Septocaine® with epinephrine 1:100,000
Septocaine® with epinephrine 1:200,000

(articaine hydrochloride 4% (40 mg/ml) with epinephrine 1:100,000 or 1:200,000 injection)
BRIEF SUMMARY. [See Package Insert For Full Prescribing Information]

USE
Septocaine® is indicated for local, infiltrative, or conductive anesthesia in both simple and complex dental procedures. For most routine dental procedures, Septocaine® with epinephrine 1:200,000 is preferred. Septocaine® with epinephrine 1:100,000 is preferred during operative or surgical procedures when improved visualization of the surgical field is desirable.

CONTRAINDICATIONS
Septocaine® is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type, or in patients with known hypersensitivity to sodium metabisulfite.

WARNINGS
Accidental intravascular injection may be associated with convulsions, followed by central nervous system or cardiorespiratory depression and coma, progressing ultimately to respiratory arrest. Dental practitioners and/or clinicians who employ local anesthetic agents should be well versed in diagnosis and management of emergencies that may arise from their use. Resuscitative equipment, oxygen, and other resuscitative drugs should be available for immediate use.

Intravascular injections should be avoided. To avoid intravascular injection, aspiration should be performed before Septocaine® is injected. The needle must be repositioned until no return of blood can be elicited by aspiration. Note, however, that the absence of blood in the syringe does not guarantee that intravascular injection has been avoided.

Septocaine® contains epinephrine that can cause local tissue necrosis or systemic toxicity. Usual precautions for epinephrine administration should be observed.

Septocaine® contains 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. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.

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

The American Heart Association has made the following recommendation regarding the use of local anesthetics with vasoconstrictors in patients with ischemic heart disease: "Vasoconstrictor agents should be used in local anesthesia 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: Resuscitative equipment, oxygen, and other resuscitative drugs should be available for immediate use (see **WARNINGS**). The lowest dosage that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. Repeated doses of Septocaine® may cause significant increases in blood levels with each repeated dose because of possible accumulation of the drug or its metabolites. Tolerance to elevated blood levels varies with the status of the patient.

Debilitated patients, elderly patients, acutely ill patients and pediatric patients should be given reduced doses commensurate with their age and physical condition.

Septocaine® should be used with caution in patients with heart block.

Local anesthetic solutions, such as Septocaine®, containing a vasoconstrictor should be used cautiously. Patients with peripheral vascular disease and those with hypertensive vascular disease may exhibit exaggerated vasoconstrictor response. Ischemic injury or necrosis may result. Septocaine® should be used with caution in patients during or following the administration of potent general anesthetic agents, since cardiac arrhythmias may occur under such conditions.

Systemic absorption of local anesthetics can produce effects on the central nervous and cardiovascular systems. At blood concentrations achieved with therapeutic doses, changes in cardiac conduction, excitability, refractoriness, contractility, and peripheral vascular resistance are minimal. However, toxic blood concentrations depress cardiac conduction and excitability, which may lead to atrioventricular block, ventricular arrhythmias, and cardiac arrest, possibly resulting in fatalities. In addition, myocardial contractility is depressed and peripheral vasodilation occurs, leading to decreased cardiac output and arterial blood pressure.

Careful and constant monitoring of cardiovascular and respiratory (adequacy of ventilation) vital signs and the patient's state of consciousness should be performed after each local anesthetic injection. It should be kept in mind at such times that restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors, depression, or drowsiness may be early warning signs of central nervous system toxicity.

In vitro studies show that about 5% to 10% of articaine is metabolized by the human liver microsomal P450 isoenzyme system. However, because no studies have been performed in patients with liver dysfunction, caution should be used in patients with severe hepatic disease.

Septocaine® should also be used with caution in patients with impaired cardiovascular function since they may be less able to compensate for functional changes associated with the prolongation of A-V conduction produced by these drugs.

Small doses of local anesthetics injected in dental blocks may produce adverse reactions similar to systemic toxicity seen with unintentional intravascular injections of larger doses. Confusion, convulsions, respiratory depression and/or respiratory arrest, and cardiovascular stimulation or depression have been reported. These reactions may be due to intra-arterial injection of the local anesthetic with retrograde flow to the cerebral circulation. Patients receiving these blocks should be observed constantly. Resuscitative equipment and personnel for treating adverse reactions should be immediately available.

Dosage recommendations should not be exceeded (see **DOSAGE AND ADMINISTRATION** in package insert).

Information for Patients:
- The patient should be informed in advance of the possibility of temporary loss of sensation and muscle function following infiltration and nerve block injections.
- Patients should be instructed not to eat or drink until normal sensation returns.

Clinically Significant Drug Interactions: The administration of local anesthetic solutions containing epinephrine to patients receiving monoamine oxidase inhibitors, nonselective beta adrenergic antagonists or tricyclic antidepressants may produce severe, prolonged hypertension. Phenothiazines and butyrophenones may reduce or reverse the pressor effect of epinephrine. Concurrent use of these agents should generally be avoided. In situations when concurrent therapy is necessary, careful patient monitoring is essential.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Studies to evaluate the carcinogenic potential of articaine HCl in animals have not been conducted. 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 micronucleous tests (one with Septocaine® with epinephrine 1:100,000 and one with articaine HCl alone) showed no mutagenic effects. No effects on male or female fertility were observed in rats for Septocaine® with epinephrine 1:100,000 administered subcutaneously in doses up to 80 mg/kg/day (approximately two times the maximum male and female recommended human dose on a mg/m2 basis).

Pregnancy: Teratogenic Effects-Pregnancy Category C.

In developmental studies, no embryofetal toxicities were observed when Septocaine® with epinephrine 1:100,000 was administered subcutaneously throughout organogenesis at doses up to 40 mg/kg in rabbits and 80 mg/kg in rats (approximately 2 times the maximum recommended human dose on a mg/m2 basis). In rabbits, 80 mg/kg (approximately 4 times the maximum recommended human dose on a mg/m2 basis) did cause fetal death and increase fetal skeletal variations, but these effects may be attributable to the severe maternal toxicity, including seizures, observed at this dose.

When articaine hydrochloride was administered subcutaneously to rats throughout gestation and lactation, 80 mg/kg (approximately 2 times the maximum recommended human dose on a mg/m2 basis) increased the number of stillbirths and adversely affected passive avoidance, a measure of learning, in pups. This dose also produced severe maternal toxicity in some animals. A dose of 40 mg/kg (approximately equal to the maximum recommended human dose on a mg/m2 basis) did not produce these effects. A similar study using Septocaine® with epinephrine 1:100,000 rather than articaine hydrochloride alone produced maternal toxicity, but no effects on offspring. There are no adequate and well-controlled studies in pregnant women. Animal reproduction studies are not always predictive of human response. Septocaine® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether articaine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Septocaine® is administered to a nursing woman.

Pediatric Use: In clinical trials, 61 pediatric patients between the ages of 4 and 16 years received Septocaine® with epinephrine 1:100,000. Among these pediatric patients, doses from 0.76 mg/kg to 5.65 mg/kg (0.9 to 5.1 mL) were administered safely to 51 patients for simple procedures and doses between 0.37 mg/kg and 7.48 mg/kg (0.7 to 3.9 mL) were administered safely to 10 patients for complex procedures. However, there was insufficient exposure to Septocaine® with epinephrine 1:100,000 at doses greater than 7.00 mg/kg in order to assess its safety in pediatric patients. No unusual adverse events were noted in these patients. Approximately 13% of these pediatric patients required additional injections of anesthetic for complete anesthesia. Safety and effectiveness in pediatric patients below the age of 4 years have not been established. Dosages in pediatric patients should be reduced, commensurate with age, body weight, and physical condition. See **DOSAGE AND ADMINISTRATION** in package insert.

Geriatric Use: In clinical trials, 54 patients between the ages of 65 and 75 years, and 11 patients 75 years and over received Septocaine® with epinephrine 1:100,000. Among all patients between 65 and 75 years, doses from 0.43 mg/kg to 4.76 mg/kg (0.9 to 11.9 mL) were administered safely to 35 patients for simple procedures and doses from 1.05 mg/kg to 4.27 mg/kg (1.3 to 6.8 mL) were administered safely to 19 patients for complex procedures. Among the 11 patients ³ 75 years old, doses from 0.78 mg/kg to 4.76 mg/kg (1.3 to 11.9 mL) were administered safely to 7 patients for simple procedures and doses of 1.12 mg/kg to 2.17 mg/kg (1.3 to 5.1 mL) were safely administered to 4 patients for complex procedures.

No overall differences in safety or effectiveness were observed between elderly subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. Approximately 6% of patients between the ages of 65 and 75 years and none of the 11 patients 75 years of age or older required additional injections of anesthetic for complete anesthesia compared with 11% of patients between 17 and 65 years old who required additional injections.

ADVERSE REACTIONS
Reactions to Septocaine® are characteristic of those associated with other amide-type local anesthetics. Adverse reactions to this group of drugs may also result from excessive plasma levels (which may be due to overdosage, unintentional intravascular injection, or slow metabolic degradation), injection technique, volume of injection, hypersensitivity, or may be idiosyncratic.

The reported adverse events are derived from clinical trials in the US and UK. Table 1 displays the adverse events reported in clinical trials where 882 individuals were exposed to Septocaine® with epinephrine 1:100,000 and Table 2 displays the adverse events reported in clinical trials where 182 individuals were exposed to Septocaine® with epinephrine 1:100,000 and 179 individuals were exposed to Septocaine® with epinephrine 1:200,000.

Table 1. Adverse Events in controlled trials with an incidence of 1% or greater in patients administered Septocaine® with epinephrine 1:100,000.

Body System	Septocaine® with epinephrine 1:100,000 N (%)
Number of patients	882 (100%)
Body as a whole	
Face Edema	13 (1%)
Headache	31 (4%)
Infection	10 (1%)
Pain	114 (13%)
Digestive system	
Gingivitis	13 (1%)
Nervous system	
Paresthesia	11 (1%)

Table 2. Adverse Events in controlled trials with an incidence of 1% or greater in patients administered Septocaine® with epinephrine 1:100,000 and Septocaine® with epinephrine 1:200,000.

Number of patients exposed to drug	Septocaine® with epinephrine 1:100,000 (N=182)	Septocaine® with epinephrine 1:200,000 (N=179)
Number of patients that reported any Adverse Event	35	33
Pain	14 (7.6%)	11 (6.1%)
Headache	6 (3.2%)	9 (5.0%)
Positive blood aspiration into syringe	6 (3.2%)	3 (1.6%)
Swelling	5 (2.7%)	3 (1.6%)
Trismus	3 (1.6%)	1 (0.5%)
Nausea and emesis	0 (0%)	3 (1.6%)
Sleepiness	1 (0.5%)	2 (1.1%)
Numbness and tingling	2 (1.0%)	1 (0.5%)
Palpitation	2 (1.0%)	0 (0%)
Ear symptoms (earache, otitis media)	2 (1.0%)	1 (0.5%)
Cough, persistent cough	2 (1.0%)	0 (0%)

The following list includes adverse and intercurrent events that were recorded in 1 or more patients, but occurred at an overall rate of less than one percent, and were considered clinically relevant.

Body as a Whole: abdominal pain, accidental injury, asthenia, back pain, injection site pain, burning sensation above injection site, malaise, neck pain.
Cardiovascular System: hemorrhage, migraine, syncope, tachycardia, elevated blood pressure.
Digestive System: constipation, diarrhea, dyspepsia, glossitis, gum hemorrhage, mouth ulceration, nausea, stomatitis, tongue edemas, tooth disorder, vomiting.
Hemic and Lymphatic System: ecchymosis, lymphadenopathy.
Metabolic and Nutritional System: edema, thirst.
Musculoskeletal System: arthralgia, myalgia, osteomyelitis.
Nervous System: dizziness, dry mouth, facial paralysis, hyperesthesia, increased salivation, nervousness, neuropathy, paresthesia, somnolence, exacerbation of Kearns-Sayre Syndrome.
Respiratory System: pharyngitis, rhinitis, sinus pain, sinus congestion.
Skin and Appendages: pruritus, skin disorder.
Special Senses: ear pain, taste perversion.
Urogenital System: dysmenorrhea.

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.

OVERDOSAGE
Acute emergencies from local anesthetics are generally related to high plasma levels encountered during therapeutic use of local anesthetics or to unintended subarachnoid injection of local anesthetic solution (see WARNINGS, PRECAUTIONS; General and ADVERSE REACTIONS).

Management of Local Anesthetic Emergencies: The first consideration is prevention, best accomplished by careful and constant monitoring of cardiovascular and respiratory vital signs and the patient's state of consciousness after each local anesthetic injection. At the first sign of change, oxygen should be administered.

The first step in the management of convulsions, as well as hypoventilation, consists of immediate attention to the maintenance of a patient airway and assisted or controlled ventilation as needed. The adequacy of the circulation should be assessed. Should convulsions persist despite adequate respiratory support, treatment with appropriate anticonvulsant therapy is indicated. The practitioner should be familiar, prior to the use of local anesthetics, with the use of anticonvulsant drugs. Supportive treatment of circulatory depression may require administration of intravenous fluids and, when appropriate, a vasopressor.

If not treated immediately, both convulsions and cardiovascular depression can result in hypoxia, acidosis, bradycardia, arrhythmias and cardiac arrest. If cardiac arrest should occur, standard cardiopulmonary resuscitative measures should be instituted.

HOW SUPPLIED
Septocaine® (articaine HCl 4% with epinephrine 1:100,000 or 1:200,000 injection) is available in 1.7 mL glass cartridges, in boxes of 50 cartridges. The product is formulated with a 15% overage of epinephrine.

NDC 0362-9048-02 Septocaine® with epinephrine 1:200,000 Box of 50 cartridges
NDC 0362-9049-02 Septocaine® with epinephrine 1:100,000 Box of 50 cartridges

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