

LIDOCAINE HCL 2 % AND EPINEPHRIN 1:100000

חברת הנרי שיין שוודנט מבקשת להודיע על עדכונים בעלון לרופא של התכשיר שבנדון.

התווית התכשיר:

For the production of local anaesthesia by nerve block or infiltration.
Dental infiltration injection, dental nerve block.

מרכיב פעיל:

Mepivacaine hydrochloride

DENTAL INFILTRATION INJ. , DENTAL NERVE BLOCK

**צורת המתן של התכשיר :
עלון לרופא**

4.4) Special warnings and precautions for use:

WARNINGS

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To minimize the likelihood of intravascular injection, aspiration should be performed before the local anesthetic solution is injected. If blood is aspirated, the needle must be repositioned until no return of blood can be elicited by aspiration. Note, however, that the absence of blood in the syringe does not assure that intravascular injection will be avoided.

Local anesthetic procedures should be used with caution when there is inflammation and/or sepsis in the region of the proposed injection.

Lidocaine HCL 2 % and Epinephrin 1:100000 contains potassium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

The American Heart Association has made the following recommendations regarding the use of local anesthetics with vasoconstrictors in patients with ischemic heart disease: Vasoconstrictor agents should be used in local anesthesia solutions during dental practice only when it is clear that the procedure will be shortened or the analgesia rendered more profound. When a vasoconstrictor is indicated, extreme care should be taken to avoid intravascular injection. The minimum possible amount of vasoconstrictor should be used. (Kaplan, EL, editor: Cardiovascular disease in dental practice, Dallas 1986, American Heart Association.)

Methemoglobinemia: Cases of methemoglobinemia have been reported in association with local anesthetic use; Lidocaine, along with other local anesthetics, is capable of producing this condition. 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. 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 cyanosis of the skin, nail beds and lips, and/or abnormal coloration of the blood, fatigue and weakness. 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 and any other oxidizing agents. Depending on the severity of the signs and symptoms, patients may respond to supportive care, i.e., oxygen therapy, hydration. If methemoglobinemia does not respond to administration of oxygen, a more severe clinical presentation may require treatment with methylene blue exchange transfusion, or hyperbaric oxygen.

PRECAUTIONS

General: The safety and effectiveness of lidocaine depend on proper dosage, correct technique, adequate precautions and readiness for emergencies. Consult standard textbooks for specific techniques and precautions for various regional anesthetic procedures. Resuscitative equipment, oxygen and other resuscitative drugs should be available for immediate use (See sections 4.4 and 4.8).

The lowest dosage that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. Repeated doses of lidocaine may cause significant increases in blood levels with each repeated dose due to 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.

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

Lidocaine should be used with caution in patients with severe shock or heart block. Lidocaine should also be used with caution in patients with impaired cardiovascular function. Local anesthetic solutions containing a vasoconstrictor should be used with caution in areas of the body supplied by end arteries or having otherwise compromised blood supply.

Patients with peripheral vascular disease and those with hypertensive vascular disease may exhibit exaggerated vasoconstrictor response.

Ischemic injury (such as exfoliating or ulcerating lesions) or necrosis may result. Preparations containing a vasoconstrictor should be used with caution in patients during or following the administration of potent general anesthetic agents, since cardiac arrhythmias may occur under such conditions.

Cardiovascular and respiratory (adequacy of ventilation) vital signs and the patients state of consciousness should be monitored after each local anesthetic injection. Restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors, depression or drowsiness should alert the practitioner to the possibility of central nervous system toxicity. Signs and symptoms of depressed cardiovascular function may commonly result from a vasovagal reaction, particularly if the patient is in an upright position:

placing the patient in the recumbent position is recommended when an adverse response is noted after injection of a local anesthetic (See section 4.8 - Cardiovascular System). Vasovagal reactions may elicit a range of clinical manifestations, from prodrome signs of pre-syncope (e.g. light headedness, pallor, nausea, sweating, visual disturbances, weakness) to brief loss of consciousness (i.e. syncope).

Lidocaine should be used with caution in patients with hepatic disease, since amide-type local anesthetics are metabolized by the liver. Patients with severe hepatic disease, because of their

inability to metabolize local anesthetics normally, are at greater risk of developing toxic plasma concentrations.

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 management 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 suspected triggering agent(s) and prompt treatment, including oxygen therapy, dantrolene (consult dantrolene sodium intravenous package insert before using) and other supportive measures. Lidocaine should be used with caution in persons with known drug sensitivities. Patients allergic to para-aminobenzoic acid derivatives (procaine, tetracaine, benzocaine, etc.) have not shown cross sensitivity to lidocaine Use in the Head and Neck Area: Small doses of local anesthetics injected into the head and neck area, including retrobulbar, dental and stellate ganglion blocks, may produce adverse reactions similar to systemic toxicity seen with unintentional intravascular injections of larger doses. Confusion, convulsions, respiratory depression and/or respiratory arrest, and cardiovascular stimulation or depression have been reported. These reactions may be due to intra-arterial injection of the local anesthetic with retrograde flow to the cerebral circulation. Patients receiving these blocks should have their circulation and respiration monitored and be constantly observed. Resuscitative equipment and personnel for treating adverse reactions should be immediately available. Dosage recommendations should not be exceeded (See section 4.2).

Information for Patients/Patient Counseling Information: The patient should be informed of the possibility of temporary loss of sensation and muscle function following infiltration or nerve block injections.

The patient should be advised to exert caution to avoid inadvertent trauma to the lips, tongue, cheek mucosae or soft palate when these structures are anesthetized. The ingestion of food should therefore be postponed until normal function returns. The patient should be advised to consult the dentist if anesthesia persists or if a rash develops. Inform patients that use of local anesthetics may cause methemoglobinemia, a serious condition that must be treated promptly. Advise patients or caregivers to 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.

4.5) Interaction with other medicinal products and other forms of interaction:

The administration of local anesthetic solutions containing epinephrine or norepinephrine to patients receiving monoamine oxidase inhibitors, tricyclic antidepressants or phenothiazines may produce severe prolonged hypotension or hypertension. Concurrent use of these agents should generally be avoided. In situations when concurrent therapy is necessary, careful patient monitoring is essential.

Concurrent administration of vasopressor drugs and ergot-type oxytocic drugs may cause severe, persistent hypertension or cerebrovascular accidents.

As the Lidocaine HCL 2 % and Epinephrin 1:100000 contains a vasoconstrictor (epinephrine), concurrent use of either with a Beta-adrenergic blocking agent (propranolol, timolol, etc.) may result in dose-dependent hypertension and bradycardia with possible heart block. Patients who are administered local anesthetics are at increased risk of developing methemoglobinemia when concurrently exposed to the following drugs, which could include other local anesthetics:

EXAMPLES OF DRUGS ASSOCIATED WITH METHEMOGLOBINEMIA:

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

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.

4.6) Fertility, pregnancy and lactation:

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General consideration should be given to this fact before administering lidocaine to women of childbearing potential, especially during early pregnancy when maximum organogenesis takes place.

Nursing mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when lidocaine is administered to a nursing woman.

4.7) Effects on ability to drive and use machines:

Lidocaine in combination with adrenaline solution may have minor influence on the ability to drive and use machines. Dizziness (including vertigo, vision disorder and fatigue) may occur following administration of this product (see section 4.8). Patients should not leave the dental office within 30 minutes following the dental procedure.

4.8) Undesirable effects:

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Central Nervous System: CNS manifestations are excitatory and/or depressant and may be characterized by lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred or double vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest.

The excitatory manifestations may be very brief or may not occur at all, in which case the first manifestation of toxicity may be drowsiness merging into unconsciousness and respiratory arrest.

Drowsiness following the administration of lidocaine is usually an early sign of a high blood level of the drug and may occur as a consequence of rapid absorption.

Cardiovascular system: Cardiovascular manifestations in response to lidocaine are usually depressant and are characterized by bradycardia, hypotension, and cardiovascular collapse, which may lead to cardiac arrest. In addition, the beta-adrenergic receptor- stimulating action of epinephrine may lead to excitatory cardiovascular responses, such as tachycardia, palpitations, and hypertension.

Signs and symptoms of depressed cardiovascular function may commonly result from a vasovagal reaction, particularly if the patient is in an upright position. Less commonly, they may result from a direct effect of the drug.

Failure to recognize the premonitory signs such as sweating, a feeling of faintness, changes in pulse or sensorium may result in progressive cerebral hypoxia and seizure or serious cardiovascular catastrophe.

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Allergic reactions: Allergic reactions are characterized by cutaneous lesions, urticaria, edema, anaphylactoid reactions or **dyspnea due to bronchoconstriction**. Allergic reactions as a result of sensitivity to lidocaine are extremely rare and, if they occur, should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.

Neurologic reactions: The incidences of adverse reactions (e.g., persistent neurologic deficit) associated with the use of local anesthetics may be related to the technique employed, the total dose of local anesthetic administered, the particular drug used, the route of administration, and the physical condition of the patient.

Persistent paresthesias of the lips, tongue, and oral tissues have been reported with the use of lidocaine, with slow, incomplete, or no recovery. These post-marketing events have been reported chiefly following nerve blocks in the mandible and have involved the trigeminal nerve and its branches.

השינויים המודגשים ברקע צהוב מהווים החמרה. בעלון בוצעו שינויים נוספים אשר מהווים תוספת מידע.

העלון מפורסם במאגר התרופות שבאתר משרד הבריאות:

<https://data.health.gov.il/drugs/index.html#!/byDrug>

ניתן לקבלו מודפס באמצעות פניה לבעל הרישום, חברת הנרי שיין שוודנט

בברכה,

מירי חזן

רוקחת ממונה