

PRODUCT MONOGRAPH

ORABLOC® 1:100,000 and ORABLOC® 1:200,000

(articaine hydrochloride and epinephrine bitartrate injection 40 mg/ml / 0.009 mg/ml (epinephrine 1:200,000))

and

articaine hydrochloride and epinephrine bitartrate injection 40 mg/ml / 0.018 mg/ml (epinephrine 1:100,000))

Local Anaesthetic for Dental Use

**Pierrel Pharma S.r.l.
Capua (CE), Italy 81043**

**Date of Preparation:
January 11, 2018**

**Imported by :
Wheels International Inc.
Mississauga, Ontario
L5L 5Z7**

Control#: 211716

NAME OF DRUG

ORABLOC® 1:100,000

(articaine hydrochloride and epinephrine bitartrate injection 40 mg/ml / 0.018 mg/ml
(epinephrine 1:100,000))

ORABLOC® 1:200,000

(articaine hydrochloride and epinephrine bitartrate injection 40 mg/ml / 0.009 mg/ml
(epinephrine 1:200,000))

THERAPEUTIC CLASSIFICATION

Local Anaesthetic for Dental Use

CLINICAL PHARMACOLOGY

ORABLOC (articaine hydrochloride) is a local anaesthetic that has the reversible effect of blocking the conduction of painful sensations. ORABLOC decreases nerve conduction by diminishing the sodium ion influx during the action potential period. The epinephrine is a vasoconstrictor added to ORABLOC to slow down the passage into the general circulation and thus ensure the prolonged maintenance of an active tissue concentration. The anaesthesia 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.

INDICATIONS AND CLINICAL USE

ORABLOC (articaine hydrochloride) is indicated for infiltration anaesthesia and nerve block anaesthesia in clinical dentistry. This includes local or loco-regional dental anaesthesia 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. ORABLOC is also suitable for muco-gingival operations and other surgical operations on the bone when long lasting ischaemia and analgesia are required.

CONTRAINDICATIONS

ORABLOC (articaine hydrochloride) is contraindicated in patients with known allergies to dental anaesthetics. ORABLOC is also contraindicated in patients with sepsis near the proposed injection site, severe shock, paroxysmal tachycardia, frequent arrhythmia, severe hypertension, neurological diseases, or in patients with asthma who may have bronchospastic allergic reactions induced by sulphites.

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

WARNINGS

ORABLOC, along with other local anaesthetics, is capable of producing methaemoglobinaemia. The clinical signs of methaemoglobinaemia are cyanosis of the nail beds and lips, fatigue and weakness. If methaemoglobinaemia 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.

ORABLOC contains sulphites which can cause or aggravate anaphylactic-type reactions.

Intravascular injection is strictly contraindicated: therefore, it is imperative to ensure that the needle being used for the injection does not go into a vessel. Injections should always be made slowly with frequent aspirations in order to verify the absence of intravascular injection.

Toxic reactions may occur in the case of overdosage or accidental intravenous injection.

The American Heart Association has made the following recommendations regarding the use of local anesthetics with vasoconstrictors in patients with ischemic disease: "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." (Kaplan, EL, editor: Cardiovascular disease in dental practice, Dallas 1986, American Heart Association.)

PRECAUTIONS

General

Each time a local anaesthetic 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 anaesthetics depend upon proper dosage, correct technique, adequate precautions, and readiness for emergencies. In persons with known or suspected drug allergies or sensitivities to amide-type local anaesthetics, ORABLOC should be given cautiously.

The following precautions apply to all anaesthetics: avoid injection into an inflamed or infected area. Injections should always be made slowly with frequent aspirations in order to verify the absence of intravascular injection. 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, height, 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. Avoid excessive premedication with sedatives, tranquilizers, and anti-emetic agents, especially in small children and elderly patients.

Patients with Special Diseases and Conditions

In patients with peripheral vascular disease or injection into areas with limited blood supply, the use of a local anaesthetic containing a vasoconstrictor should be made with caution.

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

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 anaphylactic shock may occur in patients with bronchial asthma due to hypersensitivity to the sulfite component.

Use in Pregnancy

Safe use of local anaesthetics 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.

Use in Children

The use of Orabloc in children under the age of 4 years is not recommended. (See **Dosage and Administration**).

Drug Interactions

Severe incompatibilities with monoamine oxydase (MAO) inhibitors and betablockers are reported. 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 or immediately following the administration of chloroform, halothane, cyclopropane, trichloroethylene or related anaesthetics may sensitize the heart to epinephrine and may cause dose-related cardiac arrhythmias.

ADVERSE REACTIONS

Reactions to ORABLOC (articaine hydrochloride) are characteristic of amide-type local anaesthetics.

Adverse reactions of this group of drugs are generally dose-related and may result from high plasma concentrations of anaesthetic 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 anaesthetic could affect the central nervous system (CNS) 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, unconsciousness, and respiratory arrest. Nausea, vomiting, chills, miosis and tinnitus may also occur.

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

Allergic reactions may be manifested by dermatologic reactions, edema, urticaria and other allergy symptoms.

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.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

The type of toxic reaction is unpredictable and depends on factors such as dosage, rate of absorption and clinical status of patient. Two types of reactions that effect stimulation and/or depression of the central cortex and medulla may result from systemic absorption.

Slow onset symptoms following overdose include stimulation leading to nervousness, dizziness, blurred vision, nausea, tremors, convulsions, hypotension, cardiovascular depression and respiratory arrest.

Rapid onset symptoms following overdose include depression leading primarily to respiratory arrest, cardiovascular collapse and cardiac arrest. Since cardiac arrest symptoms may occur rapidly and with little warning, treatment should be readily available.

Treatment

Toxic effects require symptomatic treatment, there is no specific cure:

- 1) For all symptoms: secure and maintain a patient airway, administer oxygen.

- 2) Circulatory depression: immediately resuscitate with oxygen and intravenously administer a vasopressor agent to maintain blood pressure. Cardiac massage or external cardiac stimulation is indicated if cardiac arrest occurs.
- 3) For convulsions that do not respond to respiratory support, administration of curare-like drugs, e.g. succinylcholine chloride, 40 mg intravenously or ultrashort acting barbiturates such as thiopental, 30 to 50 mg per minute. Since barbiturates may cause circulatory depression, succinylcholine chloride is preferred. I.V. muscle relaxants and barbiturates should only be administered by those familiar with their use.

DOSAGE AND ADMINISTRATION

Orabloc (articaine hydrochloride and epinephrine bitartrate injection 40 mg/ml / 0.018 mg/ml (epinephrine 1:100,000))

Orabloc (articaine hydrochloride and epinephrine bitartrate injection 40 mg/ml / 0.009 mg/ml (epinephrine 1:200,000))

As with all local anaesthetics 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 anaesthesia.

Adults

- For most common operations, one infiltration with 1.7 mL Orabloc 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 articaine hydrochloride per kilogram body weight. The duration of anaesthesia during which an operation can be performed using Orabloc 1:200,000 is up to 45minutes. The duration of anaesthesia during which an operation can be performed using Orabloc 1:100,000 is up to 75 minutes. The lowest dosage needed to provide effective anaesthesia should be administered.

Table 1

<i>Procedure</i>	<i>Orabloc 1:200,000 and Orabloc 1:100,000</i>	
	<i>Volume (mL)</i>	<i>Total Dose (mg)</i>
Infiltration	0.5 – 2.5	20 – 100
Nerve Block	0.5 – 3.4	20 – 136
Oral Surgery	1 – 5.1	40 – 204

Children

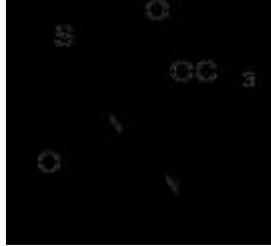
For Orabloc 1:200,000 and Orabloc 1:100,000 use in children under 4 years of age is not recommended. The quantity to be injected should be determined by the age of the child and

the size of the operation. Do not exceed the equivalent of 7 mg articaine hydrochloride per kilogram of body weight.

PHARMACEUTICAL INFORMATION

Drug Substance

Structural Formula :



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

Molecular Formula : $C_{13}H_{20}N_2O_3S \cdot HCl$

Molecular Weight : 320.84

Description : 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.

Composition per ml

Orabloc (1:100,000)

Articaine hydrochloride	40 mg
Epinephrine bitartrate (adrenaline bitartrate)	0.018 mg
corresponding in epinephrine base to	0.010 mg
Sodium chloride	1.00 mg
Sodium Metabisulfite (as antioxidant)	0.50 mg
Water for injections q. s. ad	1.0 ml

Formulated without parahydroxybenzoates

Orabloc (1:200,000)

Articaine hydrochloride	40 mg
Epinephrine bitartrate (adrenaline bitartrate)	0.009 mg
corresponding in epinephrine base to	0.005 mg
Sodium chloride	1.00 mg
Sodium Metabisulfite (as antioxidant)	0.50 mg
Water for injections q. s. ad	1.0 ml

Formulated without parahydroxybenzoates

Stability and Storage Recommendations

Store between 15°C and 25°C, protected from light.

AVAILABILITY OF DOSAGE FORMS

Orabloc® 1:100,000: articaine hydrochloride and epinephrine bitartrate injection 40 mg/ml / 0.018 mg/ml (epinephrine 1:100,000) are available in 1.7 mL glass cartridges, box of 50 or 100 cartridges.

Orabloc® 1:200,000: articaine hydrochloride and epinephrine bitartrate injection 40 mg/ml / 0.009 mg/ml (epinephrine 1:200,000) are available in 1.7 mL glass cartridges, box of 50 or 100 cartridges.

PHARMACOLOGY

Animal

Pharmacokinetics

The pharmacokinetics of articaine were studied in dwarf pigs after i.v. and i.m. administration with ³⁵S 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.

Pharmacodynamics

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 anaesthetic effect.

The anaesthesia of conduction for articaine (0.05 to 0.5%) is compared to other local anaesthetics, 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 anaesthetics had a negative inotropic effect on the heart during isovolumetric contraction.

The administration of local anaesthetics 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

Pharmacokinetics

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 ± 2.5 minutes. The peak plasma level following intramuscular injection was similar at $0.91 \pm 0.21 \mu\text{g/mL}$ but was reached more slowly at 26.2 ± 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.

Pharmacodynamics

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 $\mu\text{g/mL}$ epinephrine produced excellent analgesia with duration lasting from 40 to 62 minutes. Articaine administered without epinephrine did not produce reliable anaesthesia.

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

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 dosedependent 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 LD₅₀ levels for the rat, rabbit and dog is found in Table 2.

Table 2

<i>Species</i>	<i>Route</i>	<i>% sol.</i>	<i>LD₅₀ mg/kg</i>
Rat	I.V.	4	23.2 (22.1 – 24.3)
	I.M.	3	278 (260 – 298)
	P.O.	4	978 (868 – 1102)
Rabbit	I.V.	15	19.6 (18.6 – 20.7)
	I.M.	3	20.6 (18.6 – 22.8)
Dog	I.V.	15	Max tolerated dose 50 Min lethal dose 56
	I.M.	25	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 3.

Table 3

<i>Articaine 4 per cent</i>	<i>Male Mice</i>	<i>Female Mice</i>
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 LD₅₀ 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 anaesthesia was studied in the beagle to which 5 mL of articaine solution (2%) containing 2 mg % epinephrine was administered into the lumbar-sacral 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.

Teratology

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 foetus was normal.

Rabbit (n= 10 per dose)

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 were all normal.

REFERENCES

1. AHFS Drug Information 91. Local Anesthetics, parenteral, general statement. American Society of Hospital Pharmacists. 1991: 1944-1947.
2. Baeder C, Bahr H, Benoir W, Doerr BJ, Engelbart K, Hergott J, Kramer M, Schutz E, Schultes E, Scholz J, Sprigmen FR, Wolf GL. Untersuchungen zur Vertraglichkeit von Carticaine, einem neuen Lokalanästhetikum. *Prakt Anästh* 1975; 9: 147-52.
3. Borchard R, Drouin H. Carticaine : action of the local anesthetic on myelinated nerve fibres. *Eur J Pharmac* 1980 ; 62 : 73-9.
4. Borchard U, Greeff K, Hafner D. Quantitative evaluation of cardioactive drugs using computer analysis of the ventricular pressure curve during isovolumetric contraction. *Basic Res Cardiol* 1980 ; 75 : 378-89.
5. Den Hertog A. The effect of carticaine on mammalian non-myelinated nerve fibres. *Eur J Pharm* 1974 ; 26 : 175-8.
6. Hofer H, Eberi R, Altmann H. Pharmakokinetische Untersuchungen mit ³⁵Smarkiertem Carticaine. *Prakt Anästh* 1974 ; 9 : 157-61.
7. Kirch W, Kitteringham N, Lambers G., Hadju P, Ohnhaus EE. Die Klinische Pharmakokinetik von Articain nach intraoralen und intramuskulären Applikation. *Schweiz Mschr Zahnheilk* 1983 ; 93 : 714-9.
8. Muschaweck R, Rippel R. Ein neues Lokalanästhetikum (Carticain) aus der Thiophenreihe. *Prakt Anästh* 1974 ; 9 : 135-46.
9. USPDI. Drug information for the health care professional. Anesthetics (parenteral/local). USPDI 11 edition 1991 : 205-211.
10. Winther JE, Patirupanusara B. Evaluation of carticaine – a new local analgesic. *Int J oral Surg* 1974 ; 3 : 422-7.
11. Compendium of Pharmaceuticals and Specialities, 26th Edition, 1991 (e.d. C.M.E. Krogh), Canadian Pharmaceutical Association.
12. Product monograph for Septanest, June 26, 2007, by Septodont

Last revised: January 11, 2018