

1 **APP**

2 451106E/Revised: August 2013

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4 **Sensorcaine<sup>®</sup> (bupivacaine HCl Injection, USP)**

5 **Sensorcaine<sup>®</sup>-MPF (bupivacaine HCl Injection, USP)**

6 **Sensorcaine<sup>®</sup> with Epinephrine (bupivacaine HCl and epinephrine Injection, USP)**

7 **1:200,000 (as bitartrate)**

8 **Sensorcaine<sup>®</sup>-MPF with Epinephrine (bupivacaine HCl and epinephrine Injection,**

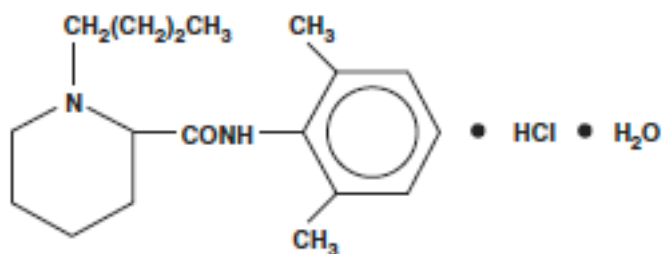
9 **USP) 1:200,000 (as bitartrate)**

10 Rx only

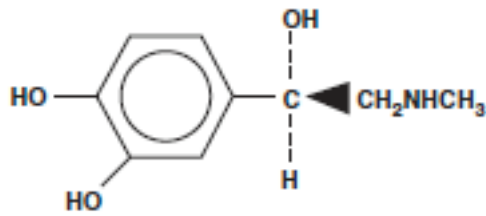
11 **DESCRIPTION:**

12 Sensorcaine<sup>®</sup> (bupivacaine HCl) injections are sterile isotonic solutions that contain a  
13 local anesthetic agent with and without epinephrine (as bitartrate) 1:200,000 and are  
14 administered parenterally by injection. See **INDICATIONS AND USAGE** for specific  
15 uses. Solutions of bupivacaine HCl may be autoclaved if they do not contain  
16 epinephrine.

17 Sensorcaine injections contain bupivacaine HCl which is chemically designated  
18 as 2-piperidinecarboxamide, 1-butyl-N-(2, 6-dimethylphenyl)-, monohydrochloride,  
19 monohydrate and has the following structure:



1 Epinephrine is (-)-3, 4-Dihydroxy- $\alpha$  [(methylamino)methyl] benzyl alcohol. It  
2 has the following structural formula:



3  
4 The pK<sub>a</sub> of bupivacaine (8.1) is similar to that of lidocaine (7.86). However,  
5 bupivacaine possesses a greater degree of lipid solubility and is protein bound to a greater  
6 extent than lidocaine.

7 Bupivacaine is related chemically and pharmacologically to the aminoacyl local  
8 anesthetics. It is a homologue of mepivacaine and is chemically related to lidocaine. All  
9 three of these anesthetics contain an amide linkage between the aromatic nucleus and the  
10 amino, or piperidine group. They differ in this respect from the procaine-type local  
11 anesthetics, which have an ester linkage.

12 **Dosage forms listed as Sensorcaine-MPF indicates single dose solutions that**  
13 **are Methyl Paraben Free (MPF).**

14 Sensorcaine-MPF is a sterile isotonic solution containing sodium chloride.  
15 Sensorcaine in multiple dose vials, each mL also contains 1 mg methylparaben as  
16 antiseptic preservative. The pH of these solutions is adjusted to between 4.0 and 6.5 with  
17 sodium hydroxide and/or hydrochloric acid.

18 Sensorcaine-MPF with Epinephrine 1:200,000 (as bitartrate) is a sterile isotonic  
19 solution containing sodium chloride. Each mL contains bupivacaine hydrochloride and  
20 0.005 mg epinephrine, with 0.5 mg sodium metabisulfite as an antioxidant and 0.2 mg  
21 citric acid (anhydrous) as stabilizer. Sensorcaine with Epinephrine 1:200,000 (as

1 bitartrate) in multiple dose vials, each mL also contains 1 mg methylparaben as antiseptic  
2 preservative. The pH of these solutions is adjusted to between 3.3 to 5.5 with sodium  
3 hydroxide and/or hydrochloric acid. Filled under nitrogen.

4 Note: The user should have an appreciation and awareness of the formulations  
5 and their intended uses (see **DOSAGE AND ADMINISTRATION**).

## 6 **CLINICAL PHARMACOLOGY:**

7 Local anesthetics block the generation and the conduction of nerve impulses, presumably  
8 by increasing the threshold for electrical excitation in the nerve, by slowing the  
9 propagation of the nerve impulse, and by reducing the rate of rise of the action potential.  
10 In general, the progression of anesthesia is related to the diameter, myelination, and  
11 conduction velocity of affected nerve fibers. Clinically, the order of loss of nerve  
12 function is as follows: (1) pain, (2) temperature, (3) touch, (4) proprioception, and (5)  
13 skeletal muscle tone.

14 Systemic absorption of local anesthetics produces effects on the cardiovascular  
15 and central nervous systems CNS. At blood concentrations achieved with normal  
16 therapeutic doses, changes in cardiac conduction, excitability, refractoriness,  
17 contractility, and peripheral vascular resistance are minimal. However, toxic blood  
18 concentrations depress cardiac conduction and excitability, which may lead to  
19 atrioventricular block, ventricular arrhythmias and cardiac arrest, sometimes resulting in  
20 fatalities. In addition, myocardial contractility is depressed and peripheral vasodilation  
21 occurs, leading to decreased cardiac output and arterial blood pressure. Recent clinical  
22 reports and animal research suggest that these cardiovascular changes are more likely to  
23 occur after unintended intravascular injection of bupivacaine. Therefore, incremental

1 dosing is necessary.

2           Following systemic absorption, local anesthetics can produce central nervous  
3 system stimulation, depression, or both. Apparent central stimulation is manifested as  
4 restlessness, tremors and shivering progressing to convulsions, followed by depression  
5 and coma progressing ultimately to respiratory arrest. However, the local anesthetics  
6 have a primary depressant effect on the medulla and on higher centers. The depressed  
7 stage may occur without a prior excited state.

### 8 *Pharmacokinetics*

9 The rate of systemic absorption of local anesthetics is dependent upon the total dose and  
10 concentration of drug administered, the route of administration, the vascularity of the  
11 administration site, and the presence or absence of epinephrine in the anesthetic solution.  
12 A dilute concentration of epinephrine (1:200,000 or 5 mcg/mL) usually reduces the rate  
13 of absorption and peak plasma concentration of bupivacaine, permitting the use of  
14 moderately larger total doses and sometimes prolonging the duration of action.

15           The onset of action with bupivacaine is rapid and anesthesia is long lasting. The  
16 duration of anesthesia is significantly longer with bupivacaine than with any other  
17 commonly used local anesthetic. It has also been noted that there is a period of analgesia  
18 that persists after the return of sensation, during which time the need for strong analgesics  
19 is reduced.

20           The onset of action following dental injections is usually 2 to 10 minutes and  
21 anesthesia may last two or three times longer than lidocaine and mepivacaine for dental  
22 use, in many patients up to 7 hours. The duration of anesthetic effect is prolonged by the  
23 addition of epinephrine 1:200,000.

1           Local anesthetics are bound to plasma proteins in varying degrees. Generally, the  
2 lower the plasma concentration of drug the higher the percentage of drug bound to  
3 plasma proteins.

4           Local anesthetics appear to cross the placenta by passive diffusion. The rate and  
5 degree of diffusion is governed by (1) the degree of plasma protein binding, (2) the  
6 degree of ionization, and (3) the degree of lipid solubility. Fetal/maternal ratios of local  
7 anesthetics appear to be inversely related to the degree of plasma protein binding,  
8 because only the free, unbound drug is available for placental transfer. Bupivacaine with  
9 a high protein binding capacity (95%) has a low fetal/maternal ratio (0.2 to 0.4). The  
10 extent of placental transfer is also determined by the degree of ionization and lipid  
11 solubility of the drug. Lipid soluble, nonionized drugs readily enter the fetal blood from  
12 the maternal circulation.

13           Depending upon the route of administration, local anesthetics are distributed to  
14 some extent to all body tissues, with high concentrations found in highly perfused organs  
15 such as the liver, lungs, heart, and brain.

16           Pharmacokinetic studies on the plasma profile of bupivacaine after direct  
17 intravenous injection suggest a three-compartment open model. The first compartment is  
18 represented by the rapid intravascular distribution of the drug. The second compartment  
19 represents the equilibration of the drug throughout the highly perfused organs such as the  
20 brain, myocardium, lungs, kidneys, and liver. The third compartment represents an  
21 equilibration of the drug with poorly perfused tissues, such as muscle and fat. The  
22 elimination of drug from tissue distribution depends largely upon the ability of binding  
23 sites in the circulation to carry it to the liver where it is metabolized.

1           After injection of Sensorcaine (bupivacaine HCl) for caudal, epidural, or  
2 peripheral nerve block in man, peak levels of bupivacaine in the blood are reached in 30  
3 to 45 minutes, followed by a decline to insignificant levels during the next 3 to 6 hours.

4           Various pharmacokinetic parameters of the local anesthetics can be significantly  
5 altered by the presence of hepatic or renal disease, addition of epinephrine, factors  
6 affecting urinary pH, renal blood flow, the route of drug administration, and the age of  
7 the patient. The half-life of bupivacaine in adults is 2.7 hours and in neonates 8.1 hours.

8           In clinical studies, elderly patients reached the maximal spread of analgesia and  
9 maximal motor blockade more rapidly than younger patients. Elderly patients also  
10 exhibited higher peak plasma concentrations following administration of this product.  
11 The total plasma clearance was decreased in these patients.

12           Amide-type local anesthetics such as bupivacaine are metabolized primarily in the  
13 liver via conjugation with glucuronic acid. Patients with hepatic disease, especially those  
14 with severe hepatic disease, may be more susceptible to the potential toxicities of the  
15 amide-type local anesthetics. Pipecoloxylidine is the major metabolite of bupivacaine.

16           The kidney is the main excretory organ for most local anesthetics and their  
17 metabolites. Urinary excretion is affected by urinary perfusion and factors affecting  
18 urinary pH. Only 6% of bupivacaine is excreted unchanged in the urine.

19           When administered in recommended doses and concentrations, Sensorcaine  
20 (bupivacaine HCl) does not ordinarily produce irritation or tissue damage and does not  
21 cause methemoglobinemia.

## 22   **INDICATIONS AND USAGE:**

23   Sensorcaine (bupivacaine HCl) is indicated for the production of local or regional

1 anesthesia or analgesia for surgery, dental and oral surgery procedures, diagnostic and  
2 therapeutic procedures, and for obstetrical procedures. Only the 0.25% and 0.5%  
3 concentrations are indicated for obstetrical anesthesia (see **WARNINGS**).

4 Experience with nonobstetrical surgical procedures in pregnant patients is not  
5 sufficient to recommend use of the 0.75% concentration of bupivacaine HCl in these  
6 patients.

7 Sensorcaine is not recommended for intravenous regional anesthesia (Bier Block)  
8 (see **WARNINGS**).

9 The routes of administration and indicated Sensorcaine concentrations are:

- 10 • local infiltration 0.25%
- 11 • peripheral nerve block 0.25% and 0.5%
- 12 • retrobulbar block 0.75%
- 13 • sympathetic block 0.25%
- 14 • lumbar epidural 0.25%, 0.5%, and 0.75% (0.75% not for obstetrical  
15 anesthesia)
- 16 • caudal 0.25% and 0.5%
- 17 • epidural test dose 0.5% with epinephrine 1:200,000
- 18 • dental blocks 0.5% with epinephrine 1:200,000

19 (See **DOSAGE AND ADMINISTRATION** for additional information).

20 Standard textbooks should be consulted to determine the accepted procedures and  
21 techniques for the administration of Sensorcaine.

## 22 **CONTRAINDICATIONS:**

23 Sensorcaine (bupivacaine HCl) is contraindicated in obstetrical paracervical block

1 anesthesia. Its use in this technique has resulted in fetal bradycardia and death.

2           Sensorcaine is contraindicated in patients with a known hypersensitivity to it or to  
3 any local anesthetic agent of the amide-type or to other components of bupivacaine  
4 solutions.

5 **WARNINGS:**

**THE 0.75% CONCENTRATION OF SENSORCAINE INJECTION IS NOT RECOMMENDED FOR OBSTETRICAL ANESTHESIA. THERE HAVE BEEN REPORTS OF CARDIAC ARREST WITH DIFFICULT RESUSCITATION OR DEATH DURING USE OF BUPIVACAINE FOR EPIDURAL ANESTHESIA IN OBSTETRICAL PATIENTS. IN MOST CASES, THIS HAS FOLLOWED USE OF THE 0.75% CONCENTRATION. RESUSCITATION HAS BEEN DIFFICULT OR IMPOSSIBLE DESPITE APPARENTLY ADEQUATE PREPARATION AND APPROPRIATE MANAGEMENT. CARDIAC ARREST HAS OCCURRED AFTER CONVULSIONS RESULTING FROM SYSTEMIC TOXICITY, PRESUMABLY FOLLOWING UNINTENTIONAL INTRAVASCULAR INJECTION. THE 0.75% CONCENTRATION SHOULD BE RESERVED FOR SURGICAL PROCEDURES WHERE A HIGH DEGREE OF MUSCLE RELAXATION AND PROLONGED EFFECT ARE NECESSARY.**

6  
7 LOCAL ANESTHETICS SHOULD ONLY BE EMPLOYED BY CLINICIANS WHO  
8 ARE WELL VERSED IN DIAGNOSIS AND MANAGEMENT OF DOSE-RELATED  
9 TOXICITY AND OTHER ACUTE EMERGENCIES WHICH MIGHT ARISE FROM



1 THE BLOCK TO BE EMPLOYED, AND THEN ONLY AFTER INSURING THE  
2 **IMMEDIATE** AVAILABILITY OF OXYGEN, OTHER RESUSCITATIVE DRUGS,  
3 CARDIOPULMONARY RESUSCITATIVE EQUIPMENT, AND THE PERSONNEL  
4 RESOURCES NEEDED FOR PROPER MANAGEMENT OF TOXIC REACTIONS  
5 AND RELATED EMERGENCIES (see also **ADVERSE REACTIONS**,  
6 **PRECAUTIONS**, and **OVERDOSAGE**). DELAY IN PROPER MANAGEMENT OF  
7 DOSE-RELATED TOXICITY, UNDERVENTILATION FROM ANY CAUSE  
8 AND/OR ALTERED SENSITIVITY MAY LEAD TO THE DEVELOPMENT OF  
9 ACIDOSIS, CARDIAC ARREST AND, POSSIBLY, DEATH.

10 Local anesthetic solutions containing antimicrobial preservatives, i.e., those  
11 supplied in multiple-dose vials, should not be used for epidural or caudal anesthesia  
12 because safety has not been established with regard to intrathecal injection, either  
13 intentionally or unintentionally, of such preservatives.

14 Intra-articular infusions of local anesthetics following arthroscopic and other  
15 surgical procedures is an unapproved use, and there have been post-marketing reports of  
16 chondrolysis in patients receiving such infusions. The majority of reported cases of  
17 chondrolysis have involved the shoulder joint; cases of gleno-humeral chondrolysis have  
18 been described in pediatric and adult patients following intra-articular infusions of local  
19 anesthetics with and without epinephrine for periods of 48 to 72 hours. There is  
20 insufficient information to determine whether shorter infusion periods are not associated  
21 with these findings. The time of onset of symptoms, such as joint pain, stiffness and loss  
22 of motion can be variable, but may begin as early as the 2<sup>nd</sup> month after surgery.  
23 Currently, there is no effective treatment for chondrolysis; patients who experienced

1 chondrolysis have required additional diagnostic and therapeutic procedures and some  
2 required arthroplasty or shoulder replacement.

3 It is essential that aspiration for blood or cerebrospinal fluid (where applicable) be  
4 done prior to injecting any local anesthetic, both the original dose and all subsequent  
5 doses, to avoid intravascular or subarachnoid injection. However, a negative aspiration  
6 does not ensure against an intravascular or subarachnoid injection.

7 Bupivacaine with Epinephrine 1:200,000 or other vasopressors should not be used  
8 concomitantly with ergot-type oxytocic drugs, because a severe persistent hypertension  
9 may occur. Likewise, solutions of bupivacaine containing a vasoconstrictor, such as  
10 epinephrine, should be used with extreme caution in patients receiving monoamine  
11 oxidase inhibitors (MAOI) or antidepressants of the triptyline or imipramine types,  
12 because severe prolonged hypertension may result.

13 Until further experience is gained in pediatric patients younger than 12 years,  
14 administration of bupivacaine in this age group is not recommended.

15 Mixing or the prior or intercurrent use of any local anesthetic with bupivacaine  
16 cannot be recommended because of insufficient data on the clinical use of such mixtures.

17 There have been reports of cardiac arrest and death during the use of bupivacaine  
18 for intravenous regional anesthesia (Bier Block). Information on safe dosages and  
19 techniques of administration of bupivacaine in this procedure is lacking. Therefore,  
20 bupivacaine is not recommended for use in this technique.

21 *Sensorcaine with epinephrine 1:200,000* solutions contains sodium metabisulfite,  
22 a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-  
23 threatening or less severe asthmatic episodes in certain susceptible people. The overall

1 prevalence of sulfite sensitivity in the general population is unknown and probably low.  
2 Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.  
3 Sensorcaine and Sensorcaine - MPF without epinephrine single dose vials do not contain  
4 sodium metabisulfite.

5 **PRECAUTIONS:**

6 ***General***

7 The safety and effectiveness of local anesthetics depend on proper dosage, correct  
8 technique, adequate precautions, and readiness for emergencies. Resuscitative  
9 equipment, oxygen, and other resuscitative drugs should be available for immediate use  
10 (see **WARNINGS, ADVERSE REACTIONS, and OVERDOSAGE**). During major  
11 regional nerve blocks, the patient should have IV fluids running via an indwelling  
12 catheter to assure a functioning intravenous pathway. The lowest dosage of local  
13 anesthetic that results in effective anesthesia should be used to avoid high plasma levels  
14 and serious adverse effects. The rapid injection of a large volume of local anesthetic  
15 solution should be avoided and fractional (incremental) doses should be used when  
16 feasible.

17 ***Epidural Anesthesia***

18 During epidural administration of Sensorcaine (bupivacaine HCl), 0.5% and 0.75%  
19 solutions should be administered in incremental doses of 3 mL to 5 mL with sufficient  
20 time between doses to detect toxic manifestations of unintentional intravascular or  
21 intrathecal injection. Injections should be made slowly, with frequent aspirations before  
22 and during the injection to avoid intravascular injection. Syringe aspirations should also  
23 be performed before and during each supplemental injection in continuous (intermittent)

1 catheter techniques. An intravascular injection is still possible even if aspirations for  
2 blood are negative.

3       During the administration of epidural anesthesia, it is recommended that a test  
4 dose be administered initially and the effects monitored before the full dose is given.  
5 When using a “continuous” catheter technique, test doses should be given prior to both  
6 the original and all reinforcing doses, because plastic tubing in the epidural space can  
7 migrate into a blood vessel or through the dura. When clinical conditions permit, the test  
8 dose should contain epinephrine (10 mcg to 15 mcg has been suggested) to serve as a  
9 warning of unintended intravascular injection. If injected into a blood vessel, this amount  
10 of epinephrine is likely to produce a transient “epinephrine response” within 45 seconds,  
11 consisting of an increase in heart rate and/or systolic blood pressure, circumoral pallor,  
12 palpitations, and nervousness in the unsedated patient. The sedated patient may exhibit  
13 only a pulse rate increase of 20 or more beats per minute for 15 or more seconds.  
14 Therefore, following the test dose, the heart rate should be monitored for a heart rate  
15 increase. Patients on beta-blockers may not manifest changes in heart rate, but blood  
16 pressure monitoring can detect a transient rise in systolic blood pressure. The test dose  
17 should also contain 10 mg to 15 mg of Sensorcaine or an equivalent amount of another  
18 local anesthetic to detect an unintended intrathecal administration. This will be  
19 evidenced within a few minutes by signs of spinal block (e.g., decreased sensation of the  
20 buttocks, paresis of the legs, or, in the sedated patient, absent knee jerk). An  
21 intravascular or subarachnoid injection is still possible even if results of the test dose are  
22 negative. The test dose itself may produce a systemic toxic reaction, high spinal or  
23 epinephrine-induced cardiovascular effects.

1           Injection of repeated doses of local anesthetics may cause significant increases in  
2 plasma levels with each repeated dose due to slow accumulation of the drug or its  
3 metabolites, or to slow metabolic degradation. Tolerance to elevated blood levels varies  
4 with the status of the patient. Debilitated, elderly patients and acutely ill patients should  
5 be given reduced doses commensurate with their age and physical status. Local  
6 anesthetics should also be used with caution in patients with hypotension or heartblock.

7           Careful and constant monitoring of cardiovascular and respiratory (adequacy of  
8 ventilation) vital signs and the patient's state of consciousness should be performed after  
9 each local anesthetic injection. It should be kept in mind at such times that restlessness,  
10 anxiety, incoherent speech, lightheadedness, numbness and tingling of the mouth and  
11 lips, metallic taste, tinnitus, dizziness, blurred vision, tremors, twitching, depression, or  
12 drowsiness may be early warning signs of central nervous system toxicity.

13           Local anesthetic solutions containing a vasoconstrictor should be used cautiously  
14 and in carefully restricted quantities in areas of the body supplied by end arteries or  
15 having otherwise compromised blood supply such as digits, nose, external ear, or penis.  
16 Patients with hypertensive vascular disease may exhibit exaggerated vasoconstrictor  
17 response. Ischemic injury or necrosis may result.

18           Because amide-local anesthetics such as bupivacaine are metabolized by the liver,  
19 these drugs, especially repeat doses, should be used cautiously in patients with hepatic  
20 disease. Patients with severe hepatic disease, because of their inability to metabolize  
21 local anesthetics normally, are at a greater risk of developing toxic plasma  
22 concentrations. Local anesthetics should also be used with caution in patients with  
23 impaired cardiovascular function because they may be less able to compensate for

1 functional changes associated with the prolongation of AV conduction produced by these  
2 drugs.

3        Serious dose-related cardiac arrhythmias may occur if preparations containing a  
4 vasoconstrictor such as epinephrine are employed in patients during or following the  
5 administration of potent inhalation anesthetics. In deciding whether to use these products  
6 concurrently in the same patient, the combined action of both agents upon the  
7 myocardium, the concentration and volume of vasoconstrictor used, and the time since  
8 injection, when applicable, should be taken into account.

9        Many drugs used during the conduct of anesthesia are considered potential  
10 triggering agents for familial malignant hyperthermia. Because it is not known whether  
11 amide-type local anesthetics may trigger this reaction and because the need for  
12 supplemental general anesthesia cannot be predicted in advance, it is suggested that a  
13 standard protocol for management should be available. Early unexplained signs of  
14 tachycardia, tachypnea, labile blood pressure, and metabolic acidosis may precede  
15 temperature elevation. Successful outcome is dependent on early diagnosis, prompt  
16 discontinuance of the suspect triggering agent(s) and prompt institution of treatment,  
17 including oxygen therapy, indicated supportive measures and dantrolene (consult  
18 dantrolene sodium intravenous package insert before using).

### 19 *Use in Head and Neck Area*

20 Small doses of local anesthetics injected into the head and neck area, including  
21 retrobulbar, dental and stellate ganglion blocks, may produce adverse reactions similar to  
22 systemic toxicity seen with unintentional intravascular injections of larger doses. The  
23 injection procedures require the utmost care. Confusion, convulsions, respiratory

1 depression, and/or respiratory arrest, and cardiovascular stimulation or depression have  
2 been reported. These reactions may be due to intra-arterial injection of the local  
3 anesthetic with retrograde flow to the cerebral circulation. They may also be due to  
4 puncture of the dural sheath of the optic nerve during retrobulbar block with diffusion of  
5 any local anesthetic along the subdural space to the midbrain. Patients receiving these  
6 blocks should have their circulation and respiration monitored and be constantly  
7 observed. Resuscitative equipment and personnel for treating adverse reactions should be  
8 immediately available. Dosage recommendations should not be exceeded (see **DOSAGE**  
9 **AND ADMINISTRATION**).

#### 10 *Use in Ophthalmic Surgery*

11 Clinicians who perform retrobulbar blocks should be aware that there have been reports  
12 of respiratory arrest following local anesthetic injection. Prior to retrobulbar block, as  
13 with all other regional procedures, the immediate availability of equipment, drugs, and  
14 personnel to manage respiratory arrest or depression, convulsions, and cardiac  
15 stimulation or depression should be assured (see also **WARNINGS** and *Use in Head and*  
16 *Neck Area*, above). As with other anesthetic procedures, patients should be constantly  
17 monitored following ophthalmic blocks for signs of these adverse reactions, which may  
18 occur following relatively low total doses.

19 A concentration of 0.75% bupivacaine is indicated for retrobulbar block;  
20 however, this concentration is not indicated for any other peripheral nerve block,  
21 including the facial nerve, and not indicated for local infiltration, including the  
22 conjunctiva (see **INDICATIONS** and **PRECAUTIONS, General**). Mixing Sensorcaine  
23 (bupivacaine HCl) with other local anesthetics is not recommended because of

1 insufficient data on the clinical use of such mixtures.

2           When Sensorcaine (bupivacaine HCl) 0.75% is used for retrobulbar block,  
3 complete corneal anesthesia usually precedes onset of clinically acceptable external  
4 ocular muscle akinesia. Therefore, presence of akinesia rather than anesthesia alone  
5 should determine readiness of the patient for surgery.

### 6 ***Use in Dentistry***

7 Because of the long duration of anesthesia, when Sensorcaine 0.5% with epinephrine is  
8 used for dental injections, patients should be cautioned about the possibility of  
9 inadvertent trauma to the tongue, lips, and buccal mucosa and advised not to chew solid  
10 foods or test the anesthetized area by biting or probing.

### 11 ***Information for Patients***

12 When appropriate, patients should be informed in advance that they may experience  
13 temporary loss of sensation and motor activity, usually in the lower half of the body,  
14 following proper administration of caudal or epidural anesthesia. Also, when  
15 appropriate, the physician should discuss other information including adverse reactions in  
16 the package insert of Sensorcaine.

17           Patients receiving dental injections of Sensorcaine should be cautioned not to  
18 chew solid foods or test the anesthetized area by biting or probing until anesthesia has  
19 worn off (up to 7 hours).

### 20 ***Clinically Significant Drug Interactions***

21 The administration of local anesthetic solutions containing epinephrine or norepinephrine  
22 to patients receiving monoamine oxidase inhibitors or tricyclic antidepressants may  
23 produce severe, prolonged hypertension. Concurrent use of these agents should generally



1 be avoided. In situations when concurrent therapy is necessary, careful patient  
2 monitoring is essential.

3 Concurrent administration of vasopressor drugs and of ergot-type oxytocic drugs  
4 may cause severe, persistent hypertension or cerebrovascular accidents.

5 Phenothiazines and butyrophenones may reduce or reverse the pressor effect of  
6 epinephrine.

### 7 ***Carcinogenesis, Mutagenesis, Impairment of Fertility***

8 Long-term studies in animals to evaluate the carcinogenic potential of bupivacaine  
9 hydrochloride have not been conducted. The mutagenic potential and the effect on  
10 fertility have not been determined.

### 11 ***Pregnancy Category C***

12 There are no adequate and well-controlled studies in pregnant women. Sensorcaine  
13 should be used during pregnancy only if the potential benefit justifies the potential risk to  
14 the fetus. Bupivacaine hydrochloride produced developmental toxicity when  
15 administered subcutaneously to pregnant rats and rabbits at clinically relevant doses.  
16 This does not exclude the use of Sensorcaine at term for obstetrical anesthesia or  
17 analgesia (see ***Labor and Delivery***).

18 Bupivacaine hydrochloride was administered subcutaneously to rats at doses of 4.4,  
19 13.3, & 40 mg/kg and to rabbits at doses of 1.3, 5.8, & 22.2 mg/kg during the period of  
20 organogenesis (implantation to closure of the hard palate). The high doses are comparable to  
21 the daily maximum recommended human dose (MRHD) of 400 mg/day on a  $\text{mg/m}^2$  body  
22 surface area (BSA) basis. No embryo-fetal effects were observed in rats at the high dose  
23 which caused increased maternal lethality. An increase in embryo-fetal deaths was observed

1 in rabbits at the high dose in the absence of maternal toxicity with the fetal No Observed  
2 Adverse Effect Level representing approximately 1/5th the MRHD on a BSA basis.

3 In a rat pre- and post-natal development study (dosing from implantation through  
4 weaning) conducted at subcutaneous doses of 4.4, 13.3, & 40 mg/kg mg/kg/day, decreased  
5 pup survival was observed at the high dose. The high dose is comparable to the daily MRHD  
6 of 400 mg/day on a BSA basis.

### 7 ***Labor and Delivery***

8 SEE **BOX WARNING** REGARDING OBSTETRICAL USE of 0.75% Sensorcaine.

9 Sensorcaine is contraindicated for obstetrical paracervical block anesthesia.

10 Local anesthetics rapidly cross the placenta, and when used for epidural, caudal,  
11 or pudendal block anesthesia, can cause varying degrees of maternal, fetal, and neonatal  
12 toxicity (see **CLINICAL PHARMACOLOGY, *Pharmacokinetics*** ). The incidence and  
13 degree of toxicity depend upon the procedure performed, the type, and amount of drug  
14 used, and the technique of drug administration. Adverse reactions in the parturient, fetus,  
15 and neonate involve alterations of the central nervous system, peripheral vascular tone,  
16 and cardiac function.

17 Maternal hypotension has resulted from regional anesthesia. Local anesthetics  
18 produce vasodilation by blocking sympathetic nerves. Elevating the patient's legs and  
19 positioning her on her left side will help prevent decreases in blood pressure. The fetal  
20 heart rate also should be monitored continuously and electronic fetal monitoring is highly  
21 advisable.

22 Epidural, caudal, or pudendal anesthesia may alter the forces of parturition  
23 through changes in uterine contractility or maternal expulsive efforts. Epidural

1 anesthesia has been reported to prolong the second stage of labor by removing the  
2 parturient's reflex urge to bear down or by interfering with motor function. The use of  
3 obstetrical anesthesia may increase the need for forceps assistance.

4 The use of some local anesthetic drug products during labor and delivery may be  
5 followed by diminished muscle strength and tone for the first day or two of life. This has  
6 not been reported with bupivacaine.

7 It is extremely important to avoid aortocaval compression by the gravid uterus  
8 during administration of regional block to parturients. To do this, the patient must be  
9 maintained in the left lateral decubitus position or a blanket roll or sandbag may be  
10 placed beneath the right hip and gravid uterus displaced to the left.

#### 11 *Nursing Mothers*

12 Bupivacaine has been reported to be excreted in human milk suggesting that the nursing  
13 infant could be theoretically exposed to a dose of the drug. Because of the potential for  
14 serious adverse reactions in nursing infants from bupivacaine, a decision should be made  
15 whether to discontinue nursing or not administer bupivacaine, taking into account the  
16 importance of the drug to the mother.

#### 17 *Pediatric Use*

18 Until further experience is gained in pediatric patients younger than 12 years,  
19 administration of Sensorcaine (bupivacaine HCl) Injection in this age group is not  
20 recommended. Continuous infusions of bupivacaine in children have been reported to  
21 result in high systemic levels of bupivacaine and seizures; high plasma levels may also be  
22 associated with cardiovascular abnormalities (see **WARNINGS, PRECAUTIONS,** and  
23 **OVERDOSAGE**).

1 ***Geriatric Use***

2 Patients over 65 years, particularly those with hypertension, may be at increased risk for  
3 developing hypotension while undergoing anesthesia with bupivacaine (see **ADVERSE**  
4 **REACTIONS**).

5 Elderly patients may require lower doses of bupivacaine (see **PRECAUTIONS**,  
6 ***Epidural Anesthesia*** and **DOSAGE AND ADMINISTRATION**).

7 In clinical studies, differences in various pharmacokinetic parameters have been  
8 observed between elderly and younger patients (see **CLINICAL PHARMACOLOGY**).

9 This product is known to be substantially excreted by the kidney, and the risk of  
10 toxic reactions to this drug may be greater in patients with impaired renal function.

11 Because elderly patients are more likely to have decreased renal function, care should be  
12 taken in dose selection, and it may be useful to monitor renal function (see **CLINICAL**  
13 **PHARMACOLOGY**).

14 **ADVERSE REACTIONS:**

15 Reactions to Sensorcaine (bupivacaine HCl) are characteristic of those associated with  
16 other amide-type local anesthetics. A major cause of adverse reactions to this group of  
17 drugs is excessive plasma levels, which may be due to overdosage, unintentional  
18 intravascular injection, or slow metabolic degradation.

19 ***Systemic***

20 The most commonly encountered acute adverse experiences which demand immediate  
21 counter-measures are related to the central nervous system and the cardiovascular system.  
22 These adverse experiences are generally dose related and due to high plasma levels which  
23 may result from overdosage, rapid absorption from the injection site, diminished

1 tolerance, or from unintentional intravascular injection of the local anesthetic solution. In  
2 addition to systemic dose-related toxicity, unintentional subarachnoid injection of drug  
3 during the intended performance of caudal or lumbar epidural block or nerve blocks near  
4 the vertebral column (especially in the head and neck region) may result in  
5 underventilation or apnea (“Total or High Spinal”). Also, hypotension due to loss of  
6 sympathetic tone and respiratory paralysis or underventilation due to cephalad extension  
7 of the motor level of anesthesia may occur. This may lead to secondary cardiac arrest if  
8 untreated. Patients over 65 years, particularly those with hypertension, may be at  
9 increased risk for experiencing the hypotensive effects of bupivacaine. Factors  
10 influencing plasma protein binding, such as acidosis, systemic diseases which alter  
11 protein production, or competition of other drugs for protein binding sites, may diminish  
12 individual tolerance.

### 13 *Central Nervous System Reactions*

14 These are characterized by excitation and/or depression. Restlessness, anxiety, dizziness,  
15 tinnitus, blurred vision, or tremors may occur, possibly proceeding to convulsions.  
16 However, excitement may be transient or absent, with depression being the first  
17 manifestation of an adverse reaction. This may quickly be followed by drowsiness  
18 merging into unconsciousness and respiratory arrest. Other central nervous system  
19 effects may be nausea, vomiting, chills, and constriction of the pupils.

20 The incidence of convulsions associated with the use of local anesthetics varies  
21 with the procedure used and the total dose administered. In a survey of studies of  
22 epidural anesthesia, overt toxicity progressing to convulsions occurred in approximately  
23 0.1% of local anesthetic administrations.

1 ***Cardiovascular System Reactions***

2 High doses or unintentional intravascular injection may lead to high plasma levels and  
3 related depression of the myocardium, decreased cardiac output, heartblock, hypotension,  
4 bradycardia, ventricular arrhythmias, including ventricular tachycardia and ventricular  
5 fibrillation, and cardiac arrest (see **WARNINGS, PRECAUTIONS,** and  
6 **OVERDOSAGE**).

7 ***Allergic***

8 Allergic-type reactions are rare and may occur as a result of sensitivity to the local  
9 anesthetic or to other formulation ingredients, such as the antimicrobial preservative  
10 methylparaben contained in multiple dose vials or sulfites in epinephrine-containing  
11 solutions. These reactions are characterized by signs such as urticaria, pruritus,  
12 erythema, angioneurotic edema (including laryngeal edema), tachycardia, sneezing,  
13 nausea, vomiting, dizziness, syncope, excessive sweating, elevated temperature, and  
14 possibly, anaphylactoid-like symptomatology (including severe hypotension). Cross  
15 sensitivity among members of the amide-type local anesthetic group has been reported.  
16 The usefulness of screening for sensitivity has not been definitely established.

17 ***Neurologic***

18 The incidence of adverse neurologic reactions associated with the use of local anesthetics  
19 may be related to the total dose of local anesthetic administered and are also dependent  
20 upon the particular drug used, the route of administration, and the physical status of the  
21 patient. Many of these effects may be related to local anesthetic techniques, with or  
22 without a contribution from the drug.

23 In the practice of caudal or lumbar epidural block, occasional unintentional

1 penetration of the subarachnoid space by the catheter or needle may occur. Subsequent  
2 adverse effects may depend partially on the amount of drug administered intrathecally  
3 and the physiological and physical effects of a dural puncture. A high spinal is  
4 characterized by paralysis of the legs, loss of consciousness, respiratory paralysis, and  
5 bradycardia.

6         Neurologic effects following epidural or caudal anesthesia may include spinal  
7 block of varying magnitude (including high or total spinal block); hypotension secondary  
8 to spinal block; urinary retention; fecal and urinary incontinence; loss of perineal  
9 sensation and sexual function; persistent anesthesia, paresthesia, weakness, paralysis of  
10 the lower extremities and loss of sphincter control all of which may have slow,  
11 incomplete, or no recovery; headache; backache; septic meningitis; meningismus;  
12 slowing of labor; increased incidence of forceps delivery; or cranial nerve palsies due to  
13 traction on nerves from loss of cerebrospinal fluid.

14         Neurologic effects following other procedures or routes of administration may  
15 include persistent anesthesia, paresthesia, weakness, paralysis, all of which may have  
16 slow, incomplete, or no recovery.

#### 17 **OVERDOSAGE:**

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

#### 22 *Management of Local Anesthetic Emergencies*

23 The first consideration is prevention, best accomplished by careful and constant

1 monitoring of cardiovascular and respiratory vital signs and the patient's state of  
2 consciousness after each local anesthetic injection. At the first sign of change, oxygen  
3 should be administered.

4 *The first step in the management of systemic toxic reactions, as well as*  
5 *underventilation or apnea due to unintentional subarachnoid injection of drug solution,*  
6 *consists of **immediate** attention to the establishment and maintenance of a patent airway*  
7 *and effective assisted or controlled ventilation with 100% oxygen with a delivery system*  
8 *capable of permitting immediate positive airway pressure by mask. This may prevent*  
9 *convulsions if they have not already occurred.*

10 If necessary, use drugs to control the convulsions. A 50 mg to 100 mg bolus IV  
11 injection of succinylcholine will paralyze the patient without depressing the central  
12 nervous or cardiovascular systems and facilitate ventilation. A bolus IV dose of 5 mg to  
13 10 mg of diazepam or 50 mg to 100 mg of thiopental will permit ventilation and  
14 counteract central nervous system stimulation, but these drugs also depress the central  
15 nervous system, respiratory, and cardiac function, add to postictal depression and may  
16 result in apnea. Intravenous barbiturates, anticonvulsant agents, or muscle relaxants  
17 should only be administered by those familiar with their use. Immediately after the  
18 institution of these ventilatory measures, the adequacy of the circulation should be  
19 evaluated. Supportive treatment of circulatory depression may require administration of  
20 intravenous fluids, and when appropriate, a vasopressor dictated by the clinical situation  
21 (such as ephedrine or epinephrine to enhance myocardial contractile force).

22 Endotracheal intubation, employing drugs and techniques familiar to the  
23 clinician, may be indicated after initial administration of oxygen by mask if difficulty is



1 encountered in the maintenance of a patent airway, or if prolonged ventilatory support  
2 (assisted or controlled) is indicated.

3         Recent clinical data from patients experiencing local anesthetic-induced  
4 convulsions demonstrated rapid development of hypoxia, hypercarbia, and acidosis with  
5 bupivacaine within a minute of the onset of convulsions. These observations suggest that  
6 oxygen consumption and carbon dioxide production are greatly increased during local  
7 anesthetic convulsions and emphasize the importance of immediate and effective  
8 ventilation with oxygen which may avoid cardiac arrest.

9         If not treated immediately, convulsions with simultaneous hypoxia, hypercarbia,  
10 and acidosis plus myocardial depression from the direct effects of the local anesthetic  
11 may result in cardiac arrhythmias, bradycardia, asystole, ventricular fibrillation, or  
12 cardiac arrest. Respiratory abnormalities, including apnea, may occur. Underventilation  
13 or apnea due to unintentional subarachnoid injection of local anesthetic solution may  
14 produce these same signs and also lead to cardiac arrest if ventilatory support is not  
15 instituted. *If cardiac arrest should occur, successful outcome may require prolonged*  
16 *resuscitative efforts.*

17         The supine position is dangerous in pregnant women at term because of  
18 aortocaval compression by the gravid uterus. Therefore during treatment of systemic  
19 toxicity, maternal hypotension or fetal bradycardia following regional block, the  
20 parturient should be maintained in the left lateral decubitus position if possible, or manual  
21 displacement of the uterus off the great vessels should be accomplished.

22         The mean seizure dosage of bupivacaine in rhesus monkeys was found to be 4.4  
23 mg/kg with mean arterial plasma concentration of 4.5 mcg/mL. The intravenous and

1 subcutaneous LD<sub>50</sub> in mice is 6 mg/kg to 8 mg/kg and 38 mg/kg to 54 mg/kg  
2 respectively.

### 3 **DOSAGE AND ADMINISTRATION:**

4 The dose of any local anesthetic administered varies with the anesthetic procedure, the  
5 area to be anesthetized, the vascularity of the tissues, the number of neuronal segments to  
6 be blocked, the depth of anesthesia and degree of muscle relaxation required, the duration  
7 of anesthesia desired, individual tolerance, and the physical condition of the patient. The  
8 smallest dose and concentration required to produce the desired result should be  
9 administered. Dosages of Sensorcaine should be reduced for elderly and/or debilitated  
10 patients and patients with cardiac and/or liver disease. The rapid injection of a large  
11 volume of local anesthetic solution should be avoided and fractional (incremental) doses  
12 should be used when feasible.

13 For specific techniques and procedures, refer to standard textbooks.

14 There have been adverse event reports of chondrolysis in patients receiving intra-  
15 articular infusions of local anesthetics following arthroscopic and other surgical  
16 procedures. Sensorcaine is not approved for this use (see **WARNINGS** and **DOSAGE**  
17 **AND ADMINISTRATION**).

18 In recommended doses, Sensorcaine (bupivacaine HCl) produces complete  
19 sensory block, but the effect on motor function differs among the three concentrations.

20 **0.25%**—when used for caudal, epidural, or peripheral nerve block, produces  
21 incomplete motor block. Should be used for operations in which muscle relaxation is not  
22 important, or when another means of providing muscle relaxation is used concurrently.

23 Onset of action may be slower than with the 0.5% or 0.75% solutions.

1           **0.5%**—provides motor blockade for caudal, epidural, or nerve block, but muscle  
2 relaxation may be inadequate for operations in which complete muscle relaxation is  
3 essential.

4           **0.75%**—produces complete motor block. Most useful for epidural block in  
5 abdominal operations requiring complete muscle relaxation, and for retrobulbar  
6 anesthesia. Not for obstetrical anesthesia.

7           The duration of anesthesia with Sensorcaine is such that for most indications, a  
8 single dose is sufficient.

9           Maximum dosage limit must be individualized in each case after evaluating the  
10 size and physical status of the patient, as well as the usual rate of systemic absorption  
11 from a particular injection site. Most experience to date is with single doses of  
12 Sensorcaine up to 225 mg with epinephrine 1:200,000 and 175 mg without epinephrine;  
13 more or less drug may be used depending on individualization of each case.

14           These doses may be repeated up to once every three hours. In clinical studies to  
15 date, total daily doses have been up to 400 mg. Until further experience is gained, this  
16 dose should not be exceeded in 24 hours. The duration of anesthetic effect may be  
17 prolonged by the addition of epinephrine.

18           The dosages in Table 1 have generally proved satisfactory and are recommended  
19 as a guide for use in the average adult. These dosages should be reduced for elderly or  
20 debilitated patients. Until further experience is gained, Sensorcaine is not recommended  
21 for pediatric patients younger than 12 years. Sensorcaine is contraindicated for  
22 obstetrical paracervical blocks, and is not recommended for intravenous regional  
23 anesthesia (Bier Block).

1    ***Use in Epidural Anesthesia***

2    During epidural administration of Sensorcaine, 0.5% and 0.75% solutions should be  
3    administered in incremental doses of 3 mL to 5 mL with sufficient time between doses to  
4    detect toxic manifestations of unintentional intravascular or intrathecal injection. In  
5    obstetrics, only the 0.5% and 0.25% concentrations should be used; incremental doses of  
6    3 mL to 5 mL of the 0.5% solution not exceeding 50 mg to 100 mg at any dosing interval  
7    are recommended. Repeat doses should be preceded by a test dose containing  
8    epinephrine if not contraindicated. Use only the single dose ampules and single dose  
9    vials for caudal or epidural anesthesia; the multiple dose vials contain a preservative and  
10   therefore should not be used for these procedures.

11

12   ***Test Dose for Caudal and Lumbar Epidural Blocks***

13   The Test Dose of Sensorcaine (0.5% bupivacaine with 1:200,000 epinephrine in a 3 mL  
14   ampule) is recommended for use as a test dose when clinical conditions permit prior to  
15   caudal and lumbar epidural blocks. This may serve as a warning of unintended  
16   intravascular or subarachnoid injection (see **PRECAUTIONS**). The pulse rate and  
17   other signs should be monitored carefully immediately following each test dose  
18   administration to detect possible intravascular injection, and adequate time for onset of  
19   spinal block should be allotted to detect possible intrathecal injection. An intravascular  
20   or subarachnoid injection is still possible even if results of the test dose are negative.  
21   The test dose itself may produce a systemic toxic reaction, high spinal or cardiovascular  
22   effects from the epinephrine (see **WARNINGS** and **OVERDOSAGE**).

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**TABLE 1. Recommended Concentrations and Doses of SENSORCAINE  
(bupivacaine HCl) INJECTIONS**

Type of Block	Conc.	Each Dose		Motor Block <sup>1</sup>
		(mL)	(mg)	
Local Infiltration	0.25% <sup>4</sup>	up to max.	up to max.	—
Epidural	0.75% <sup>2,4</sup>	10 to 20	75 to 150	complete
	0.5% <sup>4</sup>	10 to 20	50 to 100	moderate to complete
	0.25% <sup>4</sup>	10 to 20	25 to 50	partial to moderate
Caudal	0.5% <sup>4</sup>	15 to 30	75 to 150	moderate to complete
	0.25% <sup>4</sup>	15 to 30	37.5 to 75	moderate
Peripheral Nerves	0.5% <sup>4</sup>	5 to max.	25 to max.	moderate to complete
	0.25% <sup>4</sup>	5 to max.	12.5 to max.	moderate to complete
Retrobulbar <sup>3</sup>	0.75% <sup>4</sup>	2 to 4	15 to 30	complete
Sympathetic	0.25%	20 to 50	50 to 125	—
Dental <sup>3</sup>	0.5%	1.8 to 3.6	9 to 18	—
	w/epi	per site	per site	
Epidural <sup>3</sup>	0.5%	2 to 3	10 to 15	
Test Dose	w/epi		10 to 15 mcg epinephrine (see <b>PRECAUTIONS</b> )	

4  
5  
6  
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8

<sup>1</sup> With continuous (intermittent) techniques, repeat doses increase the degree of motor block. The first repeat dose of 0.5% may produce complete motor block. Intercostal nerve block with 0.25% may also produce complete motor block for intra-abdominal surgery.

1 <sup>2</sup> For single dose use, not for intermittent epidural technique. Not for obstetric  
2 anesthesia.

3 <sup>3</sup> See **PRECAUTIONS**.

4 <sup>4</sup> Solutions with or without epinephrine.

5 **HOW SUPPLIED:**

6 **These solutions are not for spinal anesthesia.**

7 Sensorcaine-MPF (methylparaben free) is available in the following forms:

8 **With Epinephrine:**

<b>Product No.</b>	<b>NDC No.</b>	<b>Strength</b>	<b>Size</b>
460837	63323-468-37	0.25%	30 mL Single Dose Vials packaged in trays of twenty-five.
460817	63323-468-17	0.25%	10 mL Single Dose Vials packaged in trays of twenty-five.
460217	63323-462-17	0.5%	10 mL Single Dose Vials packaged in trays of twenty-five.
460237	63323-462-37	0.5%	30 mL Single Dose Vials packaged in trays of twenty-five.
460231	63323-462-31	0.5%	30 mL Single Dose Vials packaged in fives.
461037	63323-460-37	0.75%	30 mL Single Dose Vials packaged in trays of twenty-five.

1 **Without Epinephrine:**

<b>Product No.</b>	<b>NDC No.</b>	<b>Strength</b>	<b>Size</b>
460417	63323-464-17	0.25%	10 mL Single Dose Vials packaged in trays of twenty-five.
460437	63323-464-37	0.25%	30 mL Single Dose Vials packaged in trays of twenty-five.
460431	63323-464-31	0.25%	30 mL Single Dose Vials packaged in fives.
460617	63323-466-17	0.5%	10 mL Single Dose Vials packaged in trays of twenty-five.
460637	63323-466-37	0.5%	30 mL Single Dose Vials packaged in trays of twenty-five.
460631	63323-466-31	0.5%	30 mL Single Dose Vials packaged in fives.
470217	63323-472-17	0.75%	10 mL Single Dose Vials packaged in trays of twenty-five.
470237	63323-472-37	0.75%	30 mL Single Dose Vials packaged in trays of twenty-five.

2 Sensorcaine (preserved with methylparaben) is available in the following forms:

3 **With Epinephrine:**

<b>Product No.</b>	<b>NDC No.</b>	<b>Strength</b>	<b>Size</b>
460157	63323-461-57	0.25%	50 mL Multiple Dose Vials packaged in trays of twenty-five.
460357	63323-463-57	0.5%	50 mL Multiple Dose Vials packaged in trays of twenty-five.

1 **Without Epinephrine:**

<b>Product No.</b>	<b>NDC No.</b>	<b>Strength</b>	<b>Size</b>
460557	63323-465-57	0.25%	50 mL Multiple Dose Vials packaged in trays of twenty-five.
460757	63323-467-57	0.5%	50 mL Multiple Dose Vials packaged in trays of twenty-five.

2

3 Solutions should be stored at 20° to 25°C (68° to 77°F) [see USP Controlled  
4 Room Temperature].

5 Solutions containing epinephrine should be protected from light.

6

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8 Manufactured for:

9

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11 **Fresenius Kabi USA, LLC**  
12 Lake Zurich, IL 60047

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14 451106E

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