1 NAME OF THE MEDICINAL PRODUCT

SCANDONEST 3% PLAIN, solution for injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution for injection contains:

Mepivacaine hydrochloride 30 mg

One cartridge of 1.8 ml of solution for injection contains 54 mg of mepivacaine hydrochloride.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection.

Clear and colourless solution.

pH adjusted to 6.4 with sodium hydroxide.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

SCANDONEST 3% PLAIN is a local anaesthetic indicated for the local and loco-regional anaesthesia in dental surgery in adults, in adolescents and in children above 4 years of age (c.a. 20 kg of body weight).

SCANDONEST 3% PLAIN is particularly indicated when the use of vasoconstrictor is contraindicated.

4.2 Posology and method of administration

For professional use by dentists and stomatologists.

4.2.1 Posology

- *Adults*

As occurs with all local anaesthetics, doses vary and depend on the area to be anaesthetised, on the vascularity of tissues, on the number of nerve segments to be blocked, on the individual tolerance and on the technique of anaesthesia. The lowest volume of injection leading to effective local anaesthesia should be administered. The necessary dosage must be determined on an individual basis.

Various volumes may be used provided that the total maximum recommended dose is not exceeded.

For a healthy adult of 70 kg, the maximum dose of mepivacaine administered by submucosal infiltration and/or nervous block should not exceed 4.4 mg/kg (0.15 ml/kg) of body weight with an absolute dose of 300 mg mepivacaine per session.

The maximum recommended doses are reported in the following table depending on the cartridge volume and on the patient's weight.

			Equivalent in cartridge numbers
Weight (kg)	Mepivacaine dose (mg)	Volume (ml)	1.8 ml
50	220	7.3	4.1
60	264	8.8	4.9
70	300	10.0	5.6
80	300	10.0	5.6
90	300	10.0	5.6
100	300	10.0	5.6

- *Children*

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 by the magnitude of the operation. The average dosage is 0.75 mg/kg =0.025 ml of mepivacaine solution per kg body weight.

Maximum recommended dosage:

Do not exceed the equivalent of 3 mg mepivacaine/kg (0.1 ml mepivacaine/kg) of body weight.

The table below illustrates the maximum recommended dose:

			Equivalent in cartridge numbers
Weight (kg)	Mepivacaine dose (mg)	Volume (ml)	1.8 ml
20	60	2	1.1
30	90	3	1.7
40	120	4	2.2
50	150	5	2.8

- *Special populations*

Due to the lack of clinical data, particular precaution should be used in order to administer the lowest dose leading to efficient anaesthesia in:

- elderly people

- patients with renal or hepatic impairment

- case of hypoxia, hyperkaliema or metabolic acidosis.

4.2.2 Method of administration:

Infiltration and perineural use in oral cavity.

The rate of injection should not exceed 1 ml of solution per minute.

4.3 Contraindications

- Hypersensitivity to mepivacaine (or to any local anaesthetics agent of the amide type) or to any of the excipients

- Children (age below 4 years old)

- Severe conduction disturbances

- Poorly controlled epileptic patient

4.4 Special warnings and precautions for use

4.4.1 Special warnings

SCANDONEST 3% PLAIN must be used with caution in:

Patients with cardiovascular disorders:

- Peripheral vascular disease
- Arrhythmias particularly of ventricular origin
- Heart failure
- Hypotension

SCANDONEST 3% PLAIN should be administered with caution in patients with impaired cardiac function since they may be less able to compensate 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, see section 4.2.

Patients receiving treatment with antiplatelets / anticoagulants:

The increased risk of severe bleeding following accidental vessel puncture and during oro-maxillo-facial surgery should be considered. INR monitoring should be increased in patients taking anticoagulants.

Patients with porphyria:

SCANDONEST 3% PLAIN should be used cautiously.

Patients with malignant hyperthermia:

Many drugs used during the conduct of anaesthesia are considered potential triggering agents for familial malignant hyperthermia. It has been shown that the use of amide local anaesthetics in malignant hyperthermia patients is safe. However, there is no guarantee that neural blockage will prevent the development of malignant hyperthermia during surgery. It is also difficult to predict the need for supplemental general anaesthesia. Therefore, a standard protocol for the management of malignant hyperthermia should be available.

Patients with bleeding diathesis due to needle / technique / surgery.

Elderly patients:

Dosages should be reduced in elderly patients over 70 years old (lack of clinical data).

SCANDONEST 3% PLAIN must be used safely and effectively under appropriate conditions:

The local anaesthetic effects may be reduced when SCANDONEST 3% PLAIN is injected into an inflamed area or into an infected area.

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.

SCANDONEST 3% PLAIN contains less than 1 mmol sodium (23 mg) per cartridge, i.e. it is considered as essentially 'sodium free'.

Sportsmen should be warned that the presence of SCANDONEST 3% PLAIN in blood may yield positive results on doping tests undergone by professional athletes.

4.4.2 Precautions for use

Before using SCANDONEST 3% PLAIN, it is important:

- To make inquiries into the patient's diathesis, current therapies and history;
- To maintain verbal contact with the patient.
- To have resuscitative equipment at hand (see section 4.9).

Risk associated with an accidental intravascular injection:

Accidental intravascular injection (e.g.: inadvertent intravenous injection into the systemic circulation, inadvertent intravenous or intra-arterial injection in the head area and neck area) may be associated with severe adverse reactions, such as convulsions, followed by central nervous system or cardiorespiratory depression and coma, progressing ultimately to respiratory arrest, due to the sudden high level of mepivacaine in the systemic circulation.

Thus, to ensure that the needle does not penetrate a blood vessel during injection, aspiration should be performed before the 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 mepivacaine's potential chemical neurotoxicity as it may impair the perineural blood supply and prevent mepivacaine local wash-out.

Concomitant use of other medicinal products may require thorough monitoring (see section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

Interactions requiring precautions for use

Other local anaesthetics: Toxicity of local anaesthetics is additive. It is not relevant considering dental anaesthesia doses and blood levels, but it is a concern in children.

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 following concomitant administration of cimetidine.

Sedatives (central nervous system depressants)***:*** Reduced doses of SCANDONEST 3% PLAIN should be used due to additive effects.

4.6 Fertility, pregnancy and lactation

4.6.1 Fertility

No relevant data reported any toxic effects on fertility in animals with mepivacaine. To date, no data are available regarding humans.

4.6.2 Pregnancy

No clinical studies were performed in pregnant women and no cases of pregnant women treated with injectable solution of mepivacaine 30 mg/ml were reported in literature. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. Therefore, as a precautionary measure, it is preferable to avoid the use of SCANDONEST 3% PLAIN during pregnancy.

4.6.3 Breastfeeding

No nursing mothers were included in clinical studies involving SCANDONEST 3% PLAIN. Only literature data concerning lidocaine passage in milk are available showing no risk. 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 SCANDONEST 3% PLAIN.

4.7 Effects on ability to drive and use machines

Patients should not leave the dental office within 30 minutes following administration of SCANDONEST 3% PLAIN.

4.8 Undesirable effects

a) Summary of the safety profile

Adverse reactions following the administration of SCANDONEST 3% PLAIN are similar to those observed with other local amide anaesthetics. These adverse reactions are, in general, dose-related and may result from high plasma levels caused by overdose, rapid absorption or unintended intra-vascular injection. They may also result from hypersensitivity, idiosyncrasy, or diminished tolerance by patient.

Serious adverse reactions are generally systemic.

b) Tabulated list of adverse reactions

The reported adverse reactions come from spontaneous reporting and literature.

The frequencies classification follows the convention: Very common (≥ 1/10), Common (≥1/100 - <1/10), Uncommon (≥1/1,000 - <1/100), Rare (≥1/10,000 - <1/1,000) and Very rare (<1/10,000). Frequency "Not known": "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 1. Anaphylactic / anaphylactoid reactions Angioedema (Face / tongue / lip / throat / larynx[1] / periorbital oedema) 2. Bronchospasm / asthma[2] Urticaria
Psychiatric disorders	Not Known	Euphoric mood Anxiety/Nervousness

MedDRA System Organ Class	Frequency	Adverse reactions (continued)
Nervous system disorders	Common	Headache
	Rare	1. Neuropathy[3] : 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 disturbance) Ageusia 2. Dizziness (light headedness) Tremor 3. Deep CNS depression: Loss of consciousness Coma Convulsion (including tonic-clonic seizure) 4. 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 disorder
	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)[4] Angina pectoris [5] Conduction disorders (atrioventricular block) Tachycardia Palpitations
Vascular disorders	Rare	Hypotension (with possible circulatory collapse)
	Very rare	Hypertension
	Not known	Vasodilatation

MedDRA System Organ Class	Frequency	Adverse reactions (continued)
Respiratory, thoracic and mediastinal disorders	Rare	Respiratory depression Bradypnoea Apnoea (respiratory arrest) Yawning Dyspnoea [2]
	Not known	Hypoxia [6] (including cerebral) Hypercapnia [6] Dysphonia (Hoarseness [1])
Gastrointestinal disorders	Rare	Nausea Vomiting Gingival / oral mucosal exfoliation (sloughing) / ulceration Swelling [7] of tongue, lip, gums
	Not known	Stomatitis, glossitis, gingivitis
Skin and subcutaneous tissue disorders	Rare	Rash (eruption) Pruritus Swelling face
Musculoskeletal and connective tissue disorders	Rare	Muscle twitching Chills (shivering)
General disorders and administration site conditions	Rare	Local swelling Injection site swelling
	Not known	Chest pain Fatigue, asthenia (weakness) Feeling hot Injection site pain Hyperthermia
Injury, poisoning and procedural complications	Not known	Nerve injury

c) Description of selected adverse reactions

[1] Laryngo-pharyngeal oedema may characteristically occur with hoarseness and / or dysphagia.

[2] Bronchospasm (bronchoconstriction) may characteristically occur with dyspnoea.

[3] These neural pathologies may occur with the various symptoms of abnormal sensations (i.e., paresthesia, hypoesthesia, dysesthesia, hyperesthesia, etc) of the lips, tongue and oral tissues. These data originated in post-marketings reports, mostly following nerve blocks in mandible, involving various branches of the trigeminal nerve.

[4] This mostly occurs in patients with underlying cardiac disease or in patients receiving certain drugs.

[5] This occurs in predisposed patients or in patients with risk factors of ischemic heart disease.

[6] Hypoxia and hypercapnia are secondary to respiratory depression and / or to seizures and sustained muscular exertion.

[7] This occurs by accidental biting or chewing of the lips or tongue while the anaesthesia persists.

4.9 Overdose

4.9.1 Types of overdose

Local anaesthetic overdose in the largest sense is often used to describe:

- absolute overdose,
- relative overdose such as:
  - inadvertent injection into a blood vessel, or
  - abnormal rapid absorption into the systemic circulation, or
  - delayed metabolism and elimination of SCANDONEST 3% PLAIN.

4.9.2 Symptomatology

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

4.9.3 Treatment of overdose

The availability of resuscitation equipment should be ensured before the onset of dental anaesthesia with local anaesthetics.

If acute toxicity is suspected, the injection of SCANDONEST 3% PLAIN must immediately be stopped.

Oxygen should rapidly be administered, if necessary assisted ventilation should be used. Change patient position to supine position if necessary.

In case of cardiac arrest, immediate initiation of cardiopulmonary resuscitation should be performed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Nervous System /Anaesthetics /Local anaesthetics /Amides /Mepivacaine

ATC code: N01 BB 03

SCANDONEST 3% PLAIN contains mepivacaine, which is an amide local anaesthetic. Mepivacaine reversibly blocks nerve impulses owing to its effects on ionic transport across the cell membrane. Mepivacaine has a rapid onset, a high potency of anaesthesia and a low toxicity.

Onset of action

When peripheral nerve block is performed, mepivacaine effect occurs within 5 minutes.

Analgesia duration

Pulp anaesthesia generally lasts 25 min following maxillary infiltration and 40 min following inferior alveolar block, whereas anaesthesia of soft tissue was maintained during 90 min and 165 min following maxillary infiltration and inferior alveolar block, respectively.

5.2 Pharmacokinetic properties

Absorption

The rate of systemic absorption of mepivacaine in humans depends mainly upon the total dose and concentration of administered drug, on the route of administration, on the vascularity of the administration site and on the concomitant administration of vasoconstrictors which decreases the rate of absorption.

Distribution

Mepivacaine is rapidly distributed into tissues. Although all tissues take up local anaesthetics, the highest concentrations are found in the more highly perfused organs such as lung and kidney.

Metabolism

As all amide-type local anaesthetics, mepivacaine is largely metabolised in the liver by microsomal enzymes. Over 50% is excreted as metabolites into the bile but these probably undergo entero-hepatic circulation as only small amounts appear in the faeces.

Elimination

The plasma elimination half-life has been reported to be 1.9 hours in adults. Metabolites are excreted in the urine with less than 10% of unchanged mepivacaine.

5.3 Preclinical safety data

General toxicity studies (single dose and repeat-dose studies) were performed with mepivacaine demonstrating a good safety margin. *In vitro* and *in vivo* testing carried out on mepivacaine did not reveal any genotoxic effect of this product. No relevant reproductive and development toxicity study demonstrated teratogenic effects with mepivacaine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride

Sodium hydroxide (for pH-adjustment)

Water for injections.

6.2 Incompatibilities

In the absence of compatibility studies, SCANDONEST 3% PLAIN must not be mixed with any other medicinal products.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do no store above 25^{o}C.

In order to protect from light, keep the cartridge in the outer carton tightly closed.

Do not freeze.

6.5 Nature and contents of container

Type I glass cartridge, sealed at its base by a mobile type I synthetic rubber and at the top by a type I synthetic rubber seal kept in place by a metal cap.

Cartridges of 1.8 ml.

Box containing 50 cartridges.

Not all pack sizes may be marketed.

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

As for any cartridge, the diaphragm should be disinfected prior to use. It should be carefully swabbed:

- either with 70% ethyl alcohol
- or with 90% pure isopropyl alcohol for pharmaceutical use.

The cartridges should under no circumstance be dipped into any solution whatsoever.

One cartridge can only be used for one single patient during one single session.

No opened cartridge of anaesthetic solution should be reused. If only a part is used, the remainder must be discarded.

Any unused product or waste material should be disposed of in accordance with local requirements.