רופא/ה נכבד/ה,
רוקח/ת נכבד/ה,

MEPIVACAINE HCl 3% INJECTION

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

התווית התכשיר:
For the production of local anaesthesia for dental procedures by infiltration or nerve block in adults and pediatric patients.
.

מרכיב פעיל:

Mepivacaine hydrochloride

צורת המתן של התכשיר : DENTAL INFILTRATION INJ. , DENTAL NERVE BLOCK

עלון לרופא):

4.3) Contraindications:

- Children weighing less than 30 lb. (= 13.6 kg),
- Severe disorders of atrioventicular conduction not compensated by pace maker,
- Poorly controlled epileptic patient.

4.4) Special warnings and precautions for use:

Mepivacaine must be used with caution in:
Patients with cardiovascular disorders:
- Peripheral vascular disease,
- Arrhythmias particularly of ventricular origin,
- Atrio-ventricular conduction disorders,
- Heart failure,
- Hypotension.

Mepivacaine should be administered with caution in patients with impaired cardiac function since they may be less able to compensate or worsen changes due to prolongation of atrio-ventricular conduction.
Epileptic patients: Because of their convulsive actions, all local anaesthetics should be used very cautiously. For poorly controlled epileptic patients, see section 4.3.
Patients with a hepatic disease: The lowest dose leading to efficient anaesthesia should be used.
Patients with a kidney disease: The lowest dose leading to efficient anaesthesia should be used.
Patients with porphyria: MEPIVACAINE HCl 3% INJECTION should only be used to patients with acute porphyria when no safer alternative is available. Caution should be taken in all patients with porphyria, as this medicinal product may trigger porphyria.
Patients with acidosis: Caution should be used in case of acidosis such as worsened of renal insufficiency or poorly control of type 1 diabetes mellitus.
Elderly patients: Dosages should be reduced in elderly patients (due to lack of clinical data).
Mepivacaine should be administered with caution in patients, who are using antiplatelet / anticoagulant medicines or are suffering from a coagulation disorder, because of

higher risk of bleeding. The higher risk of bleeding is more associated with the procedure, rather than with the medicine.
Precautions for use: Local anaesthetics should only be employed by healthcare professionals who are well versed in diagnosis and management of dose-related toxicity and other acute emergencies which might arise from the block to be employed.
…

Hypoxaemia and metabolic acidosis may potentiate the cardiovascular toxicity. Early control of seizures and aggressive airway management to treat hypoxaemia and acidosis may prevent cardiac arrest. Concomitant use of the other medicinal products may require thorough monitoring (see section 4.5).

4.5) Interaction with other medicinal products and other forms of interaction
Additive interactions with other local anaesthetics: Toxicity of local anaesthetics is additive. The total dose of administered mepivacaine should not exceed the maximum recommended dose.
H2 antihistaminics (cimetidine): Increased serum levels of amide anaesthetics have been reported after concomitant administration of cimetidine. Cimetidine reduces the clearance of mepivacaine.
…

Antiarrhythmic drugs: Patients who are being treated with antiarrhythmic drugs may encounter an accumulation of side effects after the use of mepivacaine due the similarity of structures (such as Class I drug i.e. lidocaine).
CYP1A2 inhibitors: Mepivacaine is metabolised primarily by CYP1A2 enzyme. Inhibitors of this cytochrome (e.g. ciprofloxacin, enoxacin, fluvoxamine) may decrease its metabolism, increase the risk of adverse effects and contribute to prolonged or toxic blood levels. Increased serum levels of amide anaesthetics have also been reported after concomitant administration of cimetidine, which is probably due to the inhibitory effect of cimetidine on CYP1A2. Caution is advised when associating the product of interest with these medications as dizziness may last longer (see section 4.7.).
Propranolol: The clearance of mepivacaine may be reduced when associated with propranolol and it may result in higher serum concentrations of the anaesthetic. Caution should be exercised when mepivacaine is administered concomitantly with propranolol.

4.6) Fertility, pregnancy and lactation:
…
Breastfeeding: No nursing mothers were included in the clinical studies with MEPIVACAINE HCl 3% INJECTION. However, considering the lack of data for mepivacaine, a risk to the newborns/infants cannot be excluded.
Therefore, nursing mothers are advised not to breastfeed within 10 hours following anaesthesia with MEPIVACAINE HCl 3% INJECTION.

4.7) Effects on ability to drive and use machines
MEPIVACAINE HCl 3% INJECTION may have a minor influence on the ability to drive and use machines.

Dizziness (including vertigo, vision disorder and fatigue) may occur following administration of mepivacaine (see section 4.8). So, patients should not leave the dental office until they recover their abilities (generally within 30 minutes) following the dental procedure.

4.8) Undesirable effects:

MedDRA System Organ Class	Frequency	Adverse Reactions
Immune system disorders	Rare	Angioedema (Face / tongue / lip / throat / larynx / periorbital oedema) Bronchospasm / asthma
Psychiatric disorders	Not known	Anxiety
Nervous system disorders	Common	Headache
	Rare	Neuropathy Neuralgia (Neuropathic pain) Hypoesthesia / numbness (oral and perioral) Dysesthesia (oral and perioral), including dysgeusia (e.g., taste metallic, taste distorted), ageusia Coma Presyncope, syncope; Confusional state, Speech disorder (e.g., dysarthria, logorrhea) Restlessness / agitation Balance disorder (disequilibrium)
	Not known	Nystagmus
Eye disorders	Rare	Accommodation disorder
	Not known	Horner's syndrome Eyelid ptosis Enophthalmos Diplopia (paralysis of oculomotor muscles) Amaurosis (blindness) Mydriasis Miosis
Ear and labyrinth disorders	Rare	Vertigo
	Not Known	Ear discomfort Tinnitus Hyperacusis
Cardiac disorders	Rare	Cardiac arrest Bradyarrhythmia Bradycardia Tachyarrhythmia (including ventricular extrasystoles and ventricular fibrillation) Angina pectoris Conduction disorders (atrioventricular block) Tachycardia palpitations
	Not known	Myocardial depression
Vascular disorders	Rare	Hypotension (with possible circulatory collapse)
	Very rare	Hypertension
	Not known	Vasodilatation Local / Regional hyperaemia

MedDRA System Organ Class	Frequency	Adverse Reactions
Respiratory, thoracic and mediastinal disorders	Rare	Respiratory depression Bradypnoea Yawning Dyspnoea Tachypnea
	Not known	Hypercapnia Dysphonia (Hoarseness)
Gastrointestinal disorders	Rare	Nausea Vomiting Gingival / oral mucosal exfoliation (sloughing) / ulceration
	Not known	Stomatitis, glossitis, gingivitis Salivary hypersecretion
Skin and subcutaneous tissue disorders	Rare	Erythema Pruritus
Musculoskeletal and connective tissue disorders	rare	Muscle twitching Chills (shivering)
General disorders and administration site conditions	Not known	Chest pain Fatigue, asthenia (weakness) Feeling hot Injection site pain
Injury, poisoning and procedural complications	Not known	Nerve injury

4.9) Overdose:

Symptoms: In case of relative overdose, patients generally present symptoms within 1-3 minutes. Whereas in case of absolute overdose, signs of toxicity, depending on the injection site, appear about 20-30 minutes after the injection. Toxic effects are dose-dependent, comprising progressively more severe neurological manifestations, followed by vascular, respiratory and finally cardiovascular signs such as hypotension, bradycardia, arrhythmia and cardiac arrest. CNS toxicity occurs gradually, with symptoms and reactions of progressively increasing severity. Initial symptoms include agitation, a feeling of intoxication, a sensation of numbness in the lips and tongue, paraesthesia around the mouth, dizziness, visual and hearing disturbances, and buzzing in the ears. Manifestation of these effects during injection of the product is a warning signal and the injection should be stopped immediately. Cardiovascular symptoms occur at plasma levels exceeding those inducing CNS toxicity and are therefore generally preceded by signs of CNS toxicity, unless the patient is under general anaesthesia or is heavily sedated (e.g. by a benzodiazepine or barbiturate). Loss of consciousness and the onset of generalized seizures may be preceded by premonitory symptoms such as joint and muscle stiffness, or twitching.

Seizures may last from a few seconds to several minutes and rapidly lead to hypoxia and hypercapnia, as a result of increased muscular activity and insufficient ventilation. In severe cases, respiratory arrest may occur.

Undesirable toxic effects may appear at plasma concentrations upper than 5 mg/l, and convulsions could appear with 10 mg/l or higher. Limited data of overdose are available.

Acidosis exacerbates the toxic effects of local anaesthetics. If a rapid intravascular injection is administered, a high blood concentration of mepivacaine in the coronary arteries may lead to myocardial failure, possibly followed by cardiac arrest, before the CNS is affected. The data on this effect remains controversial (see Sections 4.4 and 5.1).

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

24 Hametzu la St. Azur, 58061 Tel: 972 3 6534600 Fax: 972 3 6534040 e-mail: info@shvaden
7 a Rachel Imenu st, Jerusalem 93145 Tel: 972 2 5663627 Fax: 972 2 5671083