PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

CARBOCAINE 3 % DENTAL

Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1,8 ml contains 54 mg Mepivacaine hydrochloride.

Glucose free.

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM.

Injection

Clear, colourless, practically free from particulate matter solution for injection.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

For the production of local anaesthesia for conservative dental work and surgical interventions in the oral region.

4.2 Posology and method of administration

Posology

The dose varies and depends on the area to be anaesthetized, vascularity of the tissues, number of neuronal segments to be blocked, individual tolerances and the technique of anaesthesia. The lowest dose needed to provide effective anaesthesia should be administered.

The average dose of one dental cartridge will usually suffice. This dose may be doubled if necessary, to effect anaesthesia. The maximum adult dose should not exceed 400 mg mepivacaine hydrochloride, (approximately 7 mg/kg) at any one time and the total dose should not exceed 1g in any twenty-four hour period.

Do not exceed the recommended dose.

Any unused portion of a dental cartridge should be discarded.

Local anaesthetics should only be administered by dental medical practitioners or other suitable qualified healthcare professionals.

RESUSCITATIVE EQUIPMENT, OXYGEN AND EMERGENCY MEDICINES SHOULD BE IMMEDIATELY AVAILABLE WHEN ANY ANAESTHETIC IS USED.

DISINFECTION OF CARBOCAINE 3 % DENTAL *injection cartridges:*

The diaphragm should be disinfected before needle puncture. Immerse only the metal cap in undiluted isopropyl alcohol or 70 % ethyl alcohol for at least fifteen minutes. Only enough cartridges for one day's use should be stored in the alcohol.

4.3. Contraindications

CARBOCAINE 3 % DENTAL injection is contraindicated in patients with a known hypersensitivity to the amide type of local anaesthetic or excipients.

Children below 4 years of age (ca. 20 kg body weight).

Porphyria.

Patient with severe disorders of the atrioventricular conduction not compensated by pacemaker.

Epilepsy not controlled by appropriate treatment.

4.4 Special warnings and precautions for use

DO NOT AUTOCLAVE.

Safe use of CARBOCAINE 3 % DENTAL injections during pregnancy has not been established with respect to fetal development.

Patients with myasthenia gravis are particularly susceptible to the effects of local anaesthetics.

Warnings

Risk of anaesthesiophagia: various biting trauma (lips, cheeks, mucosa, tongue); advise the patient to avoid chewing gum or foodstuffs as long as there is no sensitivity.

In children under 4 years of age, the product is not recommended.

Athletes should be warned that this medicinal product contains an active substance likely to induce a positive reaction to tests undertaken in anti-doping controls.

Precautions for use

Practitioners who use local anaesthetic agents should be well versed in the diagnosis and management of emergencies which may arise from their use.

Resuscitation equipment, oxygen and other resuscitation medicines should be available for immediate use.

Mepivacaine use requires:

- Consultation to assess medical history and ongoing concomitant medication.
- Aspiration before the local anaesthetic solution is injected, so as to minimize the risk of intravascular injection.
- Slow injection while talking to the patient.

The lowest dosage that results in effective anaesthesia should be used to avoid high plasma levels and serious adverse effects. Repeated doses of mepivacaine may cause significant increases in blood levels with each repeat 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.

Cardiovascular and respiratory (adequacy of ventilation) vital signs and the patient's state of consciousness should be monitored after each local anaesthetic injection.

Restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors, depression of consciousness 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.

Dose should be minimised for patients suffering from hepatic (due to hepatic metabolism) or renal disease.

Use with caution when there is inflammation and/or sepsis in the area of the proposed injection site. Injection into highly vascular areas especially if these are inflamed or traumatised, may result in reduced effect and increased absorption.
The effect of mepivacaine hydrochloride may be reduced if the injection is made into an inflamed or infected area with a low tissue pH.

Monitoring should be increased in patients under anti-coagulant treatment (monitoring of the INR).

Mepivacaine should be used cautiously (reduce the dose) in case of hypoxia, hyperkalemia and acidosis.

Due to its cardiotoxicity effect, mepivacaine should be used with caution in patients with repolarisation disorders such as QT prolongation; the indication and Posology must be considered to prevent increased plasma concentration, which might cause severe ventricular arrhythmia.

In common with other local anaesthetics, Mepivacaine hydrochloride should be given with caution to patients with epilepsy, impaired cardiac conduction, or impaired respiratory function, or with liver damage.

The product is for single use on one patient during one treatment only. Any remaining contents should be discarded.

4.5 Interaction with other medicines and other forms of interaction

Increased serum levels of amide anaesthetics have been reported after concurrent administration of cimetidine.

If sedatives are employed to reduce patient apprehension, reduced doses of anaesthetic solution should be used since local anaesthetic agents, like sedatives, are central nervous system depressants which in combination may have an additive effect. There is an increased risk of myocardial depression when amide-type local anaesthetics are given with antiarrhythmics.

4.6 Fertility, pregnancy and lactation

Pregnancy

On the basis of long usage, anaesthetics of the mepivacaine type are considered to be reasonably safe for use on pregnant women.

Retrospective studies of pregnant women receiving local anaesthetics for emergency surgery early in pregnancy have not shown that local anaesthetics cause birth defects.

However, no controlled studies have been carried out in pregnant women.

Moreover, no reproduction studies have been performed with the product.

Therefore, risk to benefit consideration should be evaluated before administering this anaesthetic during early pregnancy.

Lactation

It is not known whether local anaesthetics are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when mepivacaine is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

Mepivacaine hydrochloride may have a minor influence on the ability to drive and use machines. Dizziness (including vertigo, vision disorder and fatigue) may occur following the administration of mepivacaine hydrochloride (see section 4.8). Patients experiencing these symptoms should not drive or use machinery until any such symptoms have completely resolved.

4.8 Undesirable effects

The reported adverse effects come from spontaneous reporting and literature.

The frequency classification follows the convention: Very common (≥1/10), Common (≥1/100 to <1/10), Uncommon

((≥1/1000 to <1/100), Rare ((≥1/10,000 to <1/1000) and Very rare (<1/10,000). Frequency “not known”: cannot be estimated from the available data.

MedDRA system organ classes (SOC)	**Frequency**	**Undesirable effect**
Blood and the lymphatic system disorders		Methaemoglobinaemia.
Immune system disorders	Rare	Hypersensitivity Anaphylactic / anaphylactoid reactions Angioedema (Face/ tongue/ lip/throat/ larynx/ periorbital oedema) Bronchospasm/ asthma Urticaria
Psychiatric disorders	Not known	Anxiety/ Nervousness, Euphoric mood, Apprehension
Nervous system disorders	Common Rare	Headache Neuropathy: Neuralgia (neuropathic pain) Paresthesia (i.e. burning, prickling, itching, tingling, local sensation of heat or cold, with no apparent physical cause) of oral and perioral structures Hypoesthesia / numbness of the tongue and perioral region, Dysesthesia (oral and perioral), including dysgeusia (e.g., taste metallic, taste distorted), ageusia,

		dizziness (light-headedness), Tremor. Deep CNS depression: Loss of consciousness, Coma, Convulsions (including tonic clonic seizure), Presyncope, syncope Confusional state, disorientation, Vertigo, Speech disorder (e.g. dysarthria, logorrhoea) Restlessness, agitation Balance disorder (disequilibrium), Somnolence,
	Not known	Nystagmus.
Eye disorders	Rare	Visual impairment Blurred vision Accommodation disorders
	Not known	Horner's syndrome Eyelid ptosis Enophthalmos Diplopia (paralysis of oculomotor muscles) Amaurosis, blindness Mydriasis Miosis

Ear and labyrinth disorders	Not known	Ear discomfort Tinnitus Hyperacusis
Cardiac disorders	Rare	Myocardial depression, Cardiac arrest Bradyarrhythmia Bradycardia Tachydysrhythmia (including ventricular extrasystoles and ventricular fibrillation) Angina pectoris Conduction disorders (atrioventricular block) Tachycardia Palpitations Dysrhythmia
Vascular disorders	Rare Very rare Not known	Hypotension (with possible circulatory collapse) Hypertension Vasodilatation
Respiratory, thoracic and mediastinal disorders	Rare Not known	Respiratory depression Bradypnoea Apnoea (respiratory arrest) Yawning Dyspnoea Hypoxia (including cerebral) Hypercapnia Dysphonia (hoarseness)

Gastrointestinal disorders	Rare Not known	Nausea Vomiting Gingival / oral mucosal exfoliation (sloughing) / ulceration Swelling of tongue, lip, gums Stomatitis, glossitis, gingivitis
Skin and subcutaneous disorders	Rare	Rash (eruption) Pruritus Swelling face
Musculoskeletal and connective tissue disorders	Rare	Muscle twitching Chills (shivering)
General disorders and administration site conditions	Rare Not known	Local swelling Injection site swelling Oedema Chest pain Fatigue, asthenia (weakness) Feeling hot Injection site pain
General injury, poisoning and procedural complications	Not known	Nerve injury

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://sahpra.org.za/wp-content/uploads/2020/01/6.04_ARF1_v5.1_27Jan2020.pdf

4.9 Overdose

Symptoms of overdosage correspond to the side effects. Cardio-respiratory arrest and convulsions as well as somnolence may occur. Treatment is symptomatic and supportive. Resuscitative equipment and emergency medicines should always be immediately available, as symptomatic treatment is recommended.

Acute emergencies from local anaesthetics are generally related to high plasma levels encountered during therapeutic use of excessive dosages of local anaesthetics or to unintended intravascular injections of local anaesthetic solution (see section 4.4 Special warnings and precautions for use, and section 4.8, Undesirable effects).

Symptomatology

The symptoms are dose-dependent and have progressive severity in the realm of neurological manifestations, followed by vascular, respiratory and finally cardiac toxicity (see section 4.8).

Central Nervous System toxicity is typical of the entire class of local anaesthetics. Symptoms may include light-headedness, dizziness, restlessness, auditory and visual disturbances, drowsiness,

disorientation, slurred speech, shivering, muscle twitching, tremors of the face, fingers and toes, generalized seizures and respiratory arrest. Hypoxia and hypercapnia occur rapidly following convulsions due to increased muscular activity, together with the interference with normal respiration. In severe cases, apnoea may occur. Acidosis increases the toxic effects of local anaesthetics.

Effects on the cardiovascular system may be seen in the severe cases. Hypotension, bradycardia, arrhythmia and cardiac arrest may occur as a result of high systemic concentrations, with potentially fatal outcome.

Recovery occurs as a consequence of redistribution of the local anaesthetic drug from the central nervous system and metabolism and may be rapid unless large amounts of the drug have been injected.

Management of local anaesthetic emergencies

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 anaesthetic injection. At the first sign of change, oxygen should be administered.

The first step in the management of convulsions consists of immediate attention to the maintenance of a patent airway and assisted or controlled ventilation with oxygen and a delivery system capable of permitting immediate positive airway pressure by mask.

Immediately after the institution of these ventilatory measures, the adequacy of the circulation should be evaluated, keeping in mind that drugs used to treat convulsions sometimes depress the circulation when administered intravenously. Should convulsions persist despite adequate respiratory support and if the status of the circulation permits, small increments of an ultra-short acting barbiturate or a benzodiazepine may be administered intravenously.

The clinician should be familiar, prior to use of local anaesthetics, with these anticonvulsant drugs.

Supportive treatment of circulation depression may require administration of intravenous fluids and, when appropriate, a vasopressor as directed by the clinical situation (e.g., Ephedrine).

If not treated immediately, both convulsions and cardiovascular depression can result in hypoxia, acidosis, bradycardia, arrhythmias and cardiac arrest. If cardiac arrest should occur, standard cardio-pulmonary resuscitative measures should be instituted.

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

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: A. 4. Local anaesthetics.

ATC code: N01BB03

Mepivacaine is a local anaesthetic of the amide type. It has a rapid onset causing a long duration reversible block of the motor and sensorial nervous fibres and of the heart stimulation.

Vasoconstriction reactions have been noted only in the case of intradermic administration.

Mepivacaine decreases the permeability of the membrane to the cations, more particularly sodium and potassium, when concentrations are high. The nervous fibres excitability decreases according to the concentrations, as the sudden increase of the permeability to sodium necessary to the formation of an action potential lowers. The neutral base comes through the myelinic tube more rapidly than the cation. The exact effect of the local anaesthetic effect has not yet been explained. The models

developed until now are still hypothetical. After having taken the axon internal pH, the cation is likely to induce the nerve block, as present active form of the local anaesthetic

The activity of the membrane is modified, and it will regard the local anaesthetic molecules which are not charged as cautions as well.

5.2 Pharmacokinetic properties

Absorption

The link of plasma proteins is 60-78 % for mepivacaine.

The blood half-life lasts between 2 and 3 hours. The clearance of the amides depends strongly on the liver irrigation.

Metabolism

The metabolism of mepivacaine occurs mainly through an oxidising process in the liver. The hydroxylated metabolites are eliminated mainly by the bile. The metabolites are then reabsorbed by the intestines and eliminated in the urine.

Elimination

In adults, only 5 % of mepivacaine is eliminated as the unchanged form, through the kidneys. The remaining part of the administered dose is eliminated in the urine under the form of PPX and glucuronized PPX hydroxylated metabolites. Only a small part of the metabolites is found in the faeces.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store at or below 25 ^{0}C. Protect from light.

6.5 Nature and contents of container

Available in 1,8 ml dental cartridges in cans of 100 cartridges and 10 x 10 blisters of 1,8 ml dental cartridges packed into a cardboard carton.

6.6 Special precautions for disposal and other handling

One cartridge should be used on one patient during one session of treatment only. If only part is used, the remainder must be discarded.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

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Midrand, 1685

Private Bag X69, Bryanston, 2021

www.adcock.com

8. REGISTRATION NUMBER(S)

G2753 (Act 101/1965)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18 August 1988

10. DATE OF REVISION OF THE TEXT

02 May 2022