PRESCRIBING INFORMATION

INCLUDING PATIENT MEDICATION INFORMATION

Lidocaine Hydrochloride Injection USP

Sterile solution, 1% lidocaine hydrochloride (10 mg/mL),

Sterile solution, 2% lidocaine hydrochloride (20 mg/mL)

For Parenteral use

USP

Local Anesthetic

Formative Pharma Inc.
4145 North Service Road, Suite 200,
Burlington, Ontario, L7L 6A3

Date of Initial Authorization:
January 27, 2023

Date of Revision:
May 09, 2024

Submission Control No: 278577

RECENT MAJOR LABEL CHANGES

Not applicable.

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Lidocaine Hydrochloride Injection USP (lidocaine hydrochloride) is indicated for production of local or regional anesthesia by:

- infiltration techniques including percutaneous injection,
- peripheral nerve block techniques such as brachial plexus and intercostal blocks,and
- central neural techniques including epidural and caudal blocks, when the accepted procedures for these techniques, as described in standard textbooks, are observed.

1.1 Pediatrics

Pediatrics (<18 years of age): Children should be given reduced doses commensurate with their age, weight and physical condition (see 4.2 DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment).

Lidocaine should be used with caution in children younger than two years of age as there are insufficient data to support the safety and efficacy of this product in this patient population at this time.

1.2 Geriatrics

Geriatrics (> 65 years of age): Elderly patients should be given reduced doses commensurate with their age and physical condition (see 4 DOSAGE AND ADMINISTRATION, Special Populations).

2 CONTRAINDICATIONS

Lidocaine Hydrochloride Injection USP (lidocaine hydrochloride) is contraindicated in:

- Patients with a known history of hypersensitivity to local anesthetics of the amide type or to other components of the solution (see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

General

Lidocaine Hydrochloride Injection USP should only be used by or under the supervision of

clinicians experienced in regional anesthesia.

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration, whenever solution and container permit. Solutions which are discoloured or which contain particulate matter should not be administered.

There have been adverse event reports of irreversible chondrolysis in patients receiving intra-articular infusions of local anesthetics following arthroscopic and other surgical procedures. Lidocaine Hydrochloride Injection USP is not approved for this use (see 7 WARNINGS AND PRECAUTIONS, General).

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 (see 4 DOSAGE AND ADMINISTRATION, Special Populations and 4.2 Recommended Dose and Dosage Adjustment).

The lowest concentration of anesthetic and the lowest dosage needed to provide effective anesthesia should be administered. The rapid injection of a large volume of local anesthetic solution should be avoided and fractional doses should be used when feasible.

The use of lidocaine with epinephrine will prolong the anesthetic action.

When Lidocaine Hydrochloride Injection USP is used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind.

Special Populations

Lidocaine should be used with caution in patients with epilepsy, impaired cardiac conduction, bradycardia, impaired hepatic or renal function and in severe shock (see 7 WARNINGS AND PRECAUTIONS).

Debilitated patients, elderly patients, acutely ill patients, patients with sepsis and children should be given reduced doses commensurate with their age, weight and physical condition (see 7 WARNINGS AND PRECAUTIONS).

4.2 Recommended Dose and Dosage Adjustment

Careful aspiration before and during injection is recommended to prevent intravascular injection. The main dose should be injected slowly or in incremental doses, while closely observing the patient's vital functions and maintaining verbal contact.

Adults: 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.

Children: In children the dosage should be calculated on a weight basis up to 5 mg/kg. With the addition of epinephrine, up to 7 mg/kg can be used. Individual variations occur. In children with a high body weight a gradual reduction of the dosage is often necessary and should be based on the ideal body weight. Standard textbooks should be consulted for factors affecting specific block techniques and for individual patient requirements.

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 will decrease the time to 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 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. The risk of reaching a toxic plasma concentration or inducing a local neural injury must be considered when prolonged blocks and/or repeated administration are employed.

In general, complete block of all nerve fibres in large nerves requires the higher concentrations of drug. In smaller nerves, or when a less intense block is required (e.g., in the relief of labour pain), the lower concentrations are indicated. The volume of drug used will affect the extent of spread of anesthesia.

The duration of effect can be increased by using solutions containing epinephrine (see Table 1). The risk of epinephrine systemic effects with solutions containing large volumes of epinephrine should be considered.

Epidural Anesthesia

The lowest dosage that will produce the desired effect should be given. The amount varies with the number of dermatomes to be anesthetized (generally 2-3 mL of the indicated concentration per dermatome).

Caudal and Lumbar Epidural Block

Test Dose: As a precaution against the adverse experience sometimes observed following unintentional penetration of the subarachnoid space, a test dose such as 3-5 mL of 1-2% lidocaine (50-60 mg) with epinephrine should be administered at least 5 minutes prior to injecting the total volume required for a lumbar or caudal epidural block. During the

administration of a test dose, it is recommended that constant electrocardiographic (ECG) monitoring occur. 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. An accidental intrathecal injection may be recognized by signs of a spinal block.

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 through the catheter should be avoided and when feasible, fractional doses should be administered.

The main dose should be injected slowly at a rate of 100-200 mg/min, or in incremental doses, while keeping in constant verbal contact with the patient. If toxic symptoms occur, the injection should be stopped immediately.

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.

Table 1 Dosage Recommendations In Adults

Type of Block	**Conc. (%)**	**Each Dose**		**Onset (min)**	**Duration (h) Without Epinephrine**	**Indication**
		mL	**mg**			
Local infiltration	0.5	≤ 80	≤ 400	1-2	1.5-2	Surgical operations.
	1	≤ 40	≤ 400	1-2	2-3	
Digital[1]	1	1-5	10-50	2-5	1.5-2	Surgical operations.
Intercostal (per nerve)	1	2-5	20-50	3-5	1-2	Surgical operations, postoperative pain and fractured ribs.
Maximum total dose of 480 mg	1.5	2-4	30-60	3-5	2-3	
Paracervical[2] (each side)	1	10	100	3-5	1-1.5	Surgical operations and dilation of cervix. Obstetric pain relief.
Paravertebral	1	3-5	30-50	5-10	1-1.5	Pain management,

Type of Block	Conc. (%)	Each Dose		Onset (min)	Duration (h) Without Epinephrine	Indication
		mL	mg			
(per segment)	2	3-5	60-100	5-10	1.5-2	diagnostic.
Pudendal (each side)	1	10	100	5-10	1.5-2	Instrumental delivery.
Intra-articular block[3]	0.5	≤ 60	≤ 300	5-10	0.5-1 after washout	Arthroscopy and surgical operations.
	1	≤ 40	≤ 400	5-10		
Retrobulbar[2]	2	4	80	3-5	1.5-2	Ocular surgery.
Peribulbar[2]	1	10-15	100-150	3-5	1.5-2	Ocular surgery.
Brachial plexus:						Surgical operations.
Axillary	1.0	40-50	400-500	15-30	1.5-2	
	1.5	30-50	450-600	15-30	1.5-3	
Supraclavicular interscalene and subclavian perivascular	1.0	30-40	300-400	15-30	1.5-2	
	1.5	20-30	300-450	15-30	1.5-3	
Sciatic	1.5	15-20	225-300	15-30	2-3	Surgical operations.
	2	15-20	300-400	15-30	2-3	
3-in-1 (Femoral, obturator and lateral cutaneous)	1	30-40	300-400	15-30	1.5-2	Surgical operations.
	1.5	30	450	15-30	2-3	
Epidural	1	5	50			Test dose.
	2	3	60			
Lumbar epidural[4]	2	15-25	300-500	15-20	1.5-2	Surgical operations.
Thoracic epidural[4]	1.5	10-15	150-225	10-20	1-1.5	Surgical operation and pain relief.
	2	10-15	200-300	10-20	1.5-2	Surgical operations.
Caudal epidural[4]	1	20-30	200-300	15-30	1-1.5	Surgical operations and pain relief.
	2	15-25	300-500	15-30	1.5-2	Surgical operations.

[1]Without epinephrine.

[2]See 7 WARNINGS AND PRECAUTIONS

[3]There have been post-marketing reports of irreversible chondrolysis in patients receiving post-operative intra-articular infusion of local anesthetics. Lidocaine Hydrochloride Injection USP is not approved for this indication (See 7 WARNINGS AND PRECAUTIONS).

[4]For epidural blocks, dose includes test dose.

5 OVERDOSAGE

Acute systemic toxicity from local anesthetics is generally related to high plasma levels encountered during therapeutic use of local anesthetics and originates mainly in the central nervous and the cardiovascular systems (see 8 ADVERSE REACTIONS and 7 WARNINGS AND PRECAUTIONS). It should be kept in mind that clinically relevant pharmacodynamic drug interactions (i.e., toxic effects) may occur with lidocaine and other local anesthetics or structurally related drugs, and Class I and Class III antiarrhythmic drugs due to additive effects (see 9 DRUG INTERACTIONS).

Symptoms

With accidental intravascular injections, the toxic effect will be obvious within 1-3 min, while with overdosage, peak plasma concentrations may not be reached for 20-30 min depending on the site of injection, with signs of toxicity thus being delayed.

Central nervous system toxicity is a graded response, with symptoms and signs of escalating severity. The first symptoms are circumoral paresthesia, numbness of the tongue, light-headedness, hyperacusis and tinnitus. Visual disturbance and muscular tremors are more serious and precede the onset of generalized convulsions. Unconsciousness and grand mal convulsions may follow, which may last from a few seconds to several minutes. Hypoxia and hypercarbia occur rapidly following convulsions due to the increased muscular activity, together with the interference with normal respiration. In severe cases apnea may occur. Acidosis, hyperkalaemia, hypocalcaemia and hypoxia increase and extend the toxic effects of local anesthetics.

Recovery is due to redistribution and metabolism of the local anesthetic drug. Recovery may be rapid unless large amounts of the drug have been administered.

Cardiovascular effects may be seen in cases with high systemic concentrations. Severe hypotension, bradycardia, arrhythmia and cardiovascular collapse may be the result in such cases.

Cardiovascular toxic effects are generally preceded by signs of toxicity in the central nervous system, unless the patient is receiving a general anesthetic or is heavily sedated with drugs such as a benzodiazepine or barbiturate.

Treatment

The first consideration is prevention, best accomplished by careful and constant monitoring of cardiovascular and respiratory vital signs and the patient's state of consciousness after each local anesthetic administration. At the first sign of change, oxygen should be administered. **If signs of acute systemic toxicity appear, injection of the local anesthetic should be**

immediately stopped.

The first step in the management of systemic toxic reactions, as well as underventilation or apnea due to unintentional subarachnoid injection consists of immediate attention to the establishment and 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. This may prevent convulsions if they have not already occurred.

If convulsions occur, the objective of the treatment is to maintain ventilation and oxygenation and support circulation. Oxygen must be given and ventilation assisted if necessary (mask and bag or tracheal intubation). Should convulsions not stop spontaneously after 15-20 seconds, an anticonvulsant should be given iv to facilitate adequate ventilation and oxygenation. Thiopental sodium 1-3 mg/kg iv is the first choice. Alternatively diazepam 0.1 mg/kg bw iv may be used, although its action will be slow. Prolonged convulsions may jeopardise the patient's ventilation and oxygenation. If so, injection of a muscle relaxant (e.g. succinylcholine 1 mg/kg bw) will facilitate ventilation, and oxygenation can be controlled. Early endotracheal intubation is required when succinylcholine is used to control motor seizure activity.

If cardiovascular depression is evident (hypotension, bradycardia), it should be managed according to the patient condition and standard of anaesthetic care.

Should circulatory arrest occur, immediate cardiopulmonary resuscitation should be instituted. Continual oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance, since hypoxia and acidosis will increase the systemic toxicity of local anesthetics. Epinephrine (0.1 – 0.2 mg as intravenous or intracardial injections) should be given as soon as possible and repeated, if necessary.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 2 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength / Composition	Non-medicinal Ingredients
Parenteral	Sterile solution of 10 mg/mL (1%) or 20 mg/mL (2%) lidocaine hydrochloride, which corresponds to 12 mg/mL or 23 mg/mL of	Sodium chloride (for isotonicity), water for injection, sodium hydroxide and/or hydrochloric acid to adjust pH 5.0-7.0.

	lidocaine base, respectively.	

Packaging

Lidocaine Hydrochloride Injection USP 1% is available in 5 mL (10 mg/mL) single use vials and 5 mL (10 mg/mL) single use ampoules. Lidocaine Hydrochloride Injection USP 2% is available in 5 mL (20 mg/mL) single use vials (USP Type I glass clear), closed with 20mm grey chlorobutyl rubber stopper and sealed with plastic cap Blue. Vial stopper not made with natural rubber latex.

7 WARNINGS AND PRECAUTIONS

General

LOCAL ANESTHETICS SHOULD ONLY BE EMPLOYED 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 8 ADVERSE REACTIONS and 5 OVERDOSAGE). 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.

AN INTRAVENOUS CANNULA MUST BE INSERTED BEFORE THE LOCAL ANESTHETIC IS INJECTED FOR NERVE BLOCKS WHICH MAY RESULT IN HYPOTENSION OR BRADYCARDIA, OR WHERE ACUTE SYSTEMIC TOXICITY MAY DEVELOP FOLLOWING INADVERTENT INTRAVASCULAR INJECTION.

THE LOWEST DOSAGE OF LOCAL ANESTHETIC THAT RESULTS IN EFFECTIVE ANESTHESIA OR ANALGESIA SHOULD BE USED TO AVOID HIGH PLASMA LEVELS AND SERIOUS ADVERSE REACTIONS. INJECTIONS SHOULD BE MADE SLOWLY OR IN INCREMENTAL DOSES, WITH FREQUENT ASPIRATIONS BEFORE AND DURING THE INJECTION TO AVOID INTRAVASCULAR INJECTION.

Reports of Irreversible Chondrolysis with Intra-articular Infusions of Local Anesthetics Following Surgery: Intra-articular infusions of local anesthetics following arthroscopic and other surgical procedures is an unapproved use, and there have been post-marketing reports of irreversible chondrolysis in patients receiving such infusions. The majority of reported cases of irreversible chondrolysis have involved the shoulder joint; cases of gleno-humeral irreversible 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. 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 irreversible chondrolysis; patients who experienced irreversible chondrolysis have required additional diagnostic and therapeutic procedures and some required arthroplasty or shoulder replacement. **Lidocaine Hydrochloride Injection USP should not be used for post-operative intra-articular infusion** (See 4.1 DOSAGE AND ADMINISTRATION, Dosing Considerations and 7 WARNINGS AND PRECAUTIONS).

Major Peripheral Nerve Blocks:

Major peripheral nerve blocks may imply the administration of a large volume of local anesthetic in areas of high vascularity, often close to large vessels where there is an increased risk of intravascular injection and/or rapid systemic absorption which can lead to high plasma concentrations.

Repeat Dosing:

Repeated doses of Lidocaine Hydrochloride Injection USP (lidocaine hydrochloride) 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 (see 4 DOSAGE AND ADMINISTRATION Special Populations).

Inflammation and Sepsis:

Local anesthetic procedures should not be used when there is inflammation and/or sepsis in the region of the proposed injection.

Malignant Hyperthermia:

Many drugs used during the conduct of anesthesia are considered potential triggering agents for familial malignant hyperthermia. It has been shown that the use of amide local anesthetics in malignant hyperthermia patients is safe. However, there is no guarantee that neural blockade will prevent the development of malignant hyperthermia during surgery. It is also difficult to predict the need for supplemental general anesthesia. Therefore, a standard protocol for the management of malignant hyperthermia should be available.

Acute Porphyria:

Lidocaine has been shown to be porphyrinogenic in animal models. Lidocaine Hydrochloride Injection USP should only be used in patients with acute porphyria when no safer alternative is available. Appropriate precautions should be taken for all porphyric patients.

Epidural Anesthesia

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 (see 4 DOSAGE AND ADMINISTRATION). 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. Patients on beta-blockers may not manifest changes in heart rate, but blood pressure monitoring can detect an evanescent rise in systolic blood pressure.

Carcinogenesis and Mutagenesis

Genotoxicity tests with lidocaine showed no evidence of mutagenic potential. A metabolite of lidocaine 2,6-dimethylaniline, showed weak evidence of activity in some genotoxicity tests. See 16 NON-CLINICAL TOXICOLOGY.

Cardiovascular

Lidocaine should be used with caution in patients with bradycardia or impaired cardiovascular function since they may be less able to compensate for functional changes associated with the prolongation of A-V conduction produced by amide-type local anesthetics.

Patients with partial or complete heart block require special attention since local anesthetics may depress myocardial conduction. To reduce the risk of potentially serious adverse reactions, attempts should be made to optimize the patient's condition before major blocks are performed. Dosage should be adjusted accordingly.

Lidocaine should be used with caution in patients in severe shock.

Lumbar and caudal epidural anesthesia should be used with extreme caution in persons with severe hypertension.

Central nerve blocks may cause cardiovascular depression, especially in the presence of hypovolemia. Epidural anesthesia should be used with caution in patients with impaired cardiovascular function.

Epidural anesthesia may lead to hypotension and bradycardia, which should be managed according to patient conditions and standard of anaesthetic care.

Patients treated with antiarrhythmic drugs (e.g., amiodarone, mexiletine) should be under close surveillance and ECG monitoring, since cardiac effects of these drugs and lidocaine may be additive (see 9 DRUG INTERACTIONS).

Driving and Operating Machinery

Besides the direct anesthetic effect, local anesthetics may have a very mild effect on mental function and co-ordination even in the absence of overt CNS toxicity and may temporarily

impair locomotion and alertness. Patients should be cautioned about driving a vehicle or operating potentially hazardous machinery on the day they receive local anesthetic treatment.

Ear/Nose/Throat

Small doses of local anesthetics injected into the head and neck area, including retrobulbar, dental and stellate ganglion blocks, may produce adverse reactions caused by inadvertent injection to an artery. These reactions may be similar to systemic toxicity seen with unintentional intravascular injections of larger doses. Inadvertent injections into an artery can cause cerebral symptoms even at low doses. Confusion, convulsions, respiratory depression and/or respiratory arrest, and cardiovascular stimulation or depression leading to cardiac arrest have been reported. 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 4 DOSAGE AND ADMINISTRATION).

Ophthalmic Surgery:
Retrobulbar injections may very occasionally reach the cranial subarachnoid space causing temporary blindness, cardiovascular collapse, apnea, convulsions, etc. These reactions, which may be due to intra-arterial injection or direct injection into the central nervous system via the sheaths of the optic nerve, must be diagnosed and treated promptly.

Retrobulbar and peribulbar injections of local anesthetics carry a low risk of persistent ocular muscle dysfunction. The primary causes include trauma and/or local toxic effects on muscles and/or nerves. The severity of such tissue reactions is related to the degree of trauma, the concentration of the local anesthetic and the duration of exposure of the tissue to the local anesthetic. For this reason, as with all local anesthetics, the lowest effective concentration and dose of local anesthetic should be used. Vasoconstrictors and other additives may aggravate tissue reactions and should be used only when indicated.

Clinicians who perform retrobulbar blocks should be aware that there have been reports of respiratory arrest following local anesthetic injection. Prior to retrobulbar block, as with all other regional procedures, the immediate availability of equipment, drugs, and personnel to manage respiratory arrest or depression, convulsions, and cardiac stimulation or depression should be assured (see also 7 WARNINGS AND PRECAUTIONS, General).

Hepatic/Biliary/Pancreatic

Because amide-type local anesthetics such as lidocaine are metabolized by the liver, these drugs, especially repeated doses, should be used cautiously 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.

Neurologic

Lumbar and caudal epidural anesthesia should be used with extreme caution in persons with existing neurological disease or spinal deformities.

Epilepsy: Lidocaine should be used with caution in patients with epilepsy. The risk of central nervous system side effects when using lidocaine in patients with epilepsy is very low, provided that the dose recommendations are followed.

Locomotion and Coordination: 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.

Besides the direct anesthetic effect, local anesthetics may have a very mild effect on mental function and co-ordination even in the absence of overt CNS toxicity and may temporarily impair locomotion and alertness.

Peri-Operative Considerations

It is essential that aspiration for blood or cerebrospinal fluid (where applicable) be done prior to injecting any local anesthetics, both the original and all subsequent doses, to avoid intravascular or subarachnoid injection. However, a negative aspiration does not ensure against an intravascular or subarachnoid injection.

The safety and effectiveness of Lidocaine Hydrochloride Injection USP (lidocaine hydrochloride) depends 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 5 OVERDOSAGE). During major regional nerve blocks or using large doses, the patient should be in an optimal condition and should have i.v. fluids running via an indwelling catheter to assure a functioning intravenous pathway. The clinician responsible should have adequate and appropriate training in the procedure to be performed, should take the necessary precautions to avoid intravascular injection (see 4 DOSAGE AND ADMINISTRATION), and should be familiar with the diagnosis and treatment of side effects, systemic toxicity and other complications (see 8 ADVERSE REACTIONS and 5 OVERDOSAGE). THE LOWEST DOSAGE THAT RESULTS IN EFFECTIVE ANESTHESIA SHOULD BE USED TO AVOID HIGH PLASMA LEVELS AND SERIOUS ADVERSE EFFECTS. INJECTIONS SHOULD BE MADE SLOWLY, WITH FREQUENT ASPIRATIONS BEFORE AND DURING THE INJECTION TO AVOID INTRAVASCULAR INJECTION.

Careful and constant monitoring of cardiovascular and respiratory (adequacy of ventilation) vital signs and the patient's state of consciousness should be performed after each local anesthetic injection. It should be kept in mind at such times that restlessness, anxiety, incoherent speech, light-headedness, numbness and tingling of the mouth and lips, metallic

taste, tinnitus, dizziness, blurred vision, tremors, twitching, depression or drowsiness may be early warning signs of central nervous system toxicity.

Renal

Lidocaine is metabolized primarily by the liver to monoethylglycinexylidine (MEGX, which has some CNS activity), and then further to metabolites glycinexylidine (GX) and 2,6-dimethylaniline (see 10.3 CLINICAL PHARMACOLOGY, Pharmacokinetics). Only a small fraction (3%) of lidocaine is excreted unchanged in the urine. The pharmacokinetics of lidocaine and its main metabolite were not altered significantly in haemodialysis patients (n=4) who received an intravenous dose of lidocaine. Therefore, renal impairment is not expected to significantly affect the pharmacokinetics of lidocaine when Lidocaine Hydrochloride Injection USP is used for short treatment durations, according to dosage instructions (see 4.1 DOSAGE AND ADMINISTRATION, Dosing Considerations). Caution is recommended when lidocaine is used in patients with severely impaired renal function because lidocaine metabolites may accumulate during long term treatment.

Sensitivity/Resistance

Lidocaine should be used with caution in persons with known drug sensitivities. Lidocaine solutions are contraindicated in patients with known hypersensitivities to local anesthetics of the amide type, and to other components in the formulation (see 2 CONTRAINDICATIONS).

7.1 Special Populations

Debilitated patients, acutely ill patients and patients with sepsis should be given reduced doses commensurate with their age, weight and physical condition because they may be more sensitive to systemic effects due to increased blood levels of lidocaine following repeated doses.

Lumbar and caudal epidural anesthesia should be used with extreme caution in persons with septicemia.

7.1.1 Pregnant Women

There are no adequate and well-controlled studies in pregnant women on the effect of lidocaine on the developing fetus.

It is reasonable to assume that a large number of pregnant women and women of child-bearing age have been given lidocaine. No specific disturbances to the reproductive process have so far been reported, e.g. no increased incidence of malformations. However, care should be given during early pregnancy when maximum organogenesis takes place.

Paracervical block can sometimes cause fetal bradycardia/tachycardia, and careful monitoring of the fetal heart rate is necessary.

Labour 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. 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. A vasopressor, such as ephedrine, may be indicated (see 7 WARNINGS AND PRECAUTIONS, Cardiovascular). 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 labour and facilitation of cervical dilation. However, spinal and epidural anesthesia have also been reported to prolong the second stage of labour 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.

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. 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. 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. 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.

7.1.2 Breast-feeding

Lidocaine and its metabolites are excreted in the breast milk. At therapeutic doses, the quantities of lidocaine and its metabolites in breast milk are small and generally are not expected to be a risk for the infant.

7.1.3 Pediatrics

Children should be given reduced doses commensurate with their age, weight and physical condition because they may be more sensitive to systemic effects due to increased blood levels of lidocaine following repeated doses (see 4.2 DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment).

In children, the dosage should be calculated on a weight basis up to 5 mg/kg. With the addition of epinephrine, up to 7 mg/kg can be used (see 4.2 DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment).

Lidocaine should be used with caution in children under the age of 2 as there is insufficient data to support the safety and efficacy of this product in this patient population at this time.

7.1.4 Geriatrics

Elderly patients may be more sensitive to systemic effects due to increased blood levels of lidocaine following repeated doses and may require dose reductions.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

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 overdosage, rapid absorption, or inadvertent intravascular injection, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient.

Table 3 Adverse Drug Reaction Frequencies

Common (≥ 1% and <10%)	Vascular disorders: hypotension, hypertension Gastrointestinal disorders: nausea, vomiting Nervous system disorders: parethesia, dizziness Cardiac disorders: bradycardia

Uncommon (≥ 0.1% and <1%)	Nervous system disorders: Signs and symptoms of CNS toxicity (convulsions, paresthesia circumoral, numbness of the tongue, hyperacusis,visual disturbances, tremor, tinnitus, dysarthria, CNS depression)
Rare (≥ 0.01% and <0.1%)	Cardiac disorders: cardiac arrest, cardiac arrhythmias Immune system disorders: allergic reactions, anaphylactic reaction/shock Respiratory disorders: respiratory depression Nervous system disorders: neuropathy, peripheral nerve injury, arachnoiditis Eye disorders: diplopia

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 the following signs and symptoms of escalating severity: circumoral paresthesia, light-headedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, hyperacusis, tinnitus, blurred vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest. The excitatory manifestations (e.g., twitching, tremors, convulsions) 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 lidocaine plasma level and may occur as a consequence of rapid absorption.

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

Allergic: Allergic reactions are characterized by cutaneous lesions, urticaria, edema or, in the most severe instances, anaphylactic shock. Allergic reactions of the amide type are rare (<0.1%) and may occur as a result of sensitivity either to the local anesthetic agent or to other components in the formulation (see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING).

Neurologic: The incidences of adverse reactions may be related to the total dose of local anesthetic administered but is also dependent upon the particular drug used, the route of administration and the physical status of the patient. Neuropathy and spinal cord dysfunction (e.g. anterior spinal artery syndrome, arachnoiditis, cauda equina syndrome), have been associated with regional anesthesia. Neurological effects may be related to local anesthetic techniques, with or without a contribution from the drug.

In the practice of lumbar epidural block, occasional unintentional penetration of the subarachnoid space by the catheter or needle may occur. For example, a high spinal is characterized by paralysis of the legs, loss of consciousness, respiratory paralysis and bradycardia.

Neurologic effects following unintentional subarachnoid administration during epidural anesthesia may include spinal block by varying magnitude (including total or high 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 may have slow, incomplete or no recovery; headache, backache, septic meningitis, meningismus, slowing of labour, increased incidence of forceps delivery, or cranial nerve palsies due to traction on nerves from loss of cerebrospinal fluid.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

Lidocaine is mainly metabolized in the liver by CYP1A2 and CYP3A4 to its two major metabolites, monoethylglycinexylidine (MEGX) and glycinexylidine (GX), both of which are pharmacologically active. Lidocaine has a high hepatic extraction ratio. Only a small fraction (3%) of lidocaine is excreted unchanged in the urine. The hepatic clearance of lidocaine is expected to depend largely on blood flow.

Strong inhibitors of CYP1A2, such as fluvoxamine, given concomitantly with lidocaine, can cause a metabolic interaction leading to an increased lidocaine plasma concentration. Therefore, prolonged administration of lidocaine should be avoided in patients treated with strong inhibitors of CYP1A2, such as fluvoxamine. When co-administered with intravenous lidocaine, two strong inhibitors of CYP3A4, erythromycin and itraconazole, have each been shown to have a modest effect on the pharmacokinetics of intravenous lidocaine. Other drugs such as propranolol and cimetidine have been reported to reduce intravenous lidocaine clearance, probably through effects on hepatic blood flow and/or metabolism.

Clinically relevant pharmacodynamic drug interactions may occur with lidocaine and other local anesthetics or structurally related drugs, and Class I and Class III antiarrhythmic drugs due to additive effects.

9.4 Drug-Drug Interactions

<u>Local anesthetics and agents structurally related to amide-type local anesthetics</u>

Lidocaine should be used with caution in patients receiving other local anesthetics or agents

structurally related to amide-type local anesthetics (e.g. antiarrhythmics such as mexiletine), since the toxic effects are additive.

Antiarrhythmic Drugs

Class I Antiarrhythmic drugs

Class I antiarrhythmic drugs (such as mexiletine) should be used with caution since toxic effects are additive and potentially synergistic.

Class III Antiarrhythmic drugs

Caution is advised when using Class III antiarrhythmic drugs concomitantly with lidocaine due to potential pharmacodynamic or pharmacokinetic interactions with lidocaine, or both. A drug interaction study has shown that the plasma concentration of lidocaine may be increased following administration of a therapeutic dose of intravenous lidocaine to patients treated with amiodarone (n=6). Case reports have described toxicity in patients treated concomitantly with lidocaine and amiodarone. Patients treated with Class III antiarrhythmic drugs (e.g. amiodarone) should be kept under close surveillance and ECG monitoring should be considered, since cardiac effects of these drugs and lidocaine may be additive.

Strong Inhibitors of CYP1A2 and CYP3A4

Cytochrome CYP1A2 and CYP3A4 are involved in the formation of the pharmacologically active lidocaine metabolite MEGX.

Fluvoxamine: Strong inhibitors of CYP1A2, such as fluvoxamine, given during prolonged administration of lidocaine to areas with a high extent of systemic absorption can cause a metabolic interaction leading to an increased lidocaine plasma concentration. The plasma clearance of a single intravenous dose of lidocaine was reduced by 41 to 60% during co-administration of fluvoxamine, a selective and potent CYP1A2 inhibitor, to healthy volunteers.

Erythromycin and Itraconazole: Erythromycin and itraconazole, which are strong inhibitors of CYP3A4, have been shown to reduce clearance of lidocaine by 9 to 18%, following a single intravenous dose of lidocaine to healthy volunteers.

During combined co-administration with fluvoxamine and erythromycin the plasma clearance of lidocaine was reduced by 53%.

β-blockers and cimetidine

Following a single intravenous dose of lidocaine, administered to healthy volunteers, the clearance of lidocaine has been reported to be reduced up to 47% when co-administered with propanolol and up to 30% when co-administered with cimetidine. Reduced clearance of lidocaine when co-administered with these drugs is probably due to reduced liver blood flow and/or inhibition of microsomal liver enzymes. The potential for clinically significant interactions with these drugs should be considered during long-term treatment with high doses

of lidocaine.

Monoamine Oxidase (MAO) Inhibitors

Lidocaine Hydrochloride Injection USP with added epinephrine or solutions containing lidocaine hydrochloride and another vasoconstrictor should be used with extreme caution in patients receiving monoamine oxidase inhibitors (MAO) because severe prolonged hypertension may result. In situations when concurrent therapy is necessary, careful patient monitoring is essential.

Antidepressants (triptyline, imipramine)

Lidocaine Hydrochloride Injection USP with added epinephrine or solutions containing lidocaine hydrochloride and another vasoconstrictor should be used with extreme caution in patients receiving antidepressants of the triptyline or imipramine types because severe prolonged hypertension may result. In situations when concurrent therapy is necessary, careful patient monitoring is essential.

Antipsychotics (phenothiazines, butyrophenones)

Lidocaine Hydrochloride Injection USP with added epinephrine or solutions containing lidocaine hydrochloride and another vasoconstrictor should be used with extreme caution in patients receiving phenothiazines and butyrophenones. Phenothiazines and butyrophenone may oppose the vasoconstrictor effects of epinephrine giving rise to hypotensive responses and tachycardia. In situations when concurrent therapy is necessary, careful patient monitoring is essential.

Sedatives

If sedatives are employed to reduce patient apprehension, they should be used in reduced doses, since local anesthetic agents, like sedatives, are central nervous system depressants which in combination may have an additive effect.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 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.

10 CLINICAL PHARMACOLOGY

10.1 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. Local anesthetics of the amide type are thought to act within the sodium channels of the nerve membrane.

10.2 Pharmacodynamics

The onset of action is 1-5 minutes following infiltration and 5-15 minutes following other types of administration. The duration of anesthesia depends on the concentration of lidocaine used, the dose, and the type of block. The 2% solution will last 1½-2 h when given epidurally, and up to 5 hours with peripheral nerve blocks. With the 1% concentration, there is less effect on motor nerve fibres and the duration of action is shorter. The addition of epinephrine decreases the rate of absorption, reducing toxicity and increasing the duration of effect.

Hemodynamics
Lidocaine, like other local anesthetics, may also have effects on other excitable membranes (e.g. brain and myocardium). If excessive amounts of drug reach systemic circulation, symptoms and signs of toxicity may appear, emanating from the central nervous and cardiovascular systems.

Central nervous system toxicity (see 5 OVERDOSAGE) usually precedes the cardiovascular effects since it occurs at lower plasma concentrations. Direct effects of local anesthetics on the heart include slow conduction, negative inotropism and eventually cardiac arrest.

Indirect cardiovascular effects (hypotension, bradycardia) may occur after epidural administration depending on the extent of the concomitant sympathetic block.

10.3 Pharmacokinetics

Absorption:

Lidocaine is completely absorbed following parenteral administration. The rate of absorption depends on the dose, route of administration, and the vascularity of the injection site. The highest peak plasma levels are obtained following intercostal nerve block (approximately 1.5 mcg/mL per 100 mg injected) while abdominal subcutaneous injections give the lowest (approximately 0.5 mcg/mL per 100 mg injected). Epidural and major nerve blocks are intermediate.

Absorption is considerably slowed by the addition of epinephrine, although it also depends on the site of injection. Peak plasma concentrations are reduced by 50% following subcutaneous

injection, by 30% following epidural injection and by 20% following intercostal block if epinephrine 5 mcg/mL is added.

Lidocaine shows complete and biphasic absorption from the epidural space with half lives of the two phases in the order of 9.3 min and 82 min respectively. The slow absorption is the rate limiting factor in the elimination of lidocaine, which explains why the apparent terminal half-life is longer after epidural administration. Absorption of lidocaine from the subarachnoid space is monophasic with an absorption half-life of 71 min.

Distribution:

Lidocaine has a total plasma clearance of 0.95 L/min and a volume of distribution at steady state of 91 L.

Lidocaine readily crosses the placenta, and equilibrium with regard to the unbound concentration is rapidly reached. The degree of plasma protein binding in the fetus is less than in the mother, which results in lower total plasma concentrations in the fetus.

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.

Metabolism:

Lidocaine is metabolized rapidly by the liver, and metabolites and unchanged drug are excreted by the kidneys. The main metabolites formed from lidocaine are monoethylglycine xylidide (MEGX), glycinexylidide (GX), 2,6-dimethylaniline and 4- hydroxy-2,6-dimethylaniline. The N-dealkylation to MEGX, is considered to be mediated by both CYP1A2 and CYP3A4. The metabolite 2,6-dimethylaniline is converted to 4-hydroxy- 2,6-dimethylaniline by CYP2A6, and the latter is the major urinary metabolite in man. Only 3% of lidocaine is excreted unchanged. About 70% appears in the urine as 4-hydroxy-2,6- dimethylaniline.

Elimination:

Lidocaine has a terminal half-life of 1.6 h and an estimated hepatic extraction ratio of 0.65. The clearance of lidocaine is almost entirely due to liver metabolism, and depends both on liver blood flow and the activity of metabolizing enzymes.

The pharmacological/toxicological actions of MEGX and GX are similar to, but less potent than those of lidocaine. GX has a longer half-life (about 10 h) than lidocaine and may accumulate during long-term administration.

The elimination half-life of lidocaine following intravenous bolus injection is typically 1.5 to 2.0

hours. The terminal half-life in neonates (3.2 h) is approximately twice that of adults, whereas clearance is similar (10.2 mL/min kg). 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.

Special Populations and Conditions

Acidosis increases the systemic toxicity of lidocaine while the use of CNS depressants may increase the levels of lidocaine required to produce overt CNS effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6.0 mcg free base per mL.

11 STORAGE, STABILITY AND DISPOSAL

Lidocaine Hydrochloride Injection USP should be stored at controlled room temperature (15-30ºC). Protect from freezing. Keep out of the reach and sight of children.

12 SPECIAL HANDLING INSTRUCTIONS

Sterilization, and Technical Procedures

The solubility of lidocaine is limited at pH>6.5. This must be taken into consideration when alkaline solutions, i.e. carbonates, are added, since precipitation might occur.

Do not use if solution is coloured or if it contains a precipitate.

Lidocaine Hydrochloride Injection USP without preservative is for single use only. Discard unused portion.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

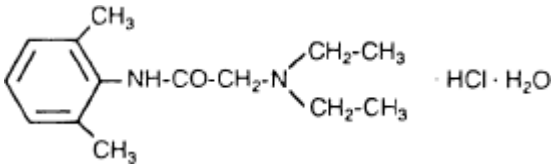
Drug Substance

Proper Name: lidocaine hydrochloride

Chemical Name: 2-Diethylamino-N-(2,6-dimethylphenyl)-acetamide monohydrochloride monohydrate

Molecular Formula and Molecular Mass: $C_{14}H_{22}N_2O.HCl.H_2O$, 288.8 g/mol

Structural formula:



Physicochemical Properties: White crystalline powder. Very soluble in water, freely soluble in alcohol. Melting range between 74 and 79°C. pHof 4.0 to 5.5 (0.5% solution in H_2O).

14 CLINICAL TRIALS

No clinical trials information is available for this product.

15 MICROBIOLOGY

No microbiological information is required for this product.

16 NON-CLINICAL TOXICOLOGY

Carcinogenicity

A chronic oral toxicity study of the metabolite 2,6-dimethylaniline (0, 14, 45, 135 mg/kg) administered in feed to rats showed that there was a significantly greater incidence of nasal cavity tumors in male and female animals that had daily oral exposure to the highest dose of 2,6-dimethylaniline for 2 years. The lowest tumor-inducing dose tested in animals (135 mg/kg) corresponds to approximately 11 times the amount of 2,6-dimethylaniline to which a 50 kg subject would be exposed following a single injection of 600 mg of lidocaine for injection,

assuming 80% conversion to 2,6-dimethylaniline. Based on a yearly exposure (once daily dosing with 2,6-dimethylaniline in animals and 5 treatment sessions with 600 mg lidocaine for injection in humans), the safety margins would be approximately 1000 times when comparing the exposure in animals to man.

17 SUPPORTING PRODUCT MONOGRAPHS

1. XYLOCAINE® (Lidocaine Hydrochloride Injection USP) parenteral solutions, 1% (10 mg/mL), 2% (20 mg/mL), submission control no. 267392, Prescribing Information, Aspen Pharmacare Canada Inc. (Mar 07, 2023).

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Lidocaine Hydrochloride Injection USP

Read this carefully before you start taking **Lidocaine Hydrochloride Injection USP** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Lidocaine Hydrochloride Injection USP**.

What is Lidocaine Hydrochloride Injection USP used for?

Lidocaine Hydrochloride Injection USP is used in adults and children (2 years of age or older), to provide pain relief by producing a temporary loss of feeling or numbness to the area that it is injected. It can be used:

- to numb the area of the body where surgery is to be performed;
- to provide pain relief in labour and after surgery.

Lidocaine Hydrochloride Injection USP should be used with caution in children younger than 2 years of age.

How does Lidocaine Hydrochloride Injection USP work?

Lidocaine Hydrochloride Injection USP belongs to a group of medicines called 'local anesthetics'. Lidocaine Hydrochloride Injection USP prevents the nerves in the injected area from transmitting signals to the brain. This causes a temporary loss of feeling or numbness, so you do not feel sensations such as pain, heat or cold.

What are the ingredients in Lidocaine Hydrochloride Injection USP?
Medicinal ingredients: lidocaine hydrochloride.
Non-medicinal ingredients: sodium chloride, water for injection, sodium hydroxide and/or hydrochloric acid (to adjust pH).

Lidocaine Hydrochloride Injection USP comes in the following dosage forms:
Sterile solution: 1% lidocaine hydrochloride contains 10 mg/mL lidocaine hydrochloride, and 2% lidocaine hydrochloride contains 20 mg/mL lidocaine hydrochloride.

Do not use Lidocaine Hydrochloride Injection USP if:

- you are allergic to lidocaine, any other "-caine" type anesthetics, or any of the non-medicinal ingredients in the product;

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Lidocaine Hydrochloride Injection USP. Talk about any health conditions or

problems you may have, including if you:

- are allergic to any other drugs, including any other local anesthetics;
- have an irregular heartbeat (arrhythmias) or other heart problems such as heart block;
- have inflammation and/or sepsis in the region of the injection;
- have sepsis;
- have liver disease;
- have severe kidney problems;
- have untreated heart disease;
- have untreated or severe high blood pressure;
- have a neurological disease or spinal deformities;
- have uncontrolled hyperthyroidism (an overactive thyroid) or diabetes;
- have epilepsy;
- have or have a family history of porphyria;
- have a condition called hypovolemia;
- have a blood circulation condition called 'peripheral vascular disorder';
- have problems with the blood supply to your brain because of obstructed arteries;
- are experiencing severe shock;
- are pregnant, think you are pregnant, or plan to become pregnant;
- are breastfeeding.

Other warnings you should know about:

Driving and using machines: In addition to the temporary loss of feeling and numbness, Lidocaine Hydrochloride Injection USP may have an effect on your mental function and coordination. This may impair your ability to move and decrease your alertness. Avoid driving or operating machinery on the day you receive Lidocaine Hydrochloride Injection USP.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Lidocaine Hydrochloride Injection USP:

- other local anesthetics;
- erythromycin, a medication used to treat bacterial infections;
- itraconazole, a medication used to treat fungal infections;
- propranolol, a medication used to treat high blood pressure;
- cimetidine, a medication used to treat heartburn and peptic ulcers;
- medications used to treat irregular heartbeat such as mexiletine or amiodarone;
- medications used to treat depression such as fluvoxamine, imipramine, triptyline drugs and monoamine oxidase inhibitors;
- certain medications used to treat headaches and migraines
- medications used to treat psychosis such as phenothiazine or butyphenones
- sedative medications
- inhaled anesthetics such as halothane or enflurane

How to take Lidocaine Hydrochloride Injection USP:

Usual Dose:
Lidocaine Hydrochloride Injection USP is given to you by a healthcare professional who is experienced in the use of anesthesia. The dose is decided by the healthcare professional and is based on the clinical need and your physical condition. In children, the dose is based on the child's weight, age and physical condition.

Overdose:

Lidocaine Hydrochloride Injection USP is only given by healthcare professionals who are well experienced in the use of anesthesia. If you experience an overdose or any serious side effects after receiving Lidocaine Hydrochloride Injection USP, the proper equipment and personnel will be immediately available to help you. Symptoms of an overdose may include:

- numbness of the lips and around the mouth,
- light-headedness or dizziness
- blurred vision
- hearing problems or tingling in the ears

In the event of a serious overdosage or a misplaced injection, trembling, seizures or unconsciousness may occur.

If the early signs of overdosage are noticed and no further Lidocaine Hydrochloride Injection USP is given, the risk of serious side effects occurring rapidly decreases. If you have any of these symptoms, **tell your healthcare professional immediately.**

If you think you, or a person you are caring for, have been given too much Lidocaine Hydrochloride Injection USP, contact a healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using Lidocaine Hydrochloride Injection USP?

These are not all the possible side effects you may have when taking Lidocaine Hydrochloride Injection USP. If you experience any side effects not listed here, tell your healthcare professional.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
COMMON			
Bradycardia (abnormally slow heartbeat)		**X**	
Dizziness, abnormal sensations (pins and needles)		**X**	
Feeling of sickness/nausea, vomiting (These side effects occur more frequently after epidural block).	**X**		
Hypertension (high blood pressure): shortness of breath, fatigue, dizziness or fainting, chest pain or pressure, swelling in your ankles and legs, bluish colour to your lips and skin, racing pulse or heart palpitations		**X**	
Hypotension (low blood pressure): dizziness, fainting, light-headedness, blurred vision, nausea, vomiting, fatigue (may occur when you go from lying or sitting to standing up)		**X**	
UNCOMMON			
Toxicity symptoms: convulsions, seizures, light-headedness, numbness of the lips and around the mouth, hearing, visual, or speech disturbances, trembling.			**X**
RARE			
Allergic reaction: difficulty swallowing or breathing, wheezing, feeling sick to your stomach and throwing up, hives or rash, swelling of the face, lips, tongue or throat			**X**
Cardiac arrest and/or irregular heartbeat			**X**
Double vision		**X**	
Nervous system disorders: weakness or paralysis of limbs or face, tingling of extremities, difficulty speaking, confusion, disorientation, trembling		**X**	

If you have a troublesome symptom or side effect that is not listed here or becomes bad

enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/healthcanada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or

- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

The healthcare professional is responsible for storing Lidocaine Hydrochloride Injection USP.

Lidocaine Hydrochloride Injection USP should be stored at controlled room temperature (15-30ºC). Protect from freezing. Keep out of the reach and sight of children.

If you want more information about Lidocaine Hydrochloride Injection USP:

- Talk to your healthcare professional
- Find the full prescribing information that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.formativepharma.com, or by calling 1-855-808-9528

This leaflet was prepared by:
Formative Pharma Inc.
Burlington, Ontario, L7L 6A3

Last revised: May 09, 2024