Orabloc®

BRIEF SUMMARY of PRESCRIBING INFORMATION
(See Package Insert For Full Prescribing Information)

Articaine hydrochloride 4% and epinephrine 1:200,000
Articaine hydrochloride 4% and epinephrine 1:100,000

USE
Orabloc is an amide local anesthetic containing a vasoconstrictor indicated for local, infiltrative, or conductive anesthesia in both simple and complex dental procedures (1).

CONTRADICATIONS
Known hypersensitivity to sulfite (4)
Dosage recommendations should not be exceeded (see DOSAGE AND ADMINISTRATION in package insert)

WARNINGS AND PRECAUTIONS
Accidental Intravascular Injection
Accidental intravascular injection of Orabloc may be associated with convulsions, followed by central nervous system or cardiorespiratory depression and coma, progressing ultimately to respiratory arrest. Dental practitioners who employ local anesthetic agents including Orabloc 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. To avoid intravascular injection, aspiration should be performed before Orabloc 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.
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 (2.1)].
Systemic Toxicity
This includes toxicity arising from accidental intravascular injection of Orabloc discussed in Section 5.1, as well as that related to higher systemic concentrations of local anesthetics or epinephrine [see Warnings and Precautions (5.3)]. Systemic absorption of local anesthetics including Orabloc can produce e_ects on the central nervous and cardiovascular systems.
At blood concentrations achieved with therapeutic doses of Orabloc, changes in cardiac conduction, excitability, refractoriness, contractility, and peripheral vascular resistance are minimal. However, toxic blood concentrations of Orabloc can 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 vasodilatation occurs, leading to decreased cardiac output and arterial blood pressure. Orabloc should also be used with caution in patients with heart block as well as those 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.
Restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors, depression, or drowsiness may be early warning signs of central nervous system toxicity.
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 Orabloc. Repeated doses of Orabloc may cause significant increases in blood levels because of possible accumulation of the drug or its metabolites. The lowest dosage that results in e_ective anesthesia should be used to decrease the risk of high plasma levels and serious adverse effects. Tolerance to elevated blood levels varies with the status of the patient. Resuscitative equipment, oxygen, and other resuscitative drugs should be available for immediate use. Precautions for epinephrine administration, discussed in Section 5.3 should be observed.
Debilitated patients, elderly patients, acutely ill patients, and pediatric patients should be given reduced doses commensurate with their age and physical condition [see Dosage and Administration (2.1, 2.3)]. No studies have been performed in patients with liver dysfunction, and caution should be used in patients with severe hepatic disease.
Vasoconstrictor Toxicity
Orabloc contains epinephrine, a vasoconstrictor that can cause local or systemic toxicity and should be used cautiously. Local toxicity may include ischemic injury or necrosis, which may be related to vascular spasm. Orabloc 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. Patients with peripheral vascular disease and those with hypertensive vascular disease may exhibit exaggerated vasoconstrictor response.
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, 1986).
It is essential to aspirate before any injection to avoid administration of the drug into the blood stream.
Methemoglobinemia
Orabloc, like other local anesthetic solutions containing a vasoconstrictor, can cause methemoglobinemia, particularly in conjunction with methemoglobin-inducing agents. Orabloc should not be used in patients with congenital or idiopathic methemoglobinemia, and in patients who are receiving treatment with methemoglobin-inducing agents since they are more susceptible to drug-induced methemoglobinemia.
Signs and symptoms of methemoglobinemia may be delayed some hours after exposure. Initial signs and symptoms of methemoglobinemia include slate grey cyanosis seen in buccal mucous membranes, lips and nail beds. In severe cases, symptoms may include central cyanosis, headache, lethargy, dizziness, fatigue, syncope, dyspnea, CNS depression, seizures, dysrythmia and shock.
Methemoglobinemia should be considered if central cyanosis unresponsive to oxygen therapy occurs, especially if methemoglobininducing agents have been used. Calculated oxygen saturation and pulse oximetry are inaccurate in the setting of methemoglobinemia. The diagnosis can be confirmed by an elevated methemoglobin level of at least 10% is present. The development of methemoglobinemia is dose-related. Management of methemoglobinemia: If methemoglobinemia does not respond to administration of oxygen, clinically signi_cant symptoms of methemoglobinemia should be treated with administration of a slow intravenous injection (over 5 minutes) of methylene blue at a dosage of 1-2 mg/kg body weight.
Anaphylaxis and Allergic-Type Reactions
Orabloc 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

ADVERSE REACTIONS
Reactions to articaine are characteristic of those associated with other amide 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, or hypersensitivity or they may be idiosyncratic.
Clinical Studies Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed cannot be directly compared to rates in other clinical trials and may not reflect the rates observed in practice.
The reported adverse events are derived from clinical trials in the United States and the United Kingdom with a similar product containing articaine and epinephrine.
Table 2 displays the adverse events reported in clinical trials where 882 individuals were exposed to articaine containing epinephrine 1:100,000.
Table 3 displays the adverse events reported in clinical trials where 182 individuals were exposed to articaine containing epinephrine 1:100,000 and 179 individuals were exposed to articaine containing epinephrine 1:200,000.
Adverse reactions observed in at least 1% of patients:
Table 2:
Adverse Reactions in Controlled Trials with an Incidence of 1% or Greater in Patients Administered articaine containing epinephrine 1:100,000

Body System/Reaction	articaine containing epinephrine 1:100,000 (N=882) Incidence
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 3:
Adverse Reactions in Controlled Trials with an Incidence of 1% or Greater in Patients Administered articaine containing epinephrine 1:200,000 and articaine containing epinephrine 1:100,000

Reaction	Articaine with epinephrine 1:200,000 (N=179) Incidence	Articaine with epinephrine 1:100,000 (N=182) Incidence
Any adverse event	33 (18%)	35 (19%)
Pain	11 (6.1%)	14 (7.6%)
Headache	9 (5%)	6 (3.2%)
Positive blood aspiration into syringe	3 (1.6%)	6 (3.2%)
Swelling	3 (1.6%)	5 (2.7%)
Trismus	1 (0.3%)	3 (1.6%)
Nausea and emesis	3 (1.6%)	0 (0%)
Sleepiness	2 (1.1%)	1 (0.5%)
Numbness and tingling	1 (0.5%)	2 (1.%)
Palpitation	0 (0%)	2 (1.%)
Ear symptoms (earache, otitis media)	1 (0.5%)	2 (1.%)
Cough, persistent cough	0 (0%)	2 (1.%)

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 and Precautions (5.1, 5.2)].
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 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 assessed. Should convulsions persist despite adequate respiratory support, treatment with appropriate anticonvulsant therapy is indicated. The practitioner should be familiar with the use of anticonvulsant drugs, prior to the use of local anesthetics. 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/or cardiac arrest. If cardiac arrest should occur, standard cardiopulmonary resuscitative measures should be instituted. For additional information about overdose treatment, call a poison control center (1-800-222-1222).

HOW SUPPLIED/STORAGE AND HANDLING
Orabloc (articaine HCl and epinephrine) Injection is available in 1.8 mL single use glass artridges, packaged in boxes of 50 and 100 cartridges in the following two strengths:
o Orabloc containing articaine HCl 4% and epinephrine 1:200,000 (NDC 45146-120-02 (50 cartridges/box), NDC 45146-120-01 (100 cartridges/box))
o Orabloc containing articaine HCl 4% and epinephrine 1:100,000 (NDC 45146-110-02 (50 cartridges/box), NDC 45146-110-01 (100 cartridges/box))
o Both products are formulated with a 10% overage of epinephrine.
Storage and Handling
Store at 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.
For chemical disinfection of the carpule, either isopropyl alcohol (91%) or ethyl alcohol (70%) is recommended. Many commercially available brands of isopropyl (rubbing) alcohol, as well as solutions of ethyl alcohol not of U.S.P. grade, contain denaturants that are injurious to rubber and therefore are not to be used. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

PATIENT COUNSELING INFORMATION
Loss of Sensation and Muscle Function:
o Inform patients in advance of the possibility of temporary loss of sensation and muscle function following infiltration and nerve block injections [see Adverse Reactions (6.2)].
o Instruct patients not to eat or drink until normal sensation returns.

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