individuals were exposed to Articaine HCl and Epinephrine containing epinephrine 1:200,000. Table 3 displays the adverse reactions reported in clinical trials where 182 individuals were exposed to Articaine HCl and Epinephrine containing epinephrine 1:100,000 and 179 observed in practice.

The minimum possible amount of vasoconstrictor should be used.” (Kaplan, 1986).

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 performed in patients with liver dysfunction, and caution should be used in patients with severe hepatic disease.

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 of Articaine HCl and Epinephrine.

Restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors, depression, or drowsiness may be early warning signs of central nervous system toxicity.

Articaine HCl and Epinephrine is contraindicated in patients who are hypersensitive to products containing sulfites. Products containing sulfites may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people [see Warnings and Precautions (5.5)].

Articaine HCl and Epinephrine may be used.

Adverse reactions observed in at least 1% of patients: Nervous system: Headache, dizziness, tinnitus, numbness and paresthesia, facial edema. Cardiovascular: Bradycardia, palpitation, flushing, chest pain, and facial erythema. Respiratory: Dyspnea, oropharyngeal edema, hiccups, rhinitis. Gastrointestinal: Nausea, vomiting, constipation, dry mouth, diarrhea. Musculoskeletal: Myalgia, muscle cramps. Other: Urinary frequency, dry throat, restlessness, anxiety, depression, drowsiness.

Dose 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 disease.

Dose 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 disease.

The recommended doses are on a page linked to the full prescribing information.
Articaine HCl and Epinephrine containing articaine HCl 4% (40 mg/mL) and epinephrine 1:200,000 (as epinephrine bitartrate 0.009 mg/mL) (NDC 390404-6625-05).  

5.4 Metabolism

Articaine HCl is metabolized by plasma carboxyesterase to its primary metabolite, articainic acid, which is inactive. In vitro studies show that the human liver microsome P450 isoenzyme system metabolizes Articaine HCl. The half-life of articainic acid following absorption is 30 to 40 minutes. Articainic acid glucuronide is also a minor metabolite.

5.5 Excretion

Articaine HCl is excreted primarily through urine with 53-57% of the administered dose eliminated in the first 24 hours following submucosal administration. Articainic acid is the primary metabolite in urine. A minor metabolite, articainic acid glucuronide, is also detected in urine and feces. In addition, small amounts of unchanged articaine HCl, articainic acid, and articainic acid glucuronide are also found in urine and feces.

5.6 Clinical Studies

Four randomized, double-blind, active-controlled studies were performed comparing Articaine HCl and Epinephrine containing epinephrine 1:100,000 versus Articaine HCl and Epinephrine containing epinephrine 1:200,000. The studies were performed in healthy surgical patients who were scheduled to receive submucosal infiltration anesthesia. Two of the studies evaluated efficacy in patients undergoing orthognathic surgery and the other two evaluated efficacy in patients undergoing periodontal surgery.

17.1 Adverse Reactions

Adverse reactions observed in less than 1% of patients:

- Pruritus; skin disorder
- Ecchymosis; lymphadenopathy
- Nervous System:
  - Dizziness
  - Somnolence
  - Pruritus; pain
  - Vomiting

17.2 Postmarketing Surveillance

Limited only to cartridges when sold without dental injector: 

Store at controlled room temperature 25°C (77°F) with brief excursions permitted between 15° and 30°C (59°F-86°F) [see USP Controlled Room Temperature].  Protect from light.  Do Not Freeze.

18 HOW SUPPLIED/STORAGE AND HANDLING

Articaine and Epinephrine solutions are available in 20 mL cartridges and 40 mL cartridges.  Each 20 mL cartridge contains articaine HCl and epinephrine solution 1:100,000 or 1:200,000 (expressed as free base).  Each 40 mL cartridge contains articaine HCl and epinephrine solution 1:200,000 or 1:100,000 (expressed as free base).

11.1 General Use

The first step in the management of convulsions, as well as hypo-ventilation, consists of immediate attention to the maintenance of a patent airway and assisted or controlled ventilation as needed.  The adequacy of the circulation should be maintained by medical intervention including premature administration of intravenous fluids and, if necessary, vasopressor therapy.

10.3 Chronic Use

There are no adequate and well-controlled studies in pregnant women with Articaine HCl and Epinephrine.  Articaine hydrochloride and epinephrine (1:100,000) has been shown to increase fetal deaths and skeletal variations in rabbits when given in doses approximately 4 times the maximum recommended human dose (MRHD).  Articaine HCl and Epinephrine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.6 Renal/Hepatic Insufficiency

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.

11.3 Pregnancy

It is not known whether Articaine HCl and Epinephrine is excreted in human milk.  Because many drugs are excreted in human milk, caution should be exercised when Articaine HCl and Epinephrine is administered to a nursing mother.

11.2 Nursing Mothers

In addition to the cardiovascular effects of local anesthetics due to systemic absorption, local anesthetics may cause excitation or hypotension with syncope.  These reactions are usually minor and transient in patients who are not cardiovascu larly compromised.  Occasionally, however, more severe and protracted cardiovascular reactions may occur.  These reactions are generally related to the amount of drug administered and the rate of administration and are consistent with local anesthetic pharmacology.  These effects can be precipitated by the administration of a drug that further potentiates the action of the local anesthetic agent.  The potential for such an interaction should be kept in mind when Articaine HCl and Epinephrine are used in patients with cardiovascular disease or with conditions that are associated with cardiovascular instability.

2.1 Pharmacology

Articaine HCl is a local anesthetic of the benzocaine family.  It is an ester-type local anesthetic with a high affinity for nerve axo soma membranes.  Articaine HCl is metabolized by plasma carboxyesterase to its primary metabolite, articainic acid, which is inactive.  In vitro studies show that the human liver microsome P450 isoenzyme system metabolizes Articaine HCl.  The half-life of articainic acid following absorption is 30 to 40 minutes.  Articainic acid glucuronide is also a minor metabolite.

2.2 Precautions

Plasma levels of articaine HCl are increased when articaine HCl is administered in combination with a vasoconstrictor such as epinephrine.  The use of articaine HCl containing epinephrine results in a decreased duration of action as compared to articaine HCl alone.

1.2 Unusual Sensitivity

An unusual sensitivity reaction to articaine HCl has been reported.  This type of reaction is characterized by the appearance of a urticarial rash, or angioedema, which may progress to anaphylactic shock.  Supportive treatment of circulatory depression may require administration of intravenous fluids and, when appropriate, a vasopressor.

1.1 Contraindications

The use of articaine HCl and epinephrine in patients with a history of allergy to local anesthetics of the benzocaine family is contraindicated.

2.5 Patient Preparation

Prior to administration of Articaine HCl and Epinephrine, patients should be instructed to avoid activities that require mental alertness, coordination, or physical activity until usual sensation has returned.  Instruct patients not to eat or drink until normal sensation returns.  

2.6 Adverse Reactions

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 64 years of age.  There were no clinically significant differences in rescue medication requirements, measured by time to first rescue medication requirement, between the two groups.