Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Scandonest 3% w/v Solution for Injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Mepivacaine hydrochloride 30.00 mg/ml.

Also contains Sodium (<1mmol/ml)

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless liquid.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Local anaesthetic for dental use.

4.2 Posology and method of administration

Administration:

Local injection (block or infiltration).

Adults:

Use 1 to a maximum of 3 cartridges.

Pediatric population:

Children from 4 years of age (ca. 20kg body weight) and older (see 4.3)

Recommended therapeutic dose:
The quantity to be injected should be determined by the age and weight of the child and the magnitude of the operation. The average dosage is 0.75mg/kg=0.025ml of mepivacaine solution per kg body weight.

Maximum recommended dosage:
Do not exceed the equivalent of 3mg mepivacaine/kg (0.1ml mepivacaine/kg) of body weight

4.3 Contraindications

- Children below 4 years of age (ca. 20 kg body weight)
- Hypersensitivity to the active ingredient or to amide type anaesthetics.
- Porphyria.
- Patient with severe disorders of the atrioventricular conduction not compensated by pace-maker.
- Epilepsy not controlled by any treatment.

4.4 Special warnings and precautions for use

Warnings
Risk of anaesthesiophagia: various biting trauma (lips, cheeks, mucosa, tongue); tell 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, due to anaesthetic procedure not suitable under this age.

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 diagnosis and management of emergencies which may arise from their use.
Resuscitation equipment, oxygen and other resuscitation drugs 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 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 metabolisation) 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.

Monitoring should be increased in patients under anti-coagulants (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 disorder such as QT prolongation; the indication and Posology must be discussed to prevent increased plasmatic concentration, which might cause severe ventricular arrhythmia.

In common with other local anaesthetics, Mepivacaine should be used cautiously in patients with epilepsy, impaired cardiac conduction, or impaired respiratory function.

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

4.5 Interaction with other medicinal products 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.

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, caution should be taken 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 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.

The seriousness of adverse reactions is classified from 1 (most serious) to 3 (less serious) in the following table:

MedDRA System Organ Class	Frequency	Adverse reactions
Immune system disorders	Rare	Hypersensitivity Anaphylactic / anaphylactoid reactions Angioedema (Face / tongue / lip / throat / larynx / periorbital oedema) Bronchospasm / asthma Urticaria
Psychiatric disorders	Not known	Euphoric mood

		Anxiety / Nervousness 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 (oral and perioral) Dysesthesia (oral and perioral), including dysgeusia (e.g., taste metallic, taste distorted), ageusia Dizziness (lightheadedness) Tremor Deep CNS depression: Loss of consciousness Coma Convulsion (including tonic clonic seizure) Presyncope, syncope Confusional state, disorientation Vertigo Speech disorder (e.g. dysarthria, logorrhea) Restlessness, agitation Balance disorder (disequilibrium) Somnolence
	Not known	Nystagmus
Eye disorders	Rare	Visual impairment Vision blurred 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, Tachyarrhythmia (including ventricular extrasystoles and ventricular fibrillation) Angina pectoris

		Conduction disorders (atrioventricular block) Tachycardia Palpitations
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

4.9 Overdose

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 (detailed in 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: Local anaesthetics for dental use
ATC Code: N01BB03

Mepivacaine is a local anaesthetic of amide type, acting rapidly and 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, as well as regards cations as the local anaesthetic molecules which are not charged.

5.2 Pharmacokinetic properties

The absorption of the local anaesthetic depends on the physico-chemical properties (as lipid solubility), on the pharmacological properties (as vasodilator effect) and on the vascularization and the irrigation of the injection area of the product.

The mepivacaine effect appears within 2 or 4 minutes in case of peripheric nerve blocks. The effect duration is determined by the progress from the tissues and by the diffusion in the blood vessels. The distribution ratio is 0.8. The plasma half-life is lengthened in patients suffering from liver disease or uraemia. The link of plasma proteins is 60-78 % for mepivacaine, mainly with α-glycoprotein acid. The mepivacaine pKa is 7.6.

The blood half-life lasts between 2 and 3 hours after the administration of 600 mg of mepivacaine for a spine anaesthesia. The clearance of the amides depends strongly on the liver irrigation.

The metabolism of mepivacaine occurs mainly through an oxidising process in the liver, following a N-demethylation pathway leading to 2'-6'-pipecoloxylidide (PPX) and an aromatic hydroxylation pathway leading to PPX-4'-hydroxymethyl and PPX-3'-hydroxymethyl. The hydroxylated metabolites are eliminated mainly by the bile and are glucuronized at 99 %. The metabolites are then reabsorbed by the intestines and eliminated in the urines.

In adults, only 5 % of mepivacaine are eliminated under the unchanged form, through the kidneys. The elimination of the unchanged form can be increased by urine acidification. The remaining part of the administered dose is eliminated in the urines under the form of PPX and glucuronized PPX hydroxylated metabolites. Only a small part of the metabolites are found in the faeces. In the new-borns, 71 % of the administered dose is excreted under unchanged mepivacaine.
In adults and neonates, 90% of the administered dose is excreted in the urines within 24 hours.

5.3 Preclinical safety data

The LD_{50} is 39.9 mg/kg in the mouse and 27.8 mg/kg in the rat in the case of intravenous injection. The toxic dose (TD_{50}) is 7.2 mg/kg in the dog in case of intravenous administration.

The mepivacaine toxic threshold in the man ranges between 5 and 10 µg/ml. The relative toxicity is 0.81, compared to lidocaine and 1, compared to procaine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25^{o}C.

6.5 Nature and contents of container

Cardboard box containing 50 cartridges of 1.8 or 2.2 ml.
Glass cartridges of type I with rubber closures.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

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 MARKETING AUTHORISATION HOLDER

Septodont
58 rue du Pont de Créteil
94100 Saint-Maur-des-Fossés
Cedex
France

8 MARKETING AUTHORISATION NUMBER

PA0196/015/001

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