



Introducing A New "Aseptically Manufactured" Articaine



Orabloc™

(articaine HCl 4% and epinephrine 1:100,000
and epinephrine 1:200,000) injection

Everything you expect from articaine with epinephrine when "aseptically manufactured"

- ◆ Rapid onset of anesthesia within 1-9 minutes
- ◆ Complete anesthesia lasts about 1 hour for infiltration, up to 2 hours for nerve block
- ◆ Only 10% overage of epinephrine¹
- ◆ A 24 month shelf life at room temperature
- ◆ Very low manufacture related degradation products such as articaine acid and epinephrine sulphonic acid
- ◆ Sodium edetate free, methylparaben free and latex free
- ◆ Each Orabloc™ cartridge is sealed individually in the blister for maximum protection during storage and handling



Box (1:100,000)
item #568-2604

Box (1:200,000)
item #568-2612

www.orabloc.com

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

Orabloc™ contains sodium metabisulfite. Orabloc™ 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.

¹ The American Heart Association (AHA) recommends using the lowest possible quantity of epinephrine (Kaplan EL ed. Cardiovascular disease in dental practice. Dallas, TX: American Heart Association, 1986.)



Orabloc™



A New Aseptically Manufactured Articaine, now introduced in the USA

Orabloc™

(articaine HCl 4% and epinephrine 1:100,000
and epinephrine 1:200,000) Injection

Indications:

- ◆ For infiltration and nerve block anesthesia
- ◆ For routine dental procedures you may use Orabloc™ 1:200,000
- ◆ When pronounced homeostasis or improved visualization of the surgical field is required, you may use Orabloc™ 1:100,000
- ◆ See prescribing information attached to this brochure

Features and benefits:

- ◆ Orabloc™ is an aseptically produced dental anaesthetic, now also available in the USA
- ◆ Rapid onset time (1-9 minutes) for fast effective anesthesia
- ◆ Articaine with epinephrine based dental anaesthetics are preferred during operative and surgical procedures, when improved visualisation of the surgical field is desirable
- ◆ Reliable/predictable anaesthesia (about 60 minutes for infiltration and about 120 minutes for nerve block)
- ◆ Sodium edetate free formulation
- ◆ Methyl paraben free formulation
- ◆ Lower epinephrine overage (+10%) with respect to USP compendial injectable anaesthetics label claim (+15%)
- ◆ Latex free and lubricated rubber closures for maximum safety, smooth plunger movement and precise control during injection
- ◆ Each Orabloc™ individual cartridge is blister packed for maximum protection during storage and handling. Mylar labelled/wrapped to minimize possibility of wounds in the event of cartridge breakage during use:
 - ✓ Packed 10 per tray with each cartridge individually sealed for maximum protection up to the moment of use
 - ✓ Avoids glass to glass contact, avoids exposure of the other cartridges to the environment when a cartridge is taken from the blister
 - ✓ Additional barrier for better protection of the epinephrine from oxidation due to permeation of air into the drug product

See package insert summary included with this handout

www.orabloc.com

Reactions to Orabloc™ (pain and headache, for example, or convulsions or respiratory arrest following accidental intravascular injection) are characteristic of those associated with other amide-type local anaesthetics. Accidental intravascular injection may be associated with convulsion, followed by central nervous system or cardio-respiratory depression and coma, progressing ultimately to respiratory arrest. Dental practitioners and/or clinicians who employ local anaesthetic agents should be well versed in diagnosis and management of emergencies that may arise from their use.

A New Aseptically Manufactured Articaine, now introduced in the USA

Orabloc™

(articaine HCl 4% and epinephrine 1:100,000
and epinephrine 1:200,000) Injection

Orabloc™ is indicated for local, infiltrative, or conductive anesthesia in both simple and complex dental procedures:

- ◆ For most routine dental procedures, Orabloc™ containing epinephrine 1:200,000 is preferred
- ◆ When more pronounced homeostasis or improved visualization of the surgical field are required, Orabloc™ containing epinephrine 1:100,000 may be used

Dosage and administration – Adults

- ◆ For normal healthy adults, the maximum dose of Orabloc™ administered by submucosal infiltration and/or nerve block should not exceed 7mg/kg (0.175 mL/kg) of articaine HCl
- ◆ Dosage should be reduced in elderly patients and in patients with cardiac or liver disease

Pediatric patients ages 4 to 16 years

- ◆ The quantity of Orabloc™ in children ages 4 to 16 years of age to be injected should be determined by the age and weight of the child and the magnitude of the operation
- ◆ The maximum dose of Orabloc™ should not exceed 7 mg/kg (0.175 mL/kg) of articaine HCl (see Use in Specific Populations). Use in pediatric patients under 4 years of age is not recommended

Both Orabloc™ strengths have a 24 month shelf life

- ◆ Store at room temperature; 25°C (77°F), with brief excursions permitted between 15°C (59°F) and 30°C (86°F)
- ◆ Protect from light
- ◆ Do not freeze

Orabloc™ packaging

- ◆ Each cartridge is individually sealed for maximum protection up to the moment of use
- ◆ Cartridges packed 10 to a blister tray to avoid glass to glass contact
- ◆ Blister trays packaged in boxes of 50

See package insert included with this handout for full prescribing information

www.orabloc.com

To purchase Orabloc™ contact your Patterson representative, local branch or call 1-800-873-7683
To learn more about Orabloc™, call Pierrel Research USA at 1-610-989-4222

Administration of Orabloc™ results in a 3 to 5 fold increase in plasma epinephrine concentrations compared to baseline. However, in healthy adults it does not appear to be associated with marked increases in blood pressure or heart rate, except in the case of accidental intravascular injection.

Inform patients in advance of the possibility of temporary loss of sensation and muscle function following infiltration and nerve block injections. Instruct patients not to eat or drink until normal sensation returns.

Manufactured in Italy by: Pierrel S.p.A. - Strada Statale Appia 46/48 - 81043 Capua (CE), Italy

Distributed in the USA by: Pierrel Research USA, Inc. - One Glenhardie Corporate Center - 1275
Drummers Lane, Suite 100 - Wayne, PA, 19087



Orabloc™





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).

CONTRADICTIONS

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 effects 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 effective 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, dysrhythmia and shock.

Methemoglobinemia should be considered if central cyanosis unresponsive to oxygen therapy occurs, especially if methemoglobin-inducing 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 significant 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 cartridges, 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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