PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

SEPTANEST SP

[Articane Hydrochloride and Epinephrine Injection]

Solution for Injection

(Articaine Hydrochloride 4% with Epinephrine 1:100,000)

Block and Infiltration use

Local Anesthetic for Dental Use

ATC Code: N01BB58

SEPTANEST N

[Articane Hydrochloride and Epinephrine Injection]

Solution for Injection

(Articaine Hydrochloride 4% with Epinephrine 1:200,000)

Block and Infiltration

Local Anesthetic for Dental Use

ATC Code: N01BB58

Septodont
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St-Maur-Des-Fosses
Val-De-Marne
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RECENT MAJOR LABEL CHANGES

Not Applicable

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

SEPTANEST (articaine hydrochloride and epinephrine injection) is indicated for infiltration anesthesia and nerve block anesthesia in clinical dentistry.

Local or loco-regional dental anesthesia suitable for operations such as: single extractions, with no complications; multiple extractions; extractions of impacted teeth; trephinement; apical resections; removal of cysts; alveolectomies; preparation of cavity; biopulpectomies; and maxillo-facial surgery Muco-gingival operations and other surgical operations on the bone when long lasting ischaemia and analgesia are required.

1.1 Pediatrics

Pediatrics (less than 4 years of age): Safety and effectiveness of SEPTANEST in pediatric patients below the age of 4 years have not been established. The use of Septanest in children under the age of 4 years is not recommended.

Pediatrics (4 to 18 years of age): Safety of doses greater than 7 mg/kg (0.175 mL/kg) in pediatric patients has not been established. [See **4 DOSAGE AND ADMINISTRATION**].

2 CONTRAINDICATIONS

Septanest (articaine hydrochloride and epinephrine injection) is contraindicated in:

- Patients with known allergies to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see **6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING**.
- Patients with a known hypersensitivity to sulphites or patients with asthma who may have bronchospastic allergic reactions induced by sulphites. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.
- Intravascular injection: therefore, it is imperative to ensure that the needle being used for the injection does not go into a vessel.
- Patients with epilepsy not controlled by treatment.

Since Septanest contains epinephrine the caution required of any vasoconstrictor drug is in order.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- As with all local anesthetics the dosage varies and depends upon the area to be anaesthetized, the vascularity of the tissues, the number of numeral segments to be blocked, individual tolerance and the technique of anesthesia.
- The lowest dosage (volume and concentration) that produces the desired results should be used to avoid high plasma levels and serious systemic side effects.
- The actual dosage and maximum dosage must be individualized, based on the age, size, and physical status of the patient and the expected rate of systemic absorption from the injection site. In highly vascular tissue, absorption is greater than other areas.

- The onset of anesthesia and the duration of anesthesia are proportional to the dosage of the local anesthetic used. Exercise caution when employing large volumes because the incidence of adverse reactions may be dose-related.
- For most routine dental procedures, SEPTANEST N containing epinephrine 1:200,000 is preferred. However, when more pronounced hemostasis or improved visualization of the surgical field are required, SEPTANEST SP containing epinephrine 1:100,000 may be used.
- Injections should always be made slowly with frequent aspirations in order to verify the absence of intravascular injection.
- Avoid excessive premedication with sedatives, tranquilizers, and anti-emetic agents, especially in small children and elderly patients.

4.2 Recommended Dose and Dosage Adjustment

Adults

- For most common operations, one infiltration with 1.7 mL Septanest is sufficient. In all cases, the injection must be administered slowly (About 1 mL/min).
- For an infiltration in the interdental septum, a quantity of 0.3 to 0.5 mL is indicated as generally sufficient.

Do not exceed the equivalent of 7 mg/kg articaine hydrochloride body weight which corresponds, for a subject weighing 60 kg, to 6 standard 1.7 mL cartridges. The duration of anesthesia during which an operation can be performed using Septanest N is up to 45 minutes. The duration of anesthesia during which an operation can be performed using Septanest SP is up to 75 minutes. The lowest dosage needed to provide effective anesthesia should be administered.

Table 1

Procedure	*Septanest N and Septanest SP*	
	Volume (mL)	*Total Dose (mg)*
Infiltration	0.5 – 2.5	20 – 100
Nerve Block	0.5 – 3.4	20 – 136
Oral Surgery	1 – 5.1	40 – 204

Children

For Septanest N and Septanest SP use in children under 4 years of age is not recommended.

For children 4 years of age or older, the quantity to be injected should be determined by the age and weight of the child, and the type of procedure. Do not exceed the equivalent of 7 mg articaine hydrochloride per kilogram of body weight.

Special Populations

Lower dosages or dosage reduction may be required in debilitated patients, acutely ill patients, elderly patients, and pediatric patients commensurate with their age and physical condition.

No studies have been performed in patients with renal or liver impairment. Exercise caution when using SEPTANEST in patients with severe liver disease.

Elevated plasma levels may occur in patients with cholinesterase deficiency or under acetylcholinesterase inhibitors treatment. Therefore, the lowest dose leading to effective anesthesia should be used. [See **7 WARNINGS AND PRECAUTIONS**].

4.4 Administration

Infiltration and nerve block anesthesia in clinical dentistry. The rate of injection should be slow (1 mL/min).

4.7 Instructions for Preparation and Use

Visually inspect SEPTANEST for particulate matter and discoloration prior to administration.

Prior to using the glass cartridges, disinfect by wiping the cap thoroughly with USP grade isopropyl alcohol (70%). Avoid use of isopropyl alcohol, as well as solutions of ethyl alcohol that are not of USP grade because they may contain denaturants that are injurious to rubber. Immersion is not recommended. Discard unused portion.

5 OVERDOSAGE

Local anesthetic 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 drug.

In case of relative overdose, patients generally present symptoms within the first minutes. Whereas in case of absolute overdose, signs of toxicity, depending on the injection site, appear later after the injection.

The type of toxic reaction depends on factors such as dosage, rate of absorption and clinical status of patient.

Adverse reactions of this group of drugs are generally dose-related and may result from high plasma concentrations of anesthetic caused by inadvertent intravascular administration, overdosage, or rapid absorption from the injection site as well as reduced patient tolerance, idiosyncrasy, or hypersensitivity.

High plasma concentrations of anesthetic affect the central nervous system and cardiovascular system. Generally, high plasma concentrations of the drug initially produce CNS stimulatory effects manifested by anxiety, apprehension, restlessness, nervousness, disorientation, confusion, dizziness, blurred vision, tremors, twitching, shivering and seizures, followed by CNS depression manifested by drowsiness, syncope, unconsciousness, and respiratory arrest. Nausea, vomiting, chills, miosis and tinnitus may also occur.

The adverse cardiovascular effects are depressant and include myocardial depression, bradycardia, cardiac arrhythmias, hypotension, cardiovascular collapse, cardiac arrest, and respiratory depression may occur tachypnea, then bradypnea, which could lead to apnea.

Treatment

Each time a local anesthetic is used, anti-convulsant medicines (benzodiazepines or barbiturates which can be injected), myorelaxants, atropine and vasopressors, resuscitating equipment (in particular a source of oxygen) enabling artificial ventilation, should be available. The safety and effectiveness of local anesthetics depend upon proper dosage, correct technique, adequate precautions, and readiness for emergencies.

Since cardiac arrest symptoms may occur rapidly and with little warning, the resuscitation equipment treatment should be readily available to enable prompt treatment of any respiratory and cardiovascular emergencies.

The patient’s state of consciousness should be monitored after each local anesthetic injection.

For management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 2 – Dosage Forms, Strengths, and Composition

Route of Administration	Dosage Form/Strength/ Composition	Non-Medicinal Ingredients
Perineural (Nerve Block) or Infiltration Use	Solution. • **Septanest SP:** 40 mg/mL (4%) of articaine hydrochloride, and 0.01 mg/mL (1:100,000) of epinephrine (as epinephrine bitartrate). • **Septanest N:** 40 mg/mL (4%) of articaine hydrochloride, and 0.005 mg/mL (1:200,000) of epinephrine (as epinephrine bitartrate).	Hydrochloric acid (as a pH adjuster), sodium chloride, sodium hydroxide (as a pH adjuster), sodium metabisulfite (as an antioxidant), and water for injection. Formulated without parahydroxybenzoates.

Packaging: Septanest SP (articaine hydrochloride 4% with epinephrine 1:100,000) and Septanest N (articaine hydrochloride 4% with epinephrine 1:200,000) are both available in 1.7 mL glass cartridges, box of 50 cartridges.

7 WARNINGS AND PRECAUTIONS

General

Toxic reactions, such as convulsions followed by coma and respiratory arrest, may occur in the case of overdosage or accidental intravenous injection. Therefore, it is imperative to ensure that the needle being used for the injection does not go into a vessel. Resuscitative equipment, oxygen and other resuscitative drugs should be available.

Avoid injection into an inflamed or infected area.

Cardiovascular

SEPTANEST N and SP contain epinephrine, a vasoconstrictor. Vasoconstrictor agents should be used in local anesthetic solutions during dental practice only when it is clear that the procedure will be shortened or the analgesia rendered more profound. When a vasoconstrictor is indicated, extreme care should be taken to avoid intravascular injection. The minimum possible amount of vasoconstrictor should be used.

It is essential to aspirate before any injection to avoid administration of the drug into the blood stream.

Local toxicity may include ischemic injury or necrosis, which may be related to vascular spasm. SEPTANEST should be used with caution in patients during and following the administration of potent general anesthetic agents. Concurrent use or immediately following the administration of chloroform, halothane, cyclopropane, trichloroethylene or related anesthetics may sensitize the heart to epinephrine and may cause dose-related cardiac arrhythmias.

Patients with peripheral vascular disease and those with hypertensive vascular disease may exhibit exaggerated vasoconstrictor response. In patients with peripheral vascular disease or injection into areas with limited blood supply, the use of a local anesthetic containing a vasoconstrictor should be made with caution.

Septanest should be used with caution in patients with cardiovascular conditions such as paroxysmal tachycardia or arrhythmias, past heart failure or myocardial infarction, hypertension or hypotension. Postponement of dental surgery should be considered if the condition is severe and/or unstable.

In patients receiving MAO inhibitors or tricyclic antidepressants, extreme care should be used with solutions containing a vasoconstrictor, e.g. epinephrine, because prolonged hypertension may result. [See section **9.4 Drug-Drug Interactions**].

Driving and Operating Machinery

Exercise caution when driving or operating a vehicle or potentially dangerous machinery.

Endocrine and Metabolism

This medicinal product must be used with special caution in patients with the following disorders and postponement of dental surgery should be considered if the condition is severe and/or unstable.

Patients with diabetes

Due to the presence of epinephrine, Septanest is not advised for diabetic subjects.

Patients with plasma cholinesterase deficiency (Pseudocholinesterase deficiency)

A plasma cholinesterase deficiency can be suspected when clinical signs of overdose occur with usual dosage of anesthesia and when a vascular injection has been excluded. In this case, caution shall be used for the next injection and reduced dose shall be applied.

Patients with myasthenia gravis treated by acetylcholinesterase inhibitors:

The lowest dose leading to effective anesthesia should be used.

Patients with pheochromocytoma:

This medicinal product should be used cautiously due to the presence of epinephrine.

Hematologic

Methemoglobinemia

Septanest, along with other local anesthetics, is capable of producing methemoglobinaemia. The clinical signs of methemoglobinaemia are cyanosis of the nail beds and lips, fatigue and weakness. If methemoglobinaemia does not respond to administration of oxygen, administration of methylene blue intravenously 1 to 2 mg/kg body weight over a 5 minute period is recommended.

Although all patients are at risk for methemoglobinemia, patients with glucose-6-phosphate dehydrogenase deficiency, congenital or idiopathic methemoglobinemia, cardiac or pulmonary compromise, infants under 6 months of age, and concurrent exposure to oxidizing agents or their metabolites are more susceptible to developing clinical manifestations of the condition.

Patients who are administered local anesthetics are at increased risk of developing methemoglobinemia when concurrently exposed to certain drugs, which could include other local anesthetics [See **9.4 Drug-Drug Interactions**].

Hepatic/Biliary/Pancreatic

This medicinal product should be used cautiously due to the presence of hepatic disease although 90% of articaine is first inactivated by unspecific plasma esterases in the tissue and blood.

Immune

Septanest contains sulphites which can cause or aggravate anaphylactic-type reactions. The overall prevalence of sulfite sensitivity in the general population is unknown. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

It is strongly recommended to question the patient to find out his background, ongoing treatment, possible allergic antecedents. Allergic-type reactions, including nausea, diarrhea, wheezing respirations, acute asthmatic attacks, impaired consciousness, or shock may occur in patients with bronchial asthma due to hypersensitivity to the sulfite component.

Ophthalmologic

This medicinal product should be used cautiously in patients with susceptibility of acute angle-closure glaucoma due to the presence of epinephrine.

Peri-Operative Considerations

Combinations of different anesthetics cause additive effects on the cardiovascular system and CNS [See **9 DRUG INTERACTIONS**].

Renal

No clinical studies have been performed in patients with severe renal. Use with caution in these patients.

Reproductive health: Female and male potential

- **Teratogenic Risk**

Teratogenic studies of articaine were carried out on the rat, rabbit and cat following intravenous administration and following subcutaneous administration in the cat [See **16 NON-CLINICAL TOXICOLOGY**].

7.1 Special Populations

7.1.1 Pregnant Women

Safe use of local anesthetics during pregnancy prior to labor has not been established with respect to adverse effects on fetal development. Careful consideration should be given before administering these drugs in pregnant women. Teratogenic studies of articaine were carried out on the rat, rabbit and cat following intravenous administration and following subcutaneous administration in the cat [See **16 NON-CLINICAL TOXICOLOGY**].

7.1.2 Breast-feeding

It is unknown if Septanest is excreted in human milk. Precaution should be exercised because many drugs can be excreted in human milk.

7.1.3 Pediatrics

The use of Septanest in children under the age of 4 years is not recommended. [See **4 DOSAGE AND ADMINISTRATION**].

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Reactions to Septanest (articaine hydrochloride) are characteristic of amide-type local anesthetics.

The most frequently adverse reactions are gingivitis, oral hypoesthesia/ numbness, dysesthesia, headache, tremor, bradycardia / tachycardia, hypotension, swelling of face and lip.

The most frequently reported serious adverse reactions are loss of consciousness, paraesthesia, dyspnoea, angioedema, hypersensitivity, syncope, dizziness.

Allergic reactions may manifest as dermatologic reactions, edema, urticaria and other allergy symptoms. [See **2 CONTRAINDICATIONS** and **7 WARNINGS AND PRECAUTIONS**]

Persistent paresthesias of the lips, tongue, and oral tissues have been reported with use of articaine hydrochloride, with slow, incomplete, or no recovery. These post-marketing events have been reported chiefly following nerve blocks in the mandible and have involved the trigeminal nerve and its branches.

8.2 Clinical Trial Adverse Reactions

This information is not available for this drug product.

8.5 Post-Market Adverse Reactions

a) Summary of the safety profile

Adverse reactions following administration of articaine / epinephrine are similar to those observed with other local amide anesthetics / vasoconstrictors.

These adverse reactions are, in general, dose-related.

They may also result from hypersensitivity, idiosyncrasy, or diminished tolerance by patient. Nervous system disorders, local injection site reaction, hypersensitivity, cardiac disorders and vascular disorders are the most frequently occurring adverse reactions.

Serious adverse reactions are generally systemic.

b) Tabulated list of adverse reactions

The reported adverse reactions come from spontaneous reports, clinical studies and literature**.**

The frequency 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).

MedDRA System Organ Class	Frequency	Adverse Reactions
Infections and infestations	Common	Gingivitis
		Conjunctivitis, rhinitis
Immune system disorders	Rare	Allergic, anaphylactic / anaphylactoid reactions; lymphadenopathy
Psychiatric disorders	Rare	Agitation/ Restlessness
		Nervousness / anxiety
Nervous system disorders	Common	Hypoesthesia/ numbness (oral and perioral)
		Dysesthesia (oral and perioral),
		Headache; sleepiness; dizziness; facial paralysis; hyperesthesia; increased salivation; neuropathy; somnolence
		Tremor

MedDRA System Organ Class	Frequency	Adverse Reactions
	Rare	Nystagmus
	Very rare	Paresthesia (persistent hypoesthesia and gustatory loss); exacerbation of Kearns-Sayre Syndrome
Eye disorders	Rare	Diplopia
		Mydriasis
		Ptosis
		Miosis
		Visual impairment (temporary blindness, vision blurred)
Ear and labyrinth disorders	Rare	Tinnitus ; ear pain
Cardiac disorders	Common	Bradycardia ; syncope
		Tachycardia
	Rare	Palpitations
	Not known	Conduction disorders (atrioventricular block)
Vascular disorders	Common	Hypotension (with possible circulatory collapse)
	Uncommon	Hypertension
	Not known	Vasodilatation ; migraine ; ecchymosis
		Vasoconstriction
Respiratory, thoracic and mediastinal disorders	Rare	Bronchospasm / asthma
		Dyspnoea ; pharyngitis; rhinitis; sinus pain; sinus congestion
Gastrointestinal disorders	Common	Swelling of face and lip
	Uncommon	Nausea, vomiting
	Rare	Gingival / oral mucosal exfoliation / ulceration
	Not known	Dysphagia
		Swelling of the cheeks ; dyspepsia; glossitis; gum hemorrhage; mouth ulceration; nausea; stomatitis; tongue edemas; tooth disorder

MedDRA System Organ Class	Frequency	Adverse Reactions
Skin and subcutaneous disorders	Uncommon	Rash (eruption)
		Pruritus
	Rare	Angioedema (face / tongue / lip / throat / larynx / periorbital oedema)
		Urticaria
	Not known	Erythema
Musculoskeletal and connective tissue disorders	Rare	Muscle twitching ; neck pain
General disorders and administration site conditions	Uncommon	Injection site pain
	Rare	Injection site exfoliation / necrosis
		Chills
	Not known	Local swelling; asthenia

Hypersensitivity may characteristically occur with various symptoms e.g., rash, urticaria, pruritus, conjunctivitis, rhinitis, bronchospasm/asthma, and angioedema including oedema of face / tongue / lip / throat / larynx / periorbital oedema. Laryngo-pharyngeal oedema may characteristically occur with dysphagia.

Bronchospasm (bronchoconstriction) may characteristically occur with dyspnoea.

Anaphylactic or anaphylactoid reactions were described with the product with a rare frequency.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

In patients receiving MAO inhibitors or tricyclic antidepressants, extreme care should be used with solutions containing a vasoconstrictor, e.g. epinephrine, because prolonged hypertension may result.

Concurrent use of other local anesthetics can increase risks of toxicity.

Concurrent use or immediately following the administration of chloroform, halothane, cyclopropane, trichloroethylene or related anesthetics may sensitize the heart to epinephrine and may cause dose-related cardiac arrhythmias.

Sedatives (central nervous system depressants e.g.: benzodiazepine, opioids) can increase the risk of adverse reactions and may mask clinical signs.

9.3 Drug-Behavioural Interactions

Driving and Operating Machinery: Besides the direct anesthetic effect, local anesthetics may have a very mild effect on mental function and coordination even in the absence of overt CNS toxicity and may temporarily impair locomotion and alertness. Patients should be cautioned about driving a vehicle or operating potentially hazardous machinery after they receive local anesthetic treatment.

Consumption of alcohol before or after local anesthesia is not recommended as it may alter its effect.

9.4 Drug-Drug Interactions

Local anesthetics

Toxicity of local anesthetics is additive; The total dose of all local anesthetics administered should not exceed the maximum recommended dose of the drugs used.

Sedatives

Sedatives (central nervous system depressants, e.g.: benzodiazepine, opioids) are central nervous system depressants that may have an additive effect.

Halogenated volatile anesthetics (e.g., halothane):

Reduced doses of this medicinal product should be used due to sensitization of the heart to the arrhythmogenic effects of catecholamines: risk of severe ventricular arrhythmia.

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 anesthesia should be given to patients on COMT inhibitors.

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.

Tricyclic antidepressants (TCAs; e.g., amitriptyline, clomipramine, desipramine, imipramine, nortriptyline, trimipramine):

Dose and rate of administration of this medicinal product should be reduced due to an increased risk of severe hypertension.

Serotoninergics and noradrenergic medicines (such as milnacipran and venlafaxine)

Increased risk of severe hypertension.

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.

Other sympathomimetics (e.g., levothyroxine, methyldopa, antihistamines (such as chlorpheniramine, diphenhydramine)

Phenothiazines (and other neuroleptics):

Use with caution in patients taking phenothiazines considering the risk of hypotension due to possible inhibition of epinephrine effect.

Methaemoglobinemia

Patients who are administered local anesthetics are at increased risk of developing methemoglobinemia when concurrently exposed to the following drugs, which could include other local anesthetics:

Examples of Drugs Associated with Methemoglobinemia	
Class	**Examples**
Nitrates/Nitrites	nitric oxide, nitroglycerin, nitroprusside, nitrous oxide
Local anesthetics	articaine, benzocaine, bupivacaine, lidocaine, mepivacaine, prilocaine, procaine, ropivacaine, tetracaine
Antineoplastic agents	cyclophosphamide, flutamide, hydroxyurea, ifosfamide, rasburicase
Antibiotics	dapsone, nitrofurantoin, para-aminosalicylic acid, sulfonamides
Antimalarials	chloroquine, primaquine
Anticonvulsants	phenobarbital, phenytoin, sodium valproate
Other drugs	acetaminophen, metoclopramide, quinine, sulfasalazine

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Septanest (articaine hydrochloride) is a local anesthetic that has the reversible effect of blocking the conduction of painful sensations. Septanest decreases nerve conduction by diminishing the sodium ion influx during the action potential period. The epinephrine is a vasoconstrictor added to Septanest to slow down the passage into the general circulation and thus ensure the prolonged maintenance of an active tissue concentration. The anesthesia is obtained rapidly (1 to 3 minutes) and lasts from 45 to 75 minutes per cartridge.

Injected in the mouth by the submucosal route with a solution containing 1:200,000 epinephrine, articaine reaches the blood concentration peak about 17 minutes after the injection. The half-life elimination is very short: about 25 minutes. Articaine is excreted mainly through the urine with total elimination of 76 % and 89 % following intramuscular and intravenous administration, respectively. Two unidentified metabolites of articaine are detected in the urine following intramuscular injection accounting for 87 % and 2 % of the administered dose. No metabolites are detected in the blood following intravenous administration.

10.2 Pharmacodynamics

Animal

In the non-myelinated C-fibres of the rabbit's dorsal vagus, articaine (0.1 to 1 mM) suppressed the action potential and reduced sodium conductance to produce a local anesthetic effect.

The anesthesia of conduction for articaine (0.05 to 0.5%) is compared to other local anesthetics, lidocaine and procaine (0.05 to 0.5%), on the sciatic nerve of a decapitated frog. Articaine showed superior effectiveness to lidocaine and procaine in the order of 1.5 and 1.9, respectively.

In cats receiving articaine and lidocaine, both anesthetics had a negative inotropic effect on the heart during isovolumetric contraction.

The administration of local anesthetics articaine, procaine, and lidocaine to cats reduced arterial blood pressure. The hypotensive effect was stronger as the speed of the injection increased.

States of shock can be produced by the administration of veratrine, histamine or acetylcholine in the cat. The intravenous injection of articaine (10 mg/kg during 2 minutes) forty minutes before veratrine injection was able to prevent the sharp fall in pressure brought about by veratrine. Articaine does not, however, affect the hypotensive action of histamine or acetylcholine.

Articaine had antispasmodic effects on the contractions of the smooth muscles of the intestinal loop from the guinea-pig induced by barium chloride, carbachol and histamine.

The intraperitoneal administration of articaine did not induce methaemoglobinaemia in the rat or cat. Prilocaine induced methaemoglobinaemia in the cat and not in the rat.

Human

The study of articaine combined with various strengths of epinephrine was evaluated for dental analgesia in healthy volunteers. Concentrations of 2-4% articaine combined with 3.3 – 10 μg/mL epinephrine produced excellent analgesia with duration lasting from 40 to 62 minutes. Articaine administered without epinephrine did not produce reliable anesthesia.

In fifty patients undergoing impacted wisdom teeth extraction, articaine hydrochloride with 1:200,000 epinephrine produced reliable anesthesia in most patients with a duration of anesthesia lasting 17-29 minutes. In another clinical trial, articaine hydrochloride with 1:100,000 epinephrine produced similar results.

10.3 Pharmacokinetics

Animal

The pharmacokinetics of articaine were studies in dwarf pigs after i.v. and i.m. administration with ^{35}S labelled articaine.

Articaine and its metabolites were eliminated principally in the urine and excretion was rapid. Following 12 hours, 64% of the intravenous and 71% if the intramuscular administered radioactivity had been eliminated through the urine. Following 48 hours, 80% and 82% of the administered radioactivity was eliminated via the urine for the intravenous and intramuscular injection respectively. Faecal elimination ranged from 8-12% for intravenous and intramuscular administration.

Human

Healthy volunteers received 240 mg articaine with 1:200,000 epinephrine by submucosal and intramuscular injection. Following submucosal injection, the mean peak plasma concentration was 1.17 $\pm$ 2.5 minutes. The peak plasma level following intramuscular injection was similar at 0.91 $\pm$ 0.21 μg/mL but was reached more slowly at 26.2 $\pm$ 4.1 minutes. The elimination half-life was short with a value of 25 minutes and 40 minutes following oral and intramuscular administration. After 3 hours, the plasma levels of non-metabolized articaine was below the limit of detection. Articaine is excreted mainly through the urine with total elimination of 76% and 89% following intramuscular and intravenous administration, respectively. The value for the plasma clearance of articaine are detected in urine following intramuscular injection accounting for 87% and 2% of the administered dose. No metabolites are detected in the blood following intravenous administration.

11 STORAGE, STABILITY AND DISPOSAL

Temperature: Store at or below 25˚C
Light: Protect from light.
Others: Do Not Freeze.

12 SPECIAL HANDLING INSTRUCTIONS

Visually inspect SEPTANEST for particulate matter and discoloration prior to administration.
Prior to using the glass cartridges, disinfect by wiping the cap thoroughly with USP grade isopropyl alcohol (70%). Avoid use of isopropyl alcohol, as well as solutions of ethyl alcohol that are not of USP grade because they may contain denaturants that are injurious to rubber. Immersion is not recommended. Discard unused portion.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

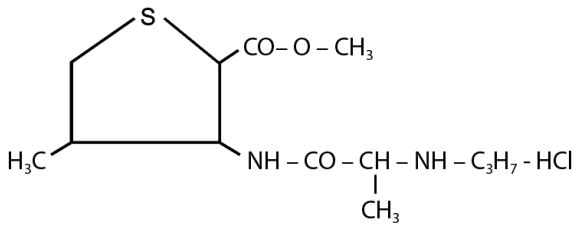
Articaine Hydrochloride

Proper name: Articaine hydrochloride

Chemical Name: Methyl 4-methyl-3-[2-(propylamino)-propionamido]-thiophene-2-carboxylate hydrochloride

Molecular formula and molecular mass: $C_{13}H_{20}N_2O_3S \bullet HCl \bullet 320.84$

Structural formula:



Physicochemical properties: Articaine hydrochloride is a white, fine odourless crystalline powder with a melting point of 177-178°C; soluble in water and ethanol and slightly soluble in chloroform.

Epinephrine Bitartrate

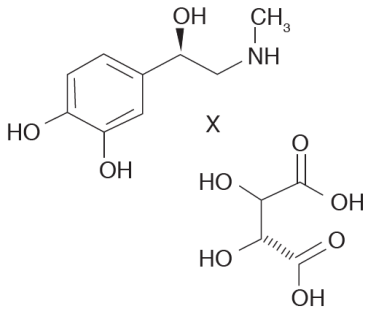
Proper name: Epinephrine bitartrate, (-)-1-(3,4-Dihydroxyphenyl)-2-methylamino-ethanol (+) tartrate (1:1) salt, is a vasoconstrictor with a concentration of 1:200,000 or 1:100,000 (expressed as free base).

Chemical Name: 1) (-)-3, 4-Dihydroxy-"-[(methylamino) methyl] benzyl alcohol (+) tartrate (1:1) salt

2) 1, 2-Benzenediol, 4-[1-hydroxy-2(methylamino) ethyl]-, (R)-, [R-(R*, R*)] -2, 3-dihydroxy-butane dionate (1:1) salt

Molecular formula and molecular mass: $C_9H_{13}NO_3C_4H_6O_6$ • 333.30

Structural formula:



Physicochemical properties: Epinephrine Bitartrate is a white to grayish-white crystalline powder. It is freely soluble in water, slightly soluble in alcohol, practically insoluble in ether. The melting point is 147 - 152 °C.

14 CLINICAL TRIALS

The clinical trial data on which the original indication was authorized is not available.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology

Acute toxicity studies in the mouse, rat, rabbit, and dog along with subchronic studies in the rat and dog were performed with articaine. Studies on the local tolerance were carried out in rabbits and dogs following subcutaneous, intravenous, intramuscular, subdural and epidural administration. Maximized skin sensitivity tests were performed to evaluate the allergenic and sensitising effects following intradermal and subcutaneous application in guinea pigs.

Acute Toxicity

Acute toxicity studies have been conducted in the mouse, rat, rabbit and dog; articaine administered parenterally with also oral administration in the rat.

The symptomatology can be characterized by tremor, vertigo, tonic and clonic convulsions appearing during injection. The duration and intensity of these manifestations are dose-dependent and regress in five to ten minutes at low dosages. At autopsy, a pulmonary edema was noted in the rats. The symptoms in the rat were identical after oral administration but varied with time. A summary of the LD_{50} levels for the rat, rabbit and dog is found in Table 4.

Table 4

Species	*Route*	*% sol.*	*LD_{50} mg/kg*
Rat	I.V. I.M. P.O.	4 3 4	23.2 (22.1 –24.3) 278 (260 – 298) 978 (868 – 1102)
Rabbit	I.V. I.M.	15 3	19.6 (18.6 – 20.7) 20.6 (18.6 – 22.8)
Dog	I.V. I.M.	15 25	Max tolerated dose 50 Min lethal dose 56 Max tolerated dose 100 Min lethal dose 160

A high dose of sub-cutaneous dose of articaine 4% without epinephrine was studied in Swiss mice. Five male and five female mice were administered 0 mg/kg, 100 mg/kg to 500 mg/kg diluted to 12.5 mL saline solution. The calculated lethal dose at various levels are listed in Table 5.

Table 5

Articaine 4 per cent	*Male Mice*	*Female Mice*
LD 0	263	360
LD 5		380
LD 16		400
LD 50	>500	440 (490-404)
LD 84		460
LD 95		475
LD 100	>500	500

The LD_{50} for the 500 mg/kg dose could not be calculated since the maximum mortality obtained for male animals was 40%.

Subchronic Toxicity

Rat

Intramuscularly, articaine was administered as an aqueous 3 per cent solution to groups of 10 male and 10 female rats at dosages of 0, 25, 50 and 100 mg/kg/day. The drug was administered at a frequency of 5 days out of 7 for 5 weeks.

Intravenously, the drug was given in aqueous 0.3 per cent solution at doses of 0, 3, 6 and 12mg/kg/day at the rate of 5 days out of 7 for 5 weeks. The injection rate was 6 mL/min.

Lethality appeared at 50 mg/kg intramuscularly and reached 80 per cent at a dose of 100 mg/kg.

At a dose of 12 mg/kg/day intravenously the drug provoked some signs of intolerance ; at a lower dose, however, no clinical or biological abnormalities were observed.

On histological examination, lesions with haematomas were observed at the site of intramuscular injection; these were sometimes infected. There was no necrosis nor damage to adjacent nerves. A dose of 100 mg/kg produced hypertrophy of the adrenals in males.

Articaine given intramuscularly is well tolerated in the rat up to a dose of 50 mg/kg/day during 5 weeks, and given intravenously, is well tolerated up to a dose of 6 mg/kg/day.

Dog

A 3 per cent solution of articaine was given intramuscularly at 25 and 50 mg/kg/day and intravenously at 5 and 10 mg/kg/day at a rate of 12 mL/min every day for 30 days to groups of three dogs, males or females in each group, with 2 animals in the control group.

Signs of acute toxicity appeared at a dose of 50 mg/kg/day given intramuscularly. These appeared at the injection site and had regressed by 45 minutes.

The symptoms persisted in an irregular manner during the study and the rate of administration of the drug affected their appearance. This was observed when a rapid intravenous injection was followed by convulsions and signs of collapse.

In conclusion, this study revealed that doses of 25 mg/kg/day given intramuscularly or 10 mg/kg/day given intravenously for 30 days were tolerated by dogs.

The experiments on subchronic toxicity demonstrated that 30 or 35 days after intramuscular or intravenous injection, the symptoms were similar to that observed for acute toxicity. Subchronic toxicity was also qualitatively identical in the two species considered.

Local Tolerance

Studies on local tolerance in the rabbit were carried out using 6 per cent solutions of articaine without vasoconstrictor, or with epinephrine (2% mg) or nonepinephrine (4.8% mg). These solutions were administered subcutaneously, intramuscularly or intravenously. The tolerance of the veins was uniformly good. Injection by the intramuscular or subcutaneous route provoked some necrosis around the injection site but these lesions consolidated themselves within two days. The articaine preparations used were regarded as tolerable since injections of NaCl solutions (0.9%) alone provoked some lesions at the injection site.

Tolerance to epidural anesthesia was studied in the beagle to which 5 mL of articaine solution (2%) containing 2 mg % epinephrine was administered into the lumbarsacral space. Histological examination of the injection site showed the solution to be well tolerated.

Tolerance to sub-dural administration was observed in dogs following injections of 200 mg of articaine in 4 mL of CSF and 200 mg of articaine in 5 mL of CSF containing 1:200,000 epinephrine into the foramen magnum sub-occipitally. Two other dogs received injections of lidocaine and two others received physiological saline under the same conditions. In none of the animals did histological examination reveal evidence of spinal or meningeal lesions.

Studies of medullary tolerance and of meningeal tolerance were carried out on ten beagles (5 males and 5 females) which received sub-occipital injections. The doses of articaine given were up to 200 mg per animal and were administered with 1:200,000 epinephrine. These doses were diluted into 4 or 5 mL of CSF which had previously been obtained by aspiration. The animals were placed under artificial respiration.

Some of the animals were sacrificed one or two days after the injection (one control and two who had received drug) and the remaining animals (one control and four who had received drug) were sacrificed eight days after the injection. In all cases, samples of medulla oblongata and cervical spinal tissue were taken at autopsy.

No articaine-induced lesion in the spinal transection or the meninges was observed.

Genotoxicity

Five standard mutagenicity tests, including three in vitro tests (the nonmammalian Ames test, the mammalian Chinese hamster ovary chromosomal aberration test, and a mammalian gene mutation test with articaine HCl) and two in vivo mouse micronucleus tests (one with articaine and epinephrine 1:100,000 and one with articaine HCl alone) showed no mutagenic effects.

Carcinogenicity

Studies to evaluate the carcinogenic potential of articaine HCI in animals have not been conducted.

Reproductive and Developmental Toxicology

No effects on male or female fertility were observed in rats for articaine and epinephrine 1:100,000 administered subcutaneously in doses up to 80 mg/kg/day (approximately 2 times the MRHD based on body surface area).

Teratogenic studies of articaine were carried out on the rat, rabbit and cat following intravenous administration and following subcutaneous administration in the cat:

Rat The dose was administered from day 7 to day 16 of gestation to groups of 20 animals, as 0; 0.8; 4 and 20 mg/kg/day in 5 mL/kg by the intravenous route. The animals were sacrificed after caesarean operation on day 21.

Examination of the maternal and fetal rats was carried out routinely. Although the dose of 20 mg/kg/day was toxic to pregnant rats, the development of the fœtus was normal.

Rabbit

Groups of 10 rabbits were dosed at 0; 0.8; 3.2 and 12.5 mg/kg/day from day 7 to day 19 of gestation. No maternal abnormalities were observed. The foetuses taken at day 29 were all normal.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Septanest SP
Articaine Hydrochloride and Epinephrine Injection
4% (40 mg/mL) of articaine hydrochloride and 1:100,000 (0.01 mg/mL) of epinephrine (as epinephrine bitartrate)

Septanest N
Articaine Hydrochloride and Epinephrine Injection
4% (40 mg/mL) of articaine hydrochloride and 1:200,000 (0.005 mg/mL) of epinephrine (as epinephrine bitartrate)

Read this carefully before you start taking **Septanest SP** and **Septanest N** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Septanest SP** and **Septanest N**.

What is Septanest SP and Septanest N used for?

Septanest SP and Septanest N are used in adults and children (4 years of age and older) to reduce pain during dental procedures.

How does Septanest SP and Septanest N work?

Septanest SP and Septanest N belong to a group of medicines known as "local anesthetics". Septanest SP and Septanest N are a combination of two medicinal ingredients:

- **Articaine hydrochloride:** This works by blocking nerve signals at the site of injection to numb a specific area.
- **Epinephrine:** This works by narrowing the blood vessels at the site of injection to enhance the effects of articaine hydrochloride and reduce bleeding during your procedure.

What are the ingredients in Septanest SP and Septanest N?

Medicinal ingredients: articaine hydrochloride and epinephrine bitartrate.

Non-medicinal ingredients: sodium chloride, sodium metabisulfite, water for injection, and hydrochloric acid and/or sodium hydroxide to adjust the pH.

Septanest SP and Septanest N comes in the following dosage forms:

- **Septanest SP (sterile solution):** 40 mg/mL of articaine hydrochloride (4%) and 0.01 mg/mL of epinephrine as epinephrine bitartrate (1:100,000).
- **Septanest N (sterile solution):** 40 mg/mL of articaine hydrochloride (4%) and 0.005 mg/mL of epinephrine as epinephrine bitartrate (1:200,000).

Do not use Septanest SP and Septanest N if:

- you are allergic to articaine hydrochloride, epinephrine, or any of the other ingredients in Septanest SP and Septanest N.
- you are allergic or have had allergic reaction to sulphite.
- you have untreated epilepsy or seizures.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Septanest SP and Septanest N. Talk about any health conditions or problems you may have, including if you:

- have low or high blood pressure.
- have any heart or blood vessel problems.

- have liver problems.
- have kidney problems.
- have asthma.
- have plasma cholinesterase deficiency (low levels of enzymes necessary for the metabolism of certain medications).
- have myasthenia gravis (a chronic autoimmune disorder that causes muscle weakness).
- have pheochromocytoma (a tumour in the adrenal gland).
- have glaucoma (increased pressure within your eyes).
- are pregnant or planning to become pregnant.
- are breastfeeding or planning to breastfeed. It is not known if Septanest SP and Septanest N are excreted in breast milk.
- have diabetes.

Other warnings you should know about:

Driving or using machinery: Septanest SP and Septanest N can affect your judgement, coordination, and alertness. You should be careful when driving or doing tasks that require special attention after receiving Septanest SP or Septanest N.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Septanest SP and Septanest N:

- acetaminophen, a medicine used to relive pain and reduce fever.
- alcohol.
- antiarrhythmics, medicines used for heart rhythm disorders (e.g., digitalis, digital glucosides, and quinidine).
- antibiotics, medicines used to treat bacterial infections (e.g., dapsone, nitrofurantoin, para-aminosalicylic acid, and sulfonamides).
- anticonvulsants, medicines used for seizures (e.g., phenobarbital, phenytoin, and sodium valproate).
- antidepressants, medicines used to treat depression and anxiety (e.g., monoamine oxidase (MAO) inhibitors, tricyclic antidepressants, amitriptyline, clomipramine, desipramine, imipramine, nortriptyline, trimipramine, milnacipran, and venlafaxine).
- antihistamines, medicines used to treat allergies (e.g., chlorpheniramine and diphenhydramine).
- antihypertensives, medicines used for high blood pressure (e.g., guanadrel, guanethidine, and rauwolfia alkaloids).
- antimalarials, medicines used to treat malaria (e.g., chloroquine and primaquine).
- antineoplastic agents, medicines used to treat cancer (e.g., cyclophosphamide, flutamide, hydroxyurea, ifosfamide, and rasburicase).
- antiparkinsonian drugs, medicines used for Parkinson's disease (e.g., entacapone and tolcapone).
- beta blockers, medicines used to treat high blood pressure and certain heart conditions (e.g., propranolol and nadolol).
- local anesthetics, medicines used for pain relief and local anesthesia (e.g., articaine, benzocaine, bupivacaine, lidocaine, mepivacaine, prilocaine, procaine, ropivacaine, and tetracaine).
- medicines used to treat migraines (e.g., methysergide, ergotamine, and ergonovine).
- metoclopramide, a medicine used to relieve nausea, vomiting, and indigestion.
- neuroleptics, medicines used to treat mental and emotional disorders (e.g., phenothiazines).
- nitrates and nitrites, medicines used to dilate blood vessels and treat certain heart conditions (e.g., nitric oxide, nitroglycerin, nitroprusside, and nitrous oxide).
- other anesthetics, medicines used for general anesthesia (e.g., chloroform, halothane, cyclopropane, and trichloroethylene).
- quinine, a medicine used to treat and prevent malaria.

- sedatives, medicines used for sleep and anxiety relief (e.g., benzodiazepine and opioids).
- sulfasalazine, a medicine used to treat bowel problems.
- sympathomimetics, medicines used to increase blood pressure, open airways, and relieve congestion (e.g., cocaine, amphetamines, phenylephrine, pseudoephedrine, oxymetazoline, levothyroxine, and methyldopa).

How to take Septanest SP and Septanest N:

Your healthcare professional will prepare and give you Septanest SP or Septanest N in a healthcare setting.

- You will receive Septanest SP or Septanest N by an injection into the area around a tooth or gums (infiltration) or near a nerve (nerve block). Any other route of administration will not be used due to the risk of dangerous side effects.
- Follow all instructions given to you by your healthcare professional.

Usual dose:

Your healthcare professional will decide the right dose for you. It will depend on your age, health, weight, and the procedure you are having. The lowest dose that produces the desired results for you will be used.

Overdose:

If you think you, or a person you are caring for, have taken too much Septanest SP and Septanest N, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using Septanest SP and Septanest N?

These are not all the possible side effects you may have when taking Septanest SP and Septanest N. If you experience any side effects not listed here, tell your healthcare professional.

Side effects of Septanest SP and Septanest N include:

- agitation or restlessness;
- anxiety or nervousness;
- bruising;
- enlarged lymph nodes;
- gum and mouth discomfort or pain, including sores or ulcers in the mouth;
- increased saliva;
- increased sensitivity;
- indigestion or upset stomach;
- loss of movement or weakness of the muscles of the face ;
- migraine;
- muscle twitching;
- neck pain;
- numbness of the lips, tongue, and mouth;
- pain or swelling at the injection site;
- ringing in the ear or ear pain;
- shaky or trembling movements (tremor);
- shivering or feeling cold (chills);
- sleepiness or drowsiness;
- sore throat;
- tooth problems.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking this drug and get immediate medical help**
	Only if severe	**In all cases**	
COMMON			
Angioedema (swelling of tissue under the skin): swelling of face, tongue, cheek, tongue, lips, throat, hands, feet, around the eyes, or difficulty breathing.			X
Bradycardia or tachycardia (abnormally slow or fast heartbeat)		X	
Dizziness	X		
Hypotension (low blood pressure): dizziness, fainting, light-headedness, blurred vision, nausea, vomiting, or fatigue (may occur when you go from lying or sitting to standing up).		X	
Syncope (fainting): a temporary loss of consciousness due to a sudden drop in blood pressure.		X	
UNCOMMON			
Hypertension (high blood pressure): shortness of breath, fatigue, dizziness, fainting, chest pain or pressure, swelling in your ankles and legs, bluish colour to your lips and skin, racing pulse, or heart palpitations.		X	
Injection site exfoliation or necrosis (peeling or death of the skin at the injection area): peeling or flaking of the skin, discoloration, severe pain, open sores, chills, or ulcers near the injection site.			X
RARE			
Allergic reactions: rash, hives, itchiness, pink eye, sneezing, stuffy nose, congestion, runny nose, difficulty swallowing, difficulty breathing, wheezing, drop in blood pressure, nausea, vomiting, or swelling of face, tongue, lip, throat, or eyes.			X
Bronchospasm (when there is a sudden narrowing of the airway): difficulty breathing, wheezing, coughing, chest tightness, or fatigue.		X	
Dyspnea (shortness of breath)		X	
Eye problems: seeing double, blurred vision, temporary or full loss of vision, itching of the eyelids, one or both pupils are larger or smaller than normal, or drooping eyelid over the eye.		X	
VERY RARE			
Paraesthesia (pins and needles): sensation of tingling, pain, or numbness in the hands, fingers and toes.		X	
UNKNOWN			
Heart conduction disorders (irregular heart rhythm): slow or irregular heartbeat, fatigue, weakness, dizziness, fainting, shortness of breath, or chest pain.		X	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Methemoglobinemia (blood disorder where not enough oxygen getting to the cells of the body): pale, gray, or blue coloured skin, headache, rapid heart rate, shortness of breath, light-headed, or fatigue.		X	
Vasoconstriction (narrowing of blood vessels): cold hands or feet, pale or bluish skin, high blood pressure, numbness, tingling, or increased heart rate.		X	
Vasodilatation (widening of blood vessels): dizziness, light-headedness, headache, warm or flushed skin, redness in the face or body, or low blood pressure.		X	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Your healthcare professional will store Septanest SP and Septanest N at or below 25°C. It will be protected from light and freezing. Keep out of reach and sight of children.

If you want more information about Septanest SP and Septanest N:

- Talk to your healthcare professional
- Find the full Product Monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website (https://www.septodont-en.ca) or by calling 1-800-647-0643.

This leaflet was prepared by Septodont.

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