDLING

Store at 20°C to 25°C (68°F 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.**

For single-dose vials and ampuls: Discard unused portion.

Single-dose products are preservative-free.

Lidocaine Hydrochloride Injection, USP is supplied as follows. This product is a clear solution.

Unit of Sale	Concentration
NDC 0409-4278-01 Tray of 25 Glass Single-dose Teartop Vials	0.5% **250 mg/50 mL** (5 mg/mL)
NDC 0409-4713-62 Case of 800 Glass Single-dose Ampuls	1% **20 mg/2 mL** (10 mg/mL)
NDC 0409-4713-65 Case of 800 Glass Single-dose Ampuls	1% **50 mg/5 mL** (10 mg/mL)
NDC 0409-4279-02 Tray of 25 Glass Single-dose Teartop Vials	1% **300 mg/30 mL** (10 mg/mL)
NDC 0409-4776-01 Carton of 25 Glass Single-dose Ampuls	1.5% **300 mg/20 mL** (15 mg/mL)
NDC 0409-4282-02 Carton of 25 Glass Single-dose Ampuls	2% **200 mg/10 mL** (20 mg/mL)

Unit of Sale	Concentration
NDC 0409-4713-02 Bundle of 5 Clamcells containing 5 Single-dose Ampuls per Clamcell	1% **50 mg/5 mL** (10 mg/mL)
NDC 0409-4713-32 Bundle of 5 Cartons containing 10 Single-dose Ampuls per Carton	1% **20 mg/2 mL** (10 mg/mL)
NDC 0409-4282-01 Bundle of 5 Clamcells containing 5 Single-dose Ampuls per Clamcell	2% **40 mg/2 mL** (20 mg/mL)

Unit of Sale	Concentration
NDC 0409-4275-01 Tray of 25 Plastic Multiple-dose Fliptop Vials	0.5% **250 mg/50 mL** (5 mg/mL)
NDC 0409-4276-01 Tray of 25 Plastic Multiple-dose Fliptop Vials	1% **200 mg/20 mL** (10 mg/mL)
NDC 0409-4276-02 Tray of 25 Plastic Multiple-dose Fliptop Vials	1% **500 mg/50 mL** (10 mg/mL)
NDC 0409-4277-01 Tray of 25 Plastic Multiple-dose Fliptop Vials	2% **400 mg/20 mL** (20 mg/mL)
NDC 0409-4277-02 Tray of 25 Plastic Multiple-dose Fliptop Vials	2% **1000 mg/50 mL** (20 mg/mL)

17 PATIENT COUNSELING INFORMATION

17.1 Allergic-Type Reactions

Assess if the patient has had allergic-type reactions to amide-type local anesthetics or to other formulation ingredients, such as the antimicrobial preservative methylparaben contained in multiple-dose vials *[see Contraindications (4), Warnings and Precautions (5.6), Adverse Reactions (6)]*.

17.2 Temporary Loss of Sensation and Motor Activity After Caudal or Epidural Anesthesia

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 caudal or epidural anesthesia.

Instructions After Dental Injection of Lidocaine Hydrochloride Injection

Advise patients receiving dental injections of Lidocaine Hydrochloride Injection not to chew solid foods or to test the anesthetized area by biting or probing until anesthesia has worn off (up to 7 hours) *[see Warnings and Precautions (5.15)]*.

17.3 Methemoglobinemia

Inform patients that use of local anesthetics may cause methemoglobinemia, a serious condition that must be treated promptly. Advise patients or caregivers to stop use and seek immediate medical attention if they or someone in their care experience the following signs or symptoms: pale, gray, or blue colored skin (cyanosis); headache; rapid heart rate; shortness of breath; lightheadedness; or fatigue *[see Warnings and Precautions (5.2)]*.

This product's labeling may have been updated. For the most recent prescribing information, please visit www.pfizer.com.

Distributed by Hospira, Inc., Lake Forest, IL 60045 USA

LAB-1118-6.0