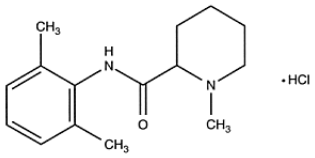
1 PRODUCT NAME

Scandonest 2% Special : Mepivacaine hydrochloride 2% (20mg/mL) with adrenaline 1:100,000, Injection Solution
Scandonest 3% : Mepivacine hydrochloride 3% (30mg/mL), Injection Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Mepivacaine hydrochloride
CAS [1722-62-9]
MW : 282.81
Chemical name : (1-Methyl-2-piperidyl)formo-2´,6´-xylidide hydrochloride



Chemical formula : $C_{15}H_{22}N_2O,HCl$

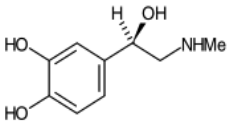
White crystalline powder, freely soluble in water and in alcohol, very slightly soluble in dichloromethane.

Mepivacaine hydrochloride is a local anaesthetic and is a racemic mixture.

Adrenaline

CAS [51-43-4]
MW : 183.2

Chemical name : (R)-1-(3,4-di-hydroxyphenyl)-2-methylaminoethanol



Chemical formula : $C_9H_{13}NO_3$

A white to greyish-white, crystalline powder, sparingly soluble in water, practically insoluble in alcohol and ether.

Adrenaline is a vasoconstrictor

Quantitative composition

SCANDONEST 2% Special

	Cartridge 2.2 mL	Cartridge 1.8 mL
Active ingredients		
Mepivacaine hydrochloride	44 mg	36 mg
Adrenaline	22 µg	18 µg
Other ingredients		
Sodium chloride	14.3 mg	11.7 mg
Potassium metabisulfite	2.64 mg	2.16 mg
Disodium edetate	0.55 mg	0.45 mg
Sodium hydroxide solution	(for pH adjustment)	(for pH adjustment)
Hydrochloric acid	(for pH adjustment)	(for pH adjustment)
Water for injections q.s.	2.2 mL	1.8 mL

SCANDONEST 3%

	Cartridge 2.2 mL	Cartridge 1.8 mL
Active ingredients		
Mepivacaine hydrochloride	66 mg	54 mg
Other ingredients		
Sodium chloride	13.2 mg	10.8 mg
Sodium hydroxide solution	(for pH adjustment)	(for pH adjustment)
Water for injections q.s.	2.2 mL	1.8 mL

Contains no anti-microbial agent.

3 PHARMACEUTICAL FORM

Injection solution

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

SCANDONEST 3% is indicated for the production of local anaesthesia in routine dental procedures and oral surgery by means of infiltration and nerve block techniques.

SCANDONEST 2% Special is recommended for oral surgery requiring prolonged duration of anaesthesia and haemostasis.

4.2 Dose and method of administration

The lowest dosage that results in effective anaesthesia for the planned treatment should be used.
The dosage will depend upon the area of the oral cavity to be anaesthetised, the vascularity of the oral tissues and the technique of anaesthesia.
Toxic doses vary widely between patients and toxic effects may occur after any local anaesthetic

procedure. Careful observation of the patient must be maintained after administration of the local anaesthetic.

Scandonest 3% and Scandonest 2% Special :

Adults : a single cartridge (2.2 mL) is generally sufficient. Do not exceed three cartridges (6.6 mL).

Adolescents between 14 and 17 years : usual dosage one cartridge (2.2 mL). Do not exceed 2 cartridges (4.4 mL) in general cases.

Children between 6 and 14 years : usual dose is 1.35 mL. Do not exceed 2.7 mL in usual cases.

Children between 3 and 6 years : do not exceed maximum recommended dose of 1.8 mL.

Do not use on children under three years of age.

Method of administration

The product is injected either locally or in the vicinity of a dental nervous trunk.
The safe dose for people with acute or chronic disease may be substantially less than that for healthy individuals.
One or more cartridges should be used on a single patient on one occasion only during each session of treatment. If only a portion of a cartridge is used, the remainder must be discarded.

4.3 CONTRAINDICATIONS

These include :

a) contraindications to Mepivacaine (SCANDONEST 2% Special and SCANDONEST 3%) :
- specific allergies to Mepivacaine or to other anaesthetics of amide type,
- allergies of cross type Procaine – Mepivacaine.

b) contraindications to Adrenaline (SCANDONEST 2% Special) :
- cerebral arteriosclerosis,
- arterial hypertension,
- coronary disease,
- valvular cardiac disease (particularly sequelae to acute rheumatic fever).
- thyrotoxicosis, untreated,
- known sensitivity to sympathomimetic amines.

c) hypersensitivity to sulfites (potassium metabisulfite is present in SCANDONEST 2% Special formula as an antioxidant),

d) injection by intravenous route is strictly contra-indicated

e) inflammation or sepsis in the region of the proposed injection

f) hypersensitivity to any other component of SCANDONEST 2% Special and SCANDONEST 3%

g) patients receiving monoamine oxidase inhibitors (or who have received such an agent within two weeks) or tricyclic antidepressants.

h) patients in whom there is a possibility that general anaesthesia might be required to complete the procedure.

4.4 Special warnings and precautions for use

General precautions:

- WHEN ANY LOCAL ANAESTHETIC AGENT IS USED, RESUSCITATIVE EQUIPMENT AND DRUGS, INCLUDING OXYGEN, SHOULD BE IMMEDIATELY AVAILABLE IN ORDER TO MANAGE POSSIBLE ADVERSE REACTIONS INVOLVING THE CARDIOVASCULAR, RESPIRATORY OR CENTRAL NERVOUS SYSTEMS. BECAUSE OF THE POSSIBILITY OF HYPOTENSION AND BRADYCARDIA FOLLOWING MAJOR BLOCKS, AN IV CANNULA SHOULD BE INSERTED BEFORE THE LOCAL ANAESTHETIC IS INJECTED. DELAY IN PROPER MANAGEMENT OF DOSE-RELATED TOXICITY, UNDER VENTILATION FROM ANY CAUSE AND/OR ALTERED SENSITIVITY MAY LEAD TO THE DEVELOPMENT OF ACIDOSIS, CARDIAC ARREST AND DEATH.
- INJECTION SHOULD ALWAYS BE MADE SLOWLY WITH FREQUENT ASPIRATIONS TO AVOID INADVERTENT INTRAVASCULAR INJECTION, WHICH CAN PRODUCE CEREBRAL SYMPTOMS EVEN AT LOW DOSES.
- Note, that the absence of blood in the syringe does not assure that intravascular injection will be avoided. There should be careful monitoring of cardiovascular and respiratory vital signs after each injection.
- Intra-vascular injection is strictly contra-indicated. An accidental injection into a blood vessel may be associated with systemic adverse effects due to the circulating levels of adrenaline and mepivacaine. Therefore, it is imperative to ensure that the needle being used for the injection does not go into a vessel.
- Since amide-type local anaesthetics are also metabolised by the liver and excreted via kidneys, **SCANDONEST 2% Special** and **SCANDONEST 3%** should be used with caution in patients with hepatic or renal disease. Patients with severe hepatic disease or renal impairment, because of their inability to metabolise or excrete local anaesthetics normally, are at greater risk of developing toxic plasma concentration.
  Due to the presence of adrenaline, the product is not advised for diabetic subjects or for patients with thyrotoxicosis.
  Many drugs used during the conduct of anaesthesia are considered potential triggering agents for familial malignant hyperthermia, since it is not known whether amide-type local anaesthetics may trigger this reaction, and since the need for supplemental general anaesthesia cannot be predicted in advance, it is suggested that a standard protocol for management should be available.

Use with caution in the following circumstances:

- local anaesthetic procedures should be used with caution when there is inflammation and/or sepsis in the region of proposed injection.
- the lowest dosage that results in effective anaesthesia should be used to avoid high plasma levels and serious adverse effects. Repeated doses may cause significant increases in blood levels with each repeated dose due to slow accumulation of the drug or its metabolites. However, this is unlikely to occur at the doses normally used in dentistry. 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.
- Mepivacaine should be used with caution in patients with epilepsy, bradycardia, digitalis intoxication, severe shock or heart block. Mepivacaine should also be used with caution in patients with impaired cardiovascular function as they may be less able to compensate for functional changes associated with prolongation of AV conduction produced by the drug. In patients with Stoke-Adams syndrome or Wolff-Parkinson-White syndrome care should be taken to avoid accidental arterio-venous injection.
- The patient should be advised to exert caution to avoid inadvertent trauma to the lips, tongue, check mucosa or soft palate when these structures are anaesthetised. Eating and drinking hot liquids should therefore be postponed until normal function returns.

Adrenaline

- Local anaesthetic solutions containing adrenaline should be used with caution in areas of the body supplied by end arteries or having otherwise compromised blood supply. Patients with peripheral vascular disease and those with hypersensitive vascular disease may exhibit exaggerated vasoconstrictor response. Ischaemic injury or necrosis may result. Preparations containing a vasoconstrictor should be used with caution in patients during or following the administration of potent general anaesthetic agents, since cardiac arrhythmias may occur under such conditions.
- Solutions containing adrenaline should be used with extreme caution in patients with severe or untreated hypertension, arteriosclerotic heart disease, heart block, cerebral vascular insufficiency, thyrotoxicosis, advanced diabetes or any other pathological condition that might be aggravated by the effects of adrenaline. Adrenaline may induce anginal pain in patients suffering from ischaemic heart disease.

Mepivacaine

- Inadvertent intravascular injection of small doses of Mepivacaine injected into the head or neck area, including retrobulbar, dental and stellate injection blocks, may produce adverse effects similar to systemic toxicity seen with unintentional intravascular injection of larger doses.
- Mepivacaine should be used with caution in patients with hepatic or renal disease, since amide-type local anaesthetics are metabolised by the liver and excreted via kidneys. Patients with hepatic or renal impairment, because of their inability to metabolise or excrete local anaesthetics normally, are at greater risk of developing toxic plasma concentrations.
- Mepivacaine should be used with caution in persons with known drug sensitivities. Patients allergic to para-aminobenzoic acid derivatives (procaine, benzocaine, etc) have not shown cross sensitivity to Mepivacaine.
- Solutions containing adrenaline should be used with extreme caution in patients with severe or untreated hypertension, arteriosclerotic heart disease, heart block, cerebral vascular insufficiency, thyrotoxicosis, advanced diabetes or any other pathological condition that might be aggravated by the effects of adrenaline. Adrenaline may induce anginal pain in patients suffering from ischaemic heart disease.
- The safety and effectiveness of Mepivacaine depend on the proper dosage, correct technique and adequate precautions. Standard textbooks should be consulted regarding specific techniques and precautions for various anaesthetic procedures.
- Mepivacaine with adrenaline solutions contain sodium metabisulfite, a sulfite that may cause allergic type reactions including anaphylactic symptoms and life threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than non-asthmatic people.

Carcinogenicity and mutagenicity:
Studies of Mepivacaine in animals to evaluate the carcinogenic and mutagenic potential or the effect on fertility have not been conducted.

4.5 Interaction with other medicines and other forms of interaction

The administration of local anaesthetic solutions containing adrenaline to patients receiving monoamine oxidase inhibitors, tricyclic antidepressants or phenothiazines may produce severe prolonged hypotension or hypertension. Phenothiazines and butyrophenones may reduce or reverse the pressor effect of adrenaline, Concurrent use of these agents should generally be avoided. In situations when concurrent therapy is necessary, careful patient monitoring is essential. Concurrent administration of vasopressor drugs and ergot-type oxytocic drugs may cause severe, persistent hypertension or cerebrovascular accidents.

As **SCANDONEST 2% Special** contains a vasoconstrictor (adrenaline), concurrent treatment with a Beta-adrenergic blocking agent (propranolol, timolol, etc.) may result in dose-dependent hypertension and bradycardia with possible heart block.
The effects of adrenaline may be potentiated by thyroid hormones.

SCANDONEST 2% Special and **SCANDONEST 3%** should be administered with caution to patients

under the following treatments:

- Hypoglycaemics: adrenaline-induced hyperglycaemia may lead to loss of blood sugar control in diabetic patients treated with hypoglycaemics.
- Anti-arrhythmic agents (e.g: procainamide, mexilitine, disopyramide) : Mepivacaine may increase their effects.
- Skeletal muscle relaxant (suxamethonium): combination with Mepivacaine may lead to excessive neuro-muscular block.
- Cardiac glycosides (e.g: digoxin) : adrenaline may interact with cardiac glycosides resulting in cardiac arrhythmias.
- Adrenergic neuron blocking agents (e.g: guanethidine) : since the product contains adrenaline.
- Quinidine: combination with adrenaline may lead to cardiac arrhythmias.
- Cimetidine: increased serum levels of Mepivacaine have been reported after concurrent cimetidine and Mepivacaine administration.
- Amiodarone: combination with Mepivacaine may reduce the clearance of Mepivacaine and seizures, sinus bradycardia and a long sinoatrial arrest have been reported. Patients receiving the combination should be carefully monitored.
- Phenytoin and other antiepileptic drugs such as phenobarbitone, primidone and carbamazepine appear to enhance the metabolism of Mepivacaine but the significance of this is not known. Phenytoin and Mepivacaine have additive cardiac depressant effects.
- Serious cardiac arrhythmias and acute pulmonary oedema if hypoxia present may occur if preparations containing adrenaline are employed in patients during or following the administration of chloroform, halothane, cyclopropane, trichlorethylene or other halogenated compounds.
- Structurally related local anaesthetics: Mepivacaine should be used with caution in patients receiving agents structurally related to local anaesthetics.
- Beta adrenoreceptor antagonists: Propranolol and metoprolol reduce the metabolism of intravenous Mepivacaine. It is possible that this effect may also occur with other beta-adrenoreceptor antagonists. If these drugs are used concurrently then the patient should be closely observed for the signs of Mepivacaine toxicity.

Effect on laboratory tests:
The intramuscular injection of Mepivacaine may result in an increase in creatine phosphokinase levels. Thus, the use of this enzyme determination without isoenzyme separation, as a diagnostic test for the presence of acute myocardial infarction may be compromised by the intramuscular injection of Mepivacaine.

4.6 Fertility, pregnancy and lactation

Use in pregnancy (Category A – Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.):

The safe use of Mepivacaine during pregnancy has not been established. Mepivacaine has however been used extensively for dental procedure during pregnancy with no proven increase in frequency of malformations or of harmful effects to mother or foetus.

Adrenaline has been administered to a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

Use in lactation :
It is not known whether mepivacaine or its metabolites appear in breast milk.
Adrenaline is excreted in the breast milk.
Therefore the use of SCANDONEST 2% Special and SCANDONEST 3% is not recommended during lactation.

4.7 Effects on ability to drive and use machines

Depending on the dosage, or, if given inadvertently intravenously, local anaesthetics may have a mild

effect on mental function and may temporarily impair locomotion and coordination.

4.8 Undesirable effects

Common reactions (≥ 1% and <10%) :
Excluding post procedural dental pain, local reactions at the injection site are the most common adverse events: infection, gingivitis, pain and oedema. Headache, paresthesia and hyperaesthesia are also reported after use of anaesthetic injections during dental procedures.

Uncommon (≥ 0.1%and <1%) :
Serious adverse experiences following the administration of Mepivacaine are similar in nature to those observed with other amide local anaesthetic agents. These adverse experiences are, in general, dose-related and may result from high plasma levels caused by excessive dosage, rapid absorption, unintended intravascular injection or may result from hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. Serious adverse experiences are generally systemic in nature. The following types are those most commonly reported:

Central nervous system
CNS manifestations are excitatory and/or depressant and may be characterised by lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred or double vision, vomiting, sensations of heat, cold or numbness, agitation, difficulty in swallowing and slurred speech, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest which are less common.
The excitatory manifestations may be very brief or may not occur at all, in which case the first manifestation of toxicity may be drowsiness merging into unconsciousness and respiratory arrest.
Drowsiness following the administration of Mepivacaine is usually an early sign of a high blood level of the drug and may occur as a consequence of rapid absorption.

Cardiovascular system
Cardiovascular manifestations are usually depressant and are characterised by bradycardia, hypotension, and cardiovascular collapse, which may lead to cardiac arrest.
Signs and symptoms of depressed cardiovascular function may commonly result from a vasovagal reaction, particularly if the patient is in an upright position.
Less commonly, they may result from a direct effect of the drug. Failure to recognize the premonitory signs such as sweating, a feeling of faintness, changes in pulse or sensorium may result in progressive cerebral hypoxia and seizure or serious cardiovascular catastrophe. Management consists of placing the patient in the recumbent position and ventilation with oxygen. Supportive treatment of circulatory depression may require the administration of intravenous fluids and, when appropriate, a vasopressor (e.g, ephedrine) as directed by the clinical situation.

Allergic reactions
Allergic reactions are characterised by cutaneous lesions, urticaria, oedema or anaphylactoid reactions.
Allergic reactions as a result of sensitivity to Mepivacaine are extremely rare and, if they occur, should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.
Caution should be taken in asthmatic patients since **SCANDONEST 2% Special** contains metabisulfites.

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 professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/,

4.9 Overdose

OVERDOSE

The injection of excessive amounts of Mepivacaine and adrenaline injection may, due to the vasoconstrictor, cause ischaemia. This can be followed by reactive hyperaemia resulting in post extraction bleeding.
Most systemic reactions to local anaesthetics are from overdose and in dentistry would most frequently be caused by accidental intravascular injection (for symptoms, see Adverse Reactions).
If unusual reactions develop resuscitative and/or supportive measures should be started promptly.

Treatment of overdose :
Contact the Poisons Information Centre (Australia 13 11 26, New Zealand 0800 764 766)

For all symptoms : If acute toxicity occurs the injection should be stopped immediately. A patent airway should be established and maintained, oxygen should be administered, and assisted or controlled ventilation should be provided as required.

Circulatory collapse : toxic cardiovascular reactions can include peripheral vasodilation, hypotension, bradycardia and cardiac arrest. Immediately resuscitate with oxygen and commence cardiovascular resuscitation procedures as appropriate.

Convulsions : Appropriate medication for the management of convulsions should be used. If not treated immediately, both convulsions and cardiovascular depression may result in hypoxia, acidosis, bradycardia, arrhythmia and cardiac arrest.

Supportive treatment should be given; standard cardiopulmonary resuscitative therapy, including respiratory support may be required to counter adverse effects on the cardiovascular and/or respiratory systems and to control convulsions. There is no specific antidote.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mepivacaine is a local anaesthetic of the amide type. It stabilises the neuronal membrane by decreasing its permeability to sodium ions and reversibly blocks the initiation and conduction of nerve impulses thereby producing local anaesthesia.
The onset – considered as rapid – and duration of anaesthesia (2 to 3 hours) depend on the route of administration and the dosage (volume & concentration) employed.

Adrenaline acts on both adrenergic receptors of tissue innervated by sympathetic nerves, except for the sweat glands and arteries of the face. It is the most important alpha receptor activator. Adrenaline stimulates the heart to increase output, raises the systolic blood pressure, lowers the diastolic blood pressure, relaxes bronchial spasm and mobilises liver glycogen, resulting in hyperglycaemia and possibly glycosuria.

The combination with adrenaline reduces the rate of local clearance of Mepivacaine from the site of injection; thereby it prolongs the duration of action of Mepivacaine.

.2 Pharmacokinetic properties

Absorption:
Information derived from diverse formulations, concentrations and usages reveals that Mepivacaine is completely absorbed following parenteral administration. Its rate of absorption depends for example, upon various factors such as the site of administration and the presence or absence of a vasoconstrictor agent.
The addition of adrenaline considerably slows the absorption of Mepivacaine.
Peak plasma concentrations are reduced following subcutaneous injection if adrenaline is included in a proportion of 5µg/mL.
Except for intravascular administration, the highest blood levels are obtained following intercostal nerve block and the lowest after subcutaneous administration.

Distribution:
Mepivacaine is highly bound to plasma protein. The plasma half-life has been reported to be about 2 to 3 hours in the adult. Mepivacaine crosses the blood-brain and placental barriers, presumably by passive diffusion.
The degree of plasma protein binding in the foetus is less than that of the mother. The free Mepivacaine concentration will be the same. Consequently, the total plasma concentration in the foetus will be greater than in the mother.
Adrenaline crosses the placenta to enter foetal circulation.

Metabolism:
Mepivacaine is rapidly metabolised by the liver.

Adrenaline is rapidly inactivated by processes which include uptake into adrenergic neurones, diffusion, and enzymatic degradation in the liver and body tissues. In general, adrenaline is methylated to metanephrine by COMT (catechol-O-methyltransferase), followed by oxidative deamination by MAO (monoamine oxidase) to 4-hydroxy-3-methoxymandelic acid or to 3,4-dihydroxymandelic acid, which, in turn, is methylated by COMT.

Excretion:
Less than 10% of a dose of Mepivacaine is reported to be excreted unchanged in the urine.
Several metabolites are also excreted via kidneys, including glucuronide conjugates of hydroxy compounds and an N-demethylated compound, 2',6'-pipecoloxylidide.
Over 50% of a dose of Mepivacaine is excreted as metabolites into the bile but these probably undergo enterohepatic circulation as only small amounts are excreted in the faeces.

The metabolites of adrenaline are excreted in the urine mainly as their glucuronide and ethereal sulphate conjugates.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

SCANDONEST 2% Special

Sodium chloride
Potassium metabisulfite
Disodium edetate
Sodium hydroxide solution
Hydrochloric acid
Water for injections q.s.

S**CANDONEST 3%**

Sodium chloride
Sodium hydroxide solution
Water for injections q.s.

6.3 Shelf life

Scandonest 3%
36 months

Scandonest 2% Special
18 months

6.4 Special precautions for storage

Store below 25ºC – Protect from light – Do Not Freeze.

6.5 Nature and contents of container

SCANDONEST 3% INJECTION

Box containing 5 blister trays of 10 x 1.8 mL (glass cartridge) with rubber closure, AUST R 49310
Box containing 5 blister trays of 10 x 2.2 mL (glass cartridge) with rubber closure, AUST R 49313
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SCANDONEST 2% SPECIAL INJECTION

Box containing 5 blister trays of 10 x 1.8 mL (glass cartridge) with rubber closure, AUST R 49318
Box containing 5 blister trays of 10 x 2.2 mL (glass cartridge) with rubber closure, AUST R 49320.

6.6 Special precautions for disposal

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

7 **MEDICINE SCHEDULE**

Prescription Medicine

8 **SPONSOR**

IVOCLAR VIVADENT Ltd
12 Omega Street, Rosedale, AUCKLAND 0632, NEW ZEALAND Telephone + 64 9 914 9990

9 **DATE OF FIRST APPROVAL**

17/07/1980

10 **DATE OF REVISION OF THE TEXT**

26/10/2017

SUMMARY TABLE OF CHANGES

Formatting changes only.