22.5.2022

רופא/ה נכבד/ה,
רוקח/ת נכבד/ה,

ARTICAINE HCL 4 % AND EPINEPHRINE 1 : 100,000
ARTICAINE HCL 4 % AND EPINEPHRINE 1 : 200,000

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

התווית התכשיר:
For infiltration anaesthesia and nerve block anaesthesia in clinical dentistry.

מרכיב פעיל:

EPINEPHRINE BITARTRATE 0.015 MG / 1.7 ML
ARTICAINE HYDROCHLORIDE 68 MG / 1.7 ML
DENTAL INFILTRATION INJ. , DENTAL NERVE BLOCK

צורת המתן של התכשיר : עלון לרופא):

4.3) Contraindications:

- Patients with epilepsy not controlled by treatment.

4.4) Special warnings and precautions for use:

Patients with renal disease: The lowest dose leading to effective anaesthesia should be used.

Patients with myasthenia gravis treated by acetylcholinesterase inhibitors: The lowest dose leading to effective anaesthesia should be used.

Patients with porphyria: Articaine HCl 4% and Epinephrine 1:200,000 and Articaine HCl 4% and Epinephrine 1:100,000 should only be used in patients with acute porphyria when no safer alternative is available. Appropriate precautions should be taken in all patients with porphyria, as this medicinal product can trigger porphyria.

Patients with concomitant treatment with halogenated inhalation anaesthetics: The lowest dose of the medicinal product leading to effective anaesthesia should be used (see section 4.5).

Elderly patients: Elevated product plasma levels may occur in elderly patients in particular after repeated use. In case of required reinjection, patient should be strictly monitored, to identity any sign of relative overdose (see section 4.9).
Therefore, the lowest dose leading to effective anaesthesia should be used.
The use of Articaine HCl 4% and Epinephrine 1:200,000 over Articaine HCl 4% and Epinephrine 1:100,000 should be considered on account of its lower epinephrine content of 5 micrograms/ml in:

- *Patients with cerebral circulation disturbances, history of strokes:* It is recommended that dental treatment with articaine/epinephrine be deferred for six months following a stroke due to the increased risk of recurrent strokes.

This medicinal product must be used safely and effectively under appropriate conditions*:* Epinephrine impairs the flow of blood in the gums, potentially causing local tissue necrosis.

Very rare cases of prolonged or irreversible nerve injury and gustatory loss have been reported after mandibular block analgesia.

The local anaesthetic effects may be reduced when this medicinal product is injected into an inflamed or infected area.

The dose must also be reduced in case of hypoxia, hyperkalaemia and metabolic acidosis.

Risk of biting trauma (lips, cheeks, mucosa, and tongue) exists, especially in children; the patient should be told to avoid chewing gum or eating until normal sensation is restored.

Precautions for use:
Risk associated with accidental intravascular injection: Accidental intravascular injection may cause sudden high levels of epinephrine and articaine in the systemic circulation. This may be associated with severe adverse reactions, such as convulsions, followed by central nervous and cardiorespiratory depression and coma, progressing to respiratory and circulatory arrest.
Thus, to ensure that the needle does not penetrate a blood vessel during injection, aspiration should be performed before the local anaesthetic medicinal product is injected. However, the absence of blood in the syringe does not guarantee that intravascular injection has been avoided.

Risk associated with intraneural injection: Accidental intraneural injection may lead the drug to move in retrograde manner along the nerve.
In order to avoid intraneural injection and to prevent nerve injuries in connection with nerve blockades, the needle should always be slightly withdrawn if electric shock sensation is felt by the patient during injection or if the injection is particularly painful. If needle nerve injuries occur, the neurotoxic effect could be aggravated by articaine potential chemical neurotoxicity and the presence of epinephrine as it may impair the perineural blood supply and prevent articaine local wash-out.

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

Interactions requiring precautions for use:
Other local anaesthetics: Toxicity of local anaesthetics is additive. The total dose of all local anaesthetics administered should not exceed the maximum recommended dose of the drugs used.

Sedatives (central nervous system depressants e.g. benzodiazepine, opioids): If sedatives are employed to reduce patient's apprehension, reduced doses of anaesthetics should be used since local anaesthetic agents, like sedatives, are central nervous system depressants which in combination may have an additive effect (see section 4.2).

Postganglionic adrenergic blocking agents (e.g., guanadrel, guanethidine, and rauwolfia alkaloids): Reduced doses of this medicinal product should be used under strict medical supervision with careful aspiration due to possible increase response to adrenergic vasoconstrictors: risk of hypertension and other cardiovascular effects.

Non-selective beta-adrenergic blockers (e.g., propranolol, nadolol): Reduced doses of this medicinal product should be used due to possible increase in blood pressure and an increased risk of bradycardia.

COMT inhibitors (Catechol-O-methyl transferase inhibitors) (e.g., entacapone, tolcapone): Arrhythmias, increased heart rate and blood pressure variations may occur.
A reduced amount of epinephrine in dental anaesthesia should be given to patients on COMT inhibitors.

Drugs causing arrhythmias (e.g., antiarrhythmics like digitalis, quinidine): Dose of administration of this medicinal product should be reduced due to the increased risk of arrhythmia when both epinephrine and digital

glucosides are administered concomitantly to patients. Careful aspiration prior to administration is recommended.

Ergot-type oxytocic drugs (e.g., methysergide, ergotamine, ergonovine): Use this medicinal product under strict medical supervision due to additive or synergistic increases in blood pressure and/or ischemic response.

Sympathomimetic vasopressors (e.g., mainly cocaine but also amphetamines, phenylephrine, pseudoephedrine, oxymetazoline): There is a risk of adrenergic toxicity. If any sympathomimetic vasopressor has been used within 24 hours, the planned dental treatment should be postponed

4.6) Fertility, pregnancy and lactation:

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Epinephrine and articaine cross the placental barrier, although articaine does so to a lesser extent than other local anaesthetics. Serum concentrations of articaine measured in newborn infants were approx. 30% of maternal levels. In the event of inadvertent intravascular administration in the mother, epinephrine can reduce uterine perfusion.

Breastfeeding: As a result of the rapid drop in serum levels and rapid elimination, clinically relevant quantities of articaine are not found in breast milk. Epinephrine passes into breast milk but also has a short half-life. It is not usually necessary to suspend breast-feeding for short-term use, starting from 5 hours following anesthesia.

4.7) Effects on ability to drive and use machines

The combination articaine hydrochloride with epinephrine bitartrate solution for 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 Articaine HCl 4% and Epinephrine 1:200,000 and Articaine HCl 4% and Epinephrine 1:100,000 (see Section 4.8 of Physician's Prescribing Information). 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**
Infections and infestations	Common	Gingivitis
Psychiatric disorders	Not known	Euphoric mood
Nervous system disorders	Common	Neuropathy: Neuralgia (neuropathic pain) Hyperesthesia Dysesthesia (oral and perioral), *including* Dysgeusia (e.g., taste metallic, taste disturbance) Ageusia Allodynia Thermohyperesthesia
	Rare	Horner's syndrome (eyelid ptosis, enophthalmos, miosis).
Eye disorders	Rare	Diplopia (paralysis of oculomotor muscles)[4] Visual impairment (temporary blindness)[4] Ptosis Miosis Enophthalmos
Ear and labyrinth disorders	Rare	Hyperacusis Tinnitus[4]
Cardiac disorders	Common	Bradycardia Tachycardia

MedDRA System Organ Class	Frequency	Adverse Reactions
	Rare	Palpitations
Vascular disorders	Common	Hypotension (with possible circulatory collapse)
	Uncommon	Hypertension
	Rare	Hot flush
	Not known	Local / Regional hyperaemia Vasodilatation Vasoconstriction
Respiratory, thoracic and mediastinal disorders	Rare	Bronchospasm / asthma Dyspnoea[2]
	Not known	Dysphonia (Hoarseness)[1]
Gastrointestinal disorders	Common	Swelling of tongue, lip, gums
	Uncommon	Stomatitis, glossitis, diarrhoea
	Rare	Gingival / oral mucosal exfoliation (sloughing) / ulceration
Skin and subcutaneous tissue disorders	Uncommon	Rash (eruption) Pruritus
	Rare	Angioedema (face / tongue / lip / throat / larynx / periorbital oedema) Urticaria
	Not known	Erythema Hyperhidrosis
Musculoskeletal and connective tissue disorders	Uncommon	Neck pain
	Not known	Aggravation of the neuromuscular manifestations in Kearns-Sayre syndrome Trismus
General disorders and administration site conditions	Uncommon	Injection site pain
	Rare	Injection site exfoliation / necrosis Fatigue, asthenia (weakness) / Chills
	Not known	Local swelling Feeling hot Feeling cold

4.9) Overdose:
Due to articaine: The symptoms are dose-dependent and have progressive severity in the realm of neurological manifestations (presyncope, syncope, headache, restlessness, agitation, confusional state, disorientation, dizziness (lightheadedness), tremor, stupor, deep CNS depression, loss of consciousness, coma, convulsion (including tonic-clonic seizure), speech disorder (e.g., dysarthria, logorrhea), vertigo, balance disorder (disequilibrium)), eyes manifestations (mydriasis, vision blurred, accommodation disorder) followed by vascular (pallor (local, regional, general)), respiratory apnoea (respiratory arrest), bradypnoea, tachypnoea, yawning, respiratory depression) and finally cardiac (cardiac arrest, myocardial depression) toxicity.
Acidosis exacerbates the toxic effects of local anaesthetics.

Due to epinephrine: The symptoms are dose-dependent and have progressive severity in the realm of neurological manifestations (restlessness, agitation, presyncope, syncope) followed by vascular (pallor (local, regional, general)), respiratory (apnoea (respiratory arrest), bradypnoea, tachypnoea, respiratory depression) and finally cardiac (cardiac arrest, myocardial depression) toxicity.

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

העלון מפורסם במאגר התרופות שבאתר משרד הבריאות:

https://israeldrugs.health.gov.il/#!/byDrug

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

בברכה,

מירי חזן
רוקחת ממונה