PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

SENSORCAINE®

Bupivacaine Hydrochloride
Solution, 0.25% (2.5 mg/mL) and 0.5% (5 mg/mL), Epidural, Block/Infiltration
USP

SENSORCAINE® with Epinephrine

Bupivacaine Hydrochloride and Epinephrine
Solution, 0.25% bupivacaine hydrochloride (2.5 mg/mL) and epinephrine bitartrate [(1:200,000) 5 mcg/mL]
and 0.5% bupivacaine hydrochloride (5 mg/mL) and epinephrine bitartrate [(1:200,000) 5 mcg/mL], Epidural, Block/Infiltration
USP

Local Anesthetics

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RECENT MAJOR LABEL CHANGES

7 Warnings and Precautions	04/2021
7.Warnings and Precautions, hepatic	04/2022

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

SENSORCAINE (bupivacaine hydrochloride) and SENSORCAINE with Epinephrine (bupivacaine hydrochloride and epinephrine) are indicated for the production of local or regional anaesthesia or analgesia with the following procedures:

- Local infiltration
- Peripheral minor or major nerve blocks
- Epidural block for surgery
- Epidural block by continuous infusion or intermittent bolus for postoperative or labour pain relief.

Standard procedures for local infiltration, minor and major nerve blocks, retrobulbar block or epidural block should be observed.

1.1 Pediatrics

Pediatrics **(< 2 years of age)**: No data are available to Health Canada; therefore, SENSORCAINE is not recommended for use.

Pediatrics **(≥2 years of age):** The safety and efficacy of SENSORCAINE have not been established; therefore, Health Canada has not authorized an indication for use (See 4 DOSAGE AND ADMINISTRATION, 7 WARNINGS AND PRECAUTIONS)

1.2 Geriatrics

Geriatrics **(> 65 years of age)**: Elderly patients should be given reduced doses commensurate with their age and physical condition.

2 CONTRAINDICATIONS

SENSORCAINE (bupivacaine hydrochloride) and SENSORCAINE with Epinephrine are contraindicated:

- In patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.
- In patients with hypersensitivity to any local anaesthetic agent of the amide type.
- For intravenous regional anaesthesia (Bier block) since unintentional leakage of bupivacaine over the tourniquet may cause systemic toxic reactions. Cardiac arrest and death have occurred (see 4 DOSAGE AND ADMINISTRATION).
- In obstetric paracervical block anaesthesia. Use of other local anaesthetics in this technique has resulted in foetal bradycardia and death.

SENSORCAINE with Epinephrine is contraindicated:

- in patients with a hypersensitivity to sodium metabisulfite (see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING, 7 WARNINGS AND PRECAUTIONS, Sensitivity/resistance).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

General

The dosage varies and depends upon the area to be anaesthetized, the number of neuronal segments to be blocked, the depth of anaesthesia and degree of muscle relaxation required, individual tolerance, tissue vascularity, and the technique of anaesthesia. The lowest concentration of anaesthetic and the lowest dosage needed to provide effective anaesthesia should be administered. The rapid injection of a large volume of local anaesthetic solution should be avoided and fractional doses should be used when feasible. In general, complete block of all nerve fibres in large nerves requires the higher concentrations of drug. In smaller nerves, or when a less intense block is required (e.g., in the relief of labour pain), the lower concentrations are indicated. The volume of drug used will affect the extent of spread of anaesthesia.

The use of bupivacaine with epinephrine will prolong the anaesthetic action.

There have been adverse event reports of irreversible chondrolysis in patients receiving intra-articular infusions of local anaesthetics following arthroscopic and other surgical procedures. SENSORCAINE (bupivacaine hydrochloride) is not approved for this use (see 7 WARNINGS AND PRECAUTIONS, General).

Special Populations

Local anaesthetics should be used with caution in patients in poor general condition due to aging or other compromising factors such as advanced liver disease or severe renal dysfunction although regional anaesthesia is frequently indicated in these patients.

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

4.2 Recommended Dose and Dosage Adjustment

Adults: The dosages in Table 1 are recommended as a guide for use in the average adult for the more commonly used techniques. The clinician's experience and knowledge of the patient's physical condition are of importance in calculating the required dose.

When prolonged blocks are used, the risks of reaching a toxic plasma concentration or inducing a local neural injury must be considered. The maximum dosage limit must be determined by evaluating the size and physical condition of the patient and considering the usual rate of systemic absorption from a specific injection site. Experience to date indicates that 400 mg administered over 24 hours is well tolerated in average adults. Until further experience is gained, this dose should not be exceeded in 24 hours.

In order to avoid intravascular injection, aspiration should be repeated prior to and during administration of the main dose, which should be injected slowly or in incremental doses, at a rate of 25-50 mg/min, while closely observing the patient's vital functions and maintaining verbal contact. An inadvertent intravascular injection may be recognized by a temporary increase in heart rate and an accidental intrathecal injection by signs of a spinal block. If toxic symptoms occur, the injection should be stopped immediately.

Intra-articular Infusion of a local anaesthetic is an unapproved use (See 7 WARNINGS AND

PRECAUTIONS). Sympathetic stellate block requires utmost caution (See 7 WARNINGS AND PRECAUTIONS, Injection in head and neck area).

SENSORCAINE with Epinephrine (3 – 5 mL) should be used only as a test dose for epidural block in labour analgesia. It should not be used for epidural block (See 7.1.1 Pregnant Women).

Table 1-Dosage recommendations in adults for SENSORCAINE or SENSORCAINE with Epinephrine

TYPE OF BLOCK	CONC. (%)	EACH DOSE mL	mg	ONSET (min.)	DURATION (h)	INDICATION
Local infiltration	0.25 0.5	up to 60[b] up to 30[b]	up to 150[b] up to 150[b]	1-3 1-3	3-4 4-8	Surgical operations and postoperative analgesia.
Lumbar epidural[a]	0.25 0.5	6-15 15-30	15-37.5 75-150	2-5 15-30	1-2 2-3	Surgical operations Postoperative analgesia Caesarean section. Labour analgesia (only epinephrine free formulations)
Thoracic epidural[a]	0.25 0.5	5-15 5-10	12.5-37.5 25-50	10-15 10-15	1.5-2 2-3	Surgical operations.
Caudal epidural[a]	0.25 0.5	20-30 20-30	50-75 100-150	20-30 15-30	1-2 2-3	Surgical operations and postoperative analgesia. Pain relief and diagnostic use.
Intercostal (per nerve)	0.5	2-3	10-15	3-5	4-8	Pain relief for surgery, postoperative and trauma.
Brachial Plexus	0.5	30	150	15-30	4-8	Surgical operations.
Sciatic	0.5	10-20	50-100	15-30	4-8	Surgical operations.
Digital[d]	0.25	1-5	2.5-12.5	2-5	3-4	Surgical operations.
Peripheral nerves	0.25 0.5	up to 40[b] up to 30[b]	up to 100[b] up to	10-20 5-10	3-5 4-8	Therapeutic (pain relief). Surgical operations.

TYPE OF BLOCK	CONC. (%)	EACH DOSE mL	mg	ONSET (min.)	DURATION (h)	INDICATION
			150[b]			
Sympathetic[c] Stellate block	0.25	5-15	12.5-37.5	10-20	3-6	Ischemic conditions or sympathetic maintained pains e.g. visceral pain conditions such as pancreatitis or cancer, pain of herpes zoster.
Lumbar	0.25	10-20	25-50	10-20	3-6	
Paravertebral block						
Coeliac plexus block	0.25	20-40	50-100	10-20	3-6	

a For epidural blocks, dose includes test dose.
b No more than 400 mg in 24 hours.
c With epinephrine 1:200,000 (5µg/mL).
d Without epinephrine.

Children: Bupivacaine is not recommended for children younger than two years of age. The safety and efficacy of SENSORCAINE or SENSORCAINE with Epinephrine in children aged between 2 - 12 years have not been established. Only limited data are available. Lower strengths may be more appropriate for administration to children aged 2 – 12 years. Pediatric regional anaesthetic procedures should be performed by qualified clinicians who are familiar with this population and the technique.

For bolus administration or intermittent injections, unless stated otherwise (see Table 2), a dose of up to 2 mg/kg of SENSORCAINE or SENSORCAINE with Epinephrine is recommended. The dose administered will depend on the age and body weight of the patient, the site of surgery, and the condition of the patient. The lowest does required for adequate analgesia should be used. The addition of epinephrine will prolong the duration of the block by 50-100%.
Risk of systemic effects of epinephrine with large volumes of epinephrine containing solutions should be considered.

Table 2- Dosage recommendations in children (over two years of age) for SENSORCAINE-SENSORCAINE with Epinephrine isotonic solutions

TYPE OF BLOCK	CONC. (%)	EACH DOSE	
		mL/kg	mg/kg
Local infiltration	0.25[a]	up to 0.8	up to 2

	0.5[a]	up to 0.4	up to 2
Caudal epidural[b]	0.25	0.6-0.8	1.5-2[c]
Lumbar epidural[b]	0.25	0.6-0.8	1.5-2[c]
Dorsal (penile)	0.25[a] 0.5[a]	0.1-0.2 0.1-0.2	0.25-0.5 0.5-1.0
Intercostal	0.25[a]	up to 0.8	up to 2

NOTE: The use of SENSORCAINE/SENSORCAINE with Epinephrine for anaesthesia and/or analgesia may be supplementary to light general anaesthesia.

a Without epinephrine.
b Consider both age and weight for calculation of dosages.
c Onset: 20-30 minutes, Duration: 2-6 hours.

In order to avoid intravascular injection, aspiration should be repeated prior to and during administration of the main dose. This should be injected slowly in incremental doses, particularly in the lumbar and thoracic epidural routes, constantly and closely observing the patient's vital functions.

The safety and efficacy of intermittent epidural bolus injection or continuous infusion have not been established. Only limited data are available.

Use in Epidural Anaesthesia

When an epidural dose is to be injected, a test dose of a local anaesthetic is recommended (see 7 WARNINGS AND PRECAUTIONS). SENSORCAINE 0.5% with Epinephrine (Table 2), or 3-5 mL lidocaine (XYLOCAINE® 1-2%) with epinephrine, can be used if a vasoconstrictor is not contraindicated. Verbal contact and repeated monitoring of heart rate and blood pressure should be maintained for five minutes after the test dose. In the absence of signs of subarachnoid or intravascular injection, the main dose may be given.

During epidural administration, bupivacaine should be administered slowly in incremental doses of 3 to 5 mL, with sufficient time between doses to detect toxic manifestations of unintentional intravascular or intrathecal injection.

SENSORCAINE with Epinephrine should not be used for epidural block in labour analgesia (apart from the use as a test dose) as the benefits from the addition of adrenaline have not been shown to outweigh the risks.

5 OVERDOSAGE

Local anaesthetic systemic toxicity is generally related to high plasma levels encountered during therapeutic use, or to unintended subarachnoid or intravascular injection, exceptionally rapid absorption from highly vascularized areas or overdosage and originates mainly in the central nervous and the cardiovascular systems (see 8 ADVERSE REACTIONS and 7 WARNINGS AND PRECAUTIONS). Central nervous system reactions are similar for all amide local anaesthetics, while cardiac reactions are more dependent on the drug, both quantitatively and qualitatively.

Symptoms

Accidental intravascular injections of local anaesthetics may cause immediate (within seconds to a few minutes) systemic toxic reactions. In the event of overdose, systemic toxicity appears later (15-60 minutes after injection) due to the slower increase in local anaesthetic blood concentration.

Central nervous system toxicity is a graded response with symptoms and signs of escalating severity. The first symptoms are usually circumoral paresthesia, numbness of the tongue, light-headedness, hyperacousis, tinnitus and visual disturbances. Dysarthria, muscular twitching or tremors are more serious and precede the onset of generalized convulsions. These signs must not be mistaken for a neurotic behaviour. Unconsciousness and grand mal convulsions may follow which may last from a few seconds to several minutes. Hypoxia and hypercarbia occur rapidly following convulsions due to the increased muscular activity, together with the interference with normal respiration and loss of the airway. In severe cases apnoea may occur. Acidosis, hyperkalaemia, hypocalcaemia and hypoxia increase and extend the toxic effects of local anaesthetics.

Recovery is due to redistribution and subsequent metabolism and excretion of the local anaesthetic drug. Recovery may be rapid unless large amounts of the drug have been administered.

Cardiovascular system toxicity may be seen in severe cases and is generally preceded by signs of toxicity in the central nervous system. In patients under heavy sedation or receiving a general anaesthetic, prodromal CNS symptoms may be absent. Hypotension, bradycardia, arrhythmia and even cardiac arrest may occur as a result of high systemic concentrations of local anaesthetics, but in rare cases cardiac arrest has occurred without prodromal CNS effects. Cardiovascular toxic reactions are usually related to depression of the conduction system of the heart and myocardium, leading to decreased cardiac output, hypotension, heart block, bradycardia and sometimes ventricular arrhythmias, including ventricular tachycardia, ventricular fibrillation and cardiac arrest.

In children, early signs of local anaesthetic toxicity may be difficult to detect in cases where the block is given during general anaesthesia.

Treatment

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 anaesthetic injection. If signs of acute systemic toxicity appear, injection of the local anaesthetic should be immediately stopped.

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

CNS symptoms (convulsion, CNS depression) must promptly be treated with appropriate airway/ respiratory support and the administration of anticonvulsant drugs.

If cardiovascular depression occurs (hypotension, bradycardia), appropriate treatment with intravenous fluids, vasopressors and/or inotropic agents should be considered as per standard practice guidance. Children should be given appropriate treatment in doses commensurate with their age and weight.

Should cardiac arrest occur, immediate cardiopulmonary resuscitation should be instituted. Optimal oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance, since hypoxia and acidosis will increase the systemic toxicity of local anaesthetics. A

successful resuscitation may require prolonged efforts.

Lipid emulsion formulations should be made immediately available as part of the anaesthetic emergency preparedness in the health care facility. When symptoms and signs of local anaesthetic system toxicity are observed, lipid emulsion therapy should be considered if clinical events warrant intervention and after the airway is secured.

The supine position is dangerous in pregnant women at term because of aortocaval compression by the gravid uterus. Therefore, during treatment of systemic toxicity, maternal hypotension or foetal bradycardia following regional block, the parturient should be maintained in the left lateral decubitus position if possible, or manual displacement of the uterus off the great vessels should be accomplished. Resuscitation of obstetrical patients may take longer than resuscitation of nonpregnant patients and closed-chest cardiac compression may be ineffective. Rapid delivery of the foetus may improve the response to resuscitative efforts.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 3– Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Parenteral	Sterile Solution / 2.5 and 5 mg/mL bupivacaine hydrochloride Solutions with epinephrine contain 5 mcg/mL (1:200,000) epinephrine as bitartrate	All SENSORCAINE presentations: Sodium chloride, sodium hydroxide and/or hydrochloric acid, water for injection SENSORCAINE with Epinephrine also contains sodium metabisulfite

Dosage Forms

SENSORCAINE (bupivacaine hydrochloride) and SENSORCAINE with Epinephrine are sterile isotonic solutions.

Packaging

Vials are supplied in units of 10 and polyethylene Polyamp® Duofit® in units of 50.

Table 4- Availability of SENSORCAINE and SENSORCAINE with Epinephrine.

SENSORCAINE (bupivacaine hydrochloride) Concentration	Epinephrine Dilution (if present)	Polyamp®Duofit® (plastic ampoules) [a] (mL)	Single-Use Vials (mL)
		10	20
0.25%		√	√
0.25%	1:200,000[b]		√
0.5%		√	√
0.5%	1:200,000[b]		√

[a] Plastic ampoules suitable for Luer fit and Luer lock syringes.
[b] Contains sodium metabisulfite as an antioxidant.
Polyamp® Duofit® are registered trademarks of the AstraZeneca group of companies.

The stopper is not made with natural rubber latex**.**

7 WARNINGS AND PRECAUTIONS

General

Local anaesthetics should only be used by clinicians who are well versed in diagnosis and management of dose-related toxicity and other acute emergencies which may arise from the block to be performed, and then only after ensuring the immediate availability of cardiopulmonary resuscitative equipment, resuscitative drugs, including oxygen, and the personnel resources needed for proper management of toxic reactions and related emergencies (see 8 ADVERSE REACTIONS and 5 OVERDOSAGE). Delay in proper management of dose-related toxicity, underventilation from any cause and/or altered sensitivity may lead to the development of acidosis, cardiac arrest and, possibly, death.

An intravenous cannula must be inserted before the local anaesthetic is injected for nerve blocks which may result in hypotension or bradycardia, or where acute systemic toxicity may develop following inadvertent intravascular injection.

The lowest dosage of local anaesthetic that results in effective anaesthesia or analgesia should be used to avoid high plasma levels and serious adverse reactions. Injections should be made slowly or in incremental doses, with frequent aspirations before and during the injection to avoid intravascular injection.

Reports of Irreversible Chondrolysis with Intra-articular Infusions of Local Anaesthetics Following Surgery: Intra-articular infusions of local anaesthetics following arthroscopic and other surgical procedures is an unapproved use, and there have been post-marketing reports of irreversible chondrolysis in patients receiving such infusions. The majority of reported cases of irreversible chondrolysis have involved the shoulder joint; cases of gleno-humeral irreversible chondrolysis have been described in pediatric and adult patients following intra-articular infusions of local anaesthetics with and without epinephrine for periods of 48 to 72 hours. The time of onset of symptoms, such as joint pain, stiffness and loss of motion can be variable, but may begin as early as the 2nd month after surgery. Currently, there is no effective treatment for irreversible chondrolysis; patients who experienced irreversible chondrolysis have required additional diagnostic and therapeutic procedures and some required arthroplasty or shoulder replacement. SENSORCAINE (bupivacaine hydrochloride) should not be used for **post-operative intra-articular infusion** (See 4 DOSAGE AND ADMINISTRATION).

Repeat Dosing: Injection of repeated doses of local anaesthetics may cause significant increases in plasma levels with each repeated dose due to slow accumulation of the drug, or its metabolites, or to slow metabolic degradation. Tolerance to elevated blood levels varies with the physical condition of the patient.

Major Peripheral Nerve Blocks: Major peripheral nerve blocks may imply the administration of a large volume of local anaesthetic in areas of high vascularity, often close to large vessels where there is an increased risk of intravascular injection and/or rapid systemic absorption which can lead to high plasma concentrations.

Use of Parenteral Solutions Containing Epinephrine: SENSORCAINE with Epinephrine should not be used in areas of the body supplied by end arteries, such as digits, nose, ears or penis, or otherwise having compromised blood supply.

Inflammation and Sepsis: Local anaesthetic procedures should be carried out sufficiently away from an inflamed region. Injections should not be performed through inflamed tissue or when there is sepsis at or near the injection site.

Cardiovascular

There have been reports of cardiac arrest or death during use of bupivacaine for epidural anaesthesia or peripheral nerve blockade. In some instances, resuscitation has been difficult or impossible despite apparently adequate preparation and management.

Ventricular arrhythmia, ventricular fibrillation, sudden cardiovascular collapse and death have been reported when bupivacaine was utilized for local anaesthetic procedures that may have resulted in high systemic concentrations of bupivacaine.

Epidural anaesthesia or analgesia may lead to hypotension and bradycardia, which should be managed according to the patient condition and standard of anaesthetic care.

SENSORCAINE with Epinephrine should be used with caution in patients who may have severe or untreated hypertension, ischemic heart disease, cerebral vascular insufficiency, heart block, peripheral vascular disorder and any other pathological condition that might be aggravated by the effects of epinephrine.

Local anaesthetics should be used with caution in patients with impaired cardiovascular function because they may be less able to compensate for functional changes associated with the prolongation of A-V conduction produced by amide-type local anaesthetics.

Patients with partial or complete heart block require special attention since local anaesthetics may depress myocardial conduction. To reduce the risk of potentially serious adverse reactions, attempts should be made to optimize the patient's condition before major blocks are performed. Dosage should be adjusted accordingly.

Central nerve blocks may cause cardiovascular depression, especially in the presence of hypovolemia. Epidural anaesthesia should be used with caution in patients with impaired cardiovascular function

Driving and Operating Machinery

Due caution should be exercised when driving or operating a vehicle or potentially dangerous machinery.

Endocrine and Metabolism

SENSORCAINE with Epinephrine should be used with caution in patients whose medical history and physical evaluation suggest the existence of poorly controlled hyperthyroidism or advanced diabetes.

Epidural Anaesthesia

It is recommended that a test dose be administered initially and the effects monitored before the full dose is given (see 4 DOSAGE AND ADMINISTRATION). When clinical conditions permit, the test dose should contain epinephrine (15 to 25 µg) as this amount of epinephrine, if injected into a blood vessel, is likely to produce a transient response within 45 seconds consisting of an increase in heart rate and systolic blood pressure. Patients on beta-blockers may not manifest changes in heart rate, but blood pressure monitoring can detect an evanescent rise in systolic blood pressure.

During epidural administration, bupivacaine should be administered in incremental doses of 3 to 5 mL with sufficient time between doses to detect toxic manifestations of unintentional intravascular or intrathecal injection. Frequent aspirations for blood or cerebrospinal fluid (where applicable, i.e., when using a "continuous" intermittent catheter technique), should be performed before and during each supplemental injection because plastic tubing in the epidural space can migrate into a blood vessel or through the dura. A negative aspiration, however, does not ensure against an intravascular or intrathecal injection.

Hepatic

Because amide-type local anaesthetics such as bupivacaine are metabolized by the liver, these drugs, especially repeat doses, should be used cautiously in patients with hepatic disease.

Patients with severe hepatic disease, because of their inability to metabolize local anaesthetics normally, are at a greater risk of developing toxic plasma concentrations.

Drug Induced Liver Injury (DILI): Serious cases of drug-induced liver injury (DILI), hepatic failure, and increased hepatic enzymes have been reported with bupivacaine, especially following repeated injections or long-term infusions. These events were not dose dependent, and patients were adults of all ages, with or without previous history of hepatic-related events.
If signs of hepatic dysfunction are observed during administration of bupivacaine, the medicinal product should be discontinued immediately. Re-challenge should be avoided (see 8 ADVERSE REACTIONS

Injection in Head and Neck Area

Inadvertent intravascular or subarachnoid injection of small doses of local anaesthetics injected into the head and neck area, including retrobulbular, dental and stellate ganglion blocks, may produce adverse reactions similar to systemic toxicity seen with unintentional intravascular injections of larger doses. The

injection procedures require the utmost care. Confusion, convulsions, respiratory depression and/or respiratory arrest, and cardiovascular stimulation or depression leading to cardiac arrest, have been reported. These reactions may be due to

intra-arterial injection of the local anaesthetic with retrograde flow to the cerebral circulation. Patients receiving these blocks should remain under constant observation and monitoring for their cardiac and pulmonary functions. Resuscitative equipment and personnel for treating adverse reactions should be immediately available. Dosage recommendations should not be exceeded (see 4 DOSAGE AND ADMINISTRATION).

Neurologic

Psychomotor effects: Local anaesthetics may have a dose-dependent effect on mental function and coordination, causing temporary impairment of locomotion and alertness, even in the absence of overt CNS toxicity.

Ophthalmic Surgery

Retrobulbar injections may very occasionally reach the cranial subarachnoid space causing temporary blindness, cardiovascular collapse, apnoea, convulsions, etc. These reactions, which may be due to intra-arterial injection or direct injection into the central nervous system via the sheaths of the optic nerve, must be diagnosed and treated promptly.

Clinicians who perform retrobulbar blocks should be aware that there have been reports of respiratory arrest following local anaesthetic injection. Prior to retrobulbar block, as with all other regional procedures, the immediate availability of equipment, drugs, and personnel to manage respiratory arrest or depression, convulsions, and cardiac stimulation or depression should be assured (see also 7 WARNINGS AND PRECAUTIONS, Injection in Head and Neck Area).

Retrobulbar injections of local anaesthetics carry a low risk of persistent ocular muscle dysfunction. The primary causes include trauma and/or local toxic effects on muscles and/or nerves. The severity of such tissue reactions is related to the degree of trauma, the concentration of the local anaesthetic and the duration of exposure of the tissue to the local anaesthetic. For this reason, as with all local anaesthetics, the lowest effective concentration and dose of local anaesthetic should be used. Vasoconstrictors, and other additives may aggravate tissue reactions and should be used only when indicated.

Peri-Operative Considerations

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

The safety and effectiveness of local anaesthetics depend on proper dosage, correct technique, adequate precautions and readiness for emergencies. Regional or local anaesthetic procedures should always be performed in a properly equipped and staffed area.

Resuscitative equipment and resuscitative drugs, including oxygen, should be available for immediate use (see 7 WARNINGS AND PRECAUTIONS and 8 ADVERSE REACTIONS and 5 OVERDOSAGE). During major regional nerve blocks, the patients should be in an optimal condition and have i.v. fluids running

via an indwelling catheter to assure a functioning intravenous pathway. The clinician responsible should have adequate and appropriate training in the procedure to be performed, should take the necessary precautions to avoid intravascular injection (see 4 DOSAGE AND ADMINISTRATION), and should be familiar with the diagnosis and treatment of side effects, systemic toxicity and other complications (see 8 ADVERSE REACTIONS and 5 OVERDOSAGE).

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

Renal

Local anaesthetics should be used with caution in patients in poor general condition due to severe renal dysfunction although regional anaesthesia is frequently indicated in these patients.

Sensitivity/Resistance

SENSORCAINE with Epinephrine contains sodium metabisulfite, that may cause allergic reactions including anaphylactic or anaphylactoid reactions or asthmatic episodes in susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.

7.1 Special Populations

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

7.1.1 Pregnant Women

There are no adequate and well-controlled studies in pregnant women of the effect of bupivacaine on the developing foetus.

Bupivacaine has been used in a large number of pregnant women and women of childbearing age for surgical, gynaecological, or obstetric procedures. No specific disturbances to the reproductive process have so far been reported, e.g., no increased incidence of malformations.

However, bupivacaine should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus. This does not exclude the use of bupivacaine at term for obstetrical anaesthesia or analgesia.

Labour and Delivery: SENSORCAINE/SENSORCAINE with Epinephrine 0.25% and 0.5% can be used at term for obstetrical anaesthesia or analgesia when benefits outweigh the risks.

However, SENSORCAINE with Epinephrine should be used only as a test dose for epidural block in labour analgesia. It should not be used for epidural block in labour analgesia as the benefits from the addition of adrenaline have not been shown to outweigh the risks.

Local anaesthetics rapidly cross the placenta, and when used for epidural block anaesthesia, can cause varying degrees of maternal, foetal and neonatal toxicity (see 10 CLINICAL PHARMACOLOGY). The incidence and degree of toxicity depend upon the procedure performed, the type and amount of drug used, and the technique of drug administration. Adverse reactions in the parturient, foetus and neonate involve alterations of the central nervous system, peripheral vascular tone and cardiac function.

Maternal hypotension has resulted from regional anaesthesia (see 7 WARNINGS AND PRECAUTIONS, Cardiovascular). Local anaesthetics produce vasodilation by blocking sympathetic nerves. It is extremely important to avoid aortocaval compression by the gravid uterus during administration of regional block to parturients. Elevating the patient's legs and positioning her on her left side will help prevent decreases in blood pressure. The foetal heart rate also should be monitored continuously, and electronic foetal monitoring is highly advisable.

Epidural anaesthesia may alter the forces of parturition through changes in uterine contractility or maternal expulsive efforts. Epidural anaesthesia has been reported to prolong the second stage of labour by removing the parturient's urge to bear down or by interfering with motor function. The use of SENSORCAINE 0.25% has been shown to interfere less than the 0.5% solution. Obstetrical anaesthesia may increase the need for forceps assistance. The addition of epinephrine may potentially decrease uterine blood flow and contractility, especially after inadvertent injection into maternal blood vessels.

7.1.2 Breast-feeding

Bupivacaine is excreted in the breast milk, but in such small quantities that there is generally no risk of affecting the infant at therapeutic doses. It is not known whether epinephrine enters breast milk or not, but it is unlikely to affect the breast-fed infant.

7.1.3 Pediatrics

Administration of any presentation of bupivacaine injection in children younger than two years is not recommended. SENSORCAINE or SENSORCAINE with Epinephrine should be used in children aged < 12 years only when potential benefits outweigh the risks. Only limited data are available.

7.1.4 Geriatrics

Elderly patients should be given reduced doses commensurate with their age and physical condition.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Reactions to bupivacaine are characteristic of those associated with other local-acting anaesthetics of the amide type.

Adverse reactions to local anaesthetics are very rare in the absence of overdose or inadvertent intravascular injection. The effects of systemic overdose and unintentional intravascular injections can be serious but should be distinguished from the physiological effects of the nerve block itself (e.g. a decrease in blood pressure and bradycardia during epidural anaesthesia).

Neurological damage, caused directly (e.g. nerve trauma) or indirectly (e.g. epidural abscess) by the needle puncture, is a rare but well recognised consequence of regional, and particularly epidural anaesthesia.

The most commonly encountered acute adverse experiences that demand immediate management are related to the central nervous system and the cardiovascular system. These adverse experiences are generally dose-related and due to high plasma levels, which may result from overdosage (see 5 OVERDOSAGE), rapid absorption from the injection site, diminished tolerance or from inadvertent intravascular injection. In addition to systemic dose-related toxicity, unintentional subarachnoid injection of drug during the intended performance of caudal or lumbar epidural block or nerve blocks near the vertebral column (especially in the head and neck region) may result in underventilation or apnoea ("Total or High Spinal").
Also, hypotension due to loss of sympathetic tone and respiratory paralysis or underventilation due to cephalad extension of the motor level of anaesthesia may occur. This may lead to secondary cardiac arrest if untreated.

Central Nervous System: These are characterized by excitation and/or depression. Restlessness, anxiety, dizziness, tinnitus, blurred vision or tremors may occur, possibly proceeding to convulsions. However, excitement may be transient or absent, with depression being the first manifestation of an adverse reaction. This may quickly be followed by drowsiness merging into unconsciousness and respiratory arrest. Other central nervous system effects may be nausea, vomiting, chills, paraesthesia, numbness of the tongue, hyperacousis, lightheadedness, dysarthria and constriction of the pupils.

Cardiovascular System: High doses or unintentional intravascular injection may lead to high plasma levels and related depression of the myocardium, decreased cardiac output, heart block, hypotension, bradycardia, hypertension, ventricular arrhythmias, including ventricular tachycardia and ventricular fibrillation, and cardiac arrest. Reactions due to systemic absorption may be either slow or rapid in onset. Cardiovascular collapse and cardiac arrest can occur rapidly (see 7 WARNINGS AND PRECAUTIONS, Cardiovascular and 5 OVERDOSAGE).

Allergic: Allergic type reactions are rare (<0.1%) and may occur as a result of sensitivity to local anaesthetics of the amide type. These reactions are characterized by signs such as urticaria, pruritis, erythema, angioneurotic oedema (including laryngeal oedema), tachycardia, sneezing, nausea, vomiting, dizziness, syncope, excessive sweating, elevated temperature, and in the most severe instances, anaphylactic shock.

Neurologic: The incidence of adverse neurologic reactions may be related to the total dose of local anaesthetic administered but is also dependent upon the particular drug used, the route of administration and the physical condition of the patient. Nerve trauma, neuropathy, urinary retention, diplopia and spinal cord dysfunction (e.g., anterior spinal artery syndrome, arachnoiditis, cauda equina syndrome, in rare cases paresis and paraplegia), have been associated with regional anaesthesia. Neurological effects may be related to local anaesthetic techniques, with or without a contribution from the drug.

High or Total Spinal Blockade: In the practice of caudal or lumbar epidural block, occasional unintentional penetration of the subarachnoid space by the catheter may occur, resulting in High or Total Spinal Blockage. Subsequent adverse effects may depend partially on the amount of drug administered subdurally.

Extensive loss of motor and sensory functions, loss of consciousness, and cardiovascular and respiratory depression may happen. The cardiovascular depression is caused by extensive sympathetic blockade which may result in profound hypotension and bradycardia, or even cardiac arrest. Respiratory depression is caused by blockade of the innervation of the respiratory muscles, including the diaphragm.

Hepatobiliary system: Drug induced liver injury (DILI), hepatic failure, jaundice and other signs of hepatic dysfunction (increased alanine aminotransferase (ALT), alkaline phosphates (AlkP) and bilirubin) have been observed following bupivacaine use (see 7 WARNINGS AND PRECAUTIONS).

9 DRUG INTERACTIONS

9.3 Drug-Behavioural Interactions

Driving and Operating Machinery: Besides the direct anaesthetic effect, local anaesthetics may have a very mild effect on mental function and co-ordination even in the absence of overt CNS toxicity and may temporarily impair locomotion and alertness. Patients should be cautioned about driving a vehicle or operating potentially hazardous machinery on the day they receive local anaesthetic treatment.

9.4 Drug-Drug Interactions

See 7 WARNINGS AND PRECAUTIONS concerning solutions containing a vasoconstrictor. Bupivacaine should be used cautiously in persons with known drug allergies or sensitivities.

Local anaesthetics and agents structurally related to amide-type local anaesthetics Bupivacaine should be used with caution in patients receiving other amide-type local anaesthetics such as lidocaine, ropivacaine, mepivacaine and prilocaine since the toxic effects are additive.

Antiarrhythmic Drugs
Bupivacaine should also be used with caution with structurally related agents such as the antiarrhythmics, procainamide, disopyramide, tocainide, mexiletine and flecainide.

Class III Antiarrhythmic drugs
Specific interaction studies with bupivacaine and class III anti-arrhythmic drugs (e.g. amiodarone) have not been performed, but caution is advised. Patients being treated with class III anti-arrhythmic drugs should be under close surveillance and ECG monitoring since cardiac affects may be additive.

Ergot-Containing Drugs
Bupivacaine with epinephrine or other vasopressors or vasoconstrictors should not be used concomitantly with ergot-type oxytocic drugs, because a severe persistent hypertension may occur and cerebrovascular and cardiac accidents are possible.

Monoamine Oxidase (MAO) Inhibitors
Bupivacaine with epinephrine or other vasopressors or vasoconstrictors should be used with extreme caution in patients receiving monoamine oxidase (MAO) inhibitors because severe prolonged hypertension may result. In situations when concurrent therapy is necessary, careful patient monitoring is essential.

Antidepressants (triptyline, imipramine)
Bupivacaine with epinephrine or other vasopressors or vasoconstrictors should be used with extreme caution in patients receiving antidepressants of the triptyline or imipramine types because severe prolonged hypertension may result. In situations when concurrent therapy is necessary, careful patient monitoring is essential

Neuroleptics (phenothiazines)
Neuroleptics such as phenothiazines may oppose the vasoconstrictor effects of epinephrine resulting in hypotensive responses and tachycardia

Sedatives
If sedatives are used to reduce patient apprehension, they should be used in reduced doses, since local anaesthetic agents, like sedatives, are central nervous system depressants which in combination may have an additive effect.

General Anaesthetics- Inhalation agents (halothane, enflurane)
Solutions containing epinephrine should be used with caution in patients undergoing general anaesthesia with inhalation agents such as halothane and enflurane, due to the risk of serious dose-related cardiac arrhythmias. In deciding whether to use these products concurrently in the same patient, the combined action of both agents upon the myocardium, the concentration and volume of vasoconstrictor used, and the time since injection, when applicable, should be taken into account.

Prior use of chloroprocaine, or any other local anaesthetic, may interfere with subsequent use of bupivacaine. Because of this, and because safety of intercurrent use with bupivacaine and other local anaesthetics has not been established, such use is not recommended.

H2-antagonists
The H2-antagonists cimetidine and ranitidine have been shown to reduce the clearance of bupivacaine; ranitidine to a lesser degree than cimetidine. Concomitant administration may increase likelihood of toxicity of bupivacaine.

Non-selective beta-blockers
Non-selective beta-blockers such as propranolol enhance the pressor effects of epinephrine, which may lead to severe hypertension and bradycardia.

9.5 Drug-Food Interactions

Interactions of bupivacaine with food have not been established.

9.6 Drug-Herb Interactions

Interactions of bupivacaine with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions of bupivacaine with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

Bupivacaine is a long-acting, amide-type local anaesthetic with both anaesthetic and analgesic effects. At high doses it produces surgical anaesthesia, while at lower doses it produces sensory block (analgesia) with less pronounced motor block.

10.1 Mechanism of Action

As with other local anaesthetics, bupivacaine causes a reversible blockade of impulse propagation along nerve fibres by preventing the inward movement of sodium ions through the cell membrane of the nerve fibres. The sodium channel of the nerve membrane is considered a receptor for local anaesthetic molecules. The threshold potential of the nerve fibre is mainly unchanged and there is a decrease in rate of rise of the action potential. When the depolarization is not sufficient to reach the threshold potential, the consequence will be conduction block.

10.2 Pharmacodynamics

Onset and Duration of Action

As with other local anaesthetics, the onset and duration of action depends on the injection site, the route of administration and the concentration and volume of anaesthetic (see 4 DOSAGE AND ADMINISTRATION). It has also been noted that there is a period of analgesia that persists after the return of sensation, during which time the need for potent analgesics is reduced. The presence of epinephrine may prolong the duration of action for infiltration and peripheral nerve blocks but has less marked effect on epidural blocks.

SENSORCAINE 0.5% has a long duration of action of 2-5 hours following a single epidural injection and up to 12 hours after peripheral nerve blocks.
The onset of blockade is slower than with lidocaine, especially when anaesthetizing large nerves. When used in low concentrations, i.e., 0.25%, there is less effect on motor nerve fibres and the duration of action is shorter.

Hemodynamics

Bupivacaine, like other local anaesthetics, may also have effects on other excitable membranes e.g. in the brain and myocardium. If excessive amounts of drug reach the systemic circulation rapidly, symptoms and signs of toxicity will appear, emanating mainly from the central nervous and cardiovascular systems.

Central nervous system toxicity (see 5 OVERDOSAGE) usually precedes the cardiovascular effects as central nervous system toxicity occurs at lower plasma concentrations. Direct effects of local anaesthetics on the heart include slow conduction, negative inotropism and eventually cardiac arrest.

Indirect cardiovascular effects (hypotension, bradycardia) may occur after epidural administration depending on the extent of the concomitant sympathetic block.

10.3 Pharmacokinetics

Absorption:

The plasma concentration of local anaesthetics is dependent upon the dose, the route of administration,

the patient's hemodynamic/circulatory condition, and the vascularity of the injection site. The addition of epinephrine to bupivacaine may decrease the peak plasma concentration, whereas the time to peak plasma concentration usually is little affected. The effect varies with the type of block, dose and concentration. In adults, epinephrine decreases peak plasma concentrations by up to 50% in brachial plexus block and by 5-25% in epidural block.

Peak levels of bupivacaine in the blood are reached in 20 to 45 minutes, depending on injection site and type of block. A decline to insignificant levels is achieved during the next three to six hours. The terminal half-life of bupivacaine in adults is 2.7 hours and in neonates it is prolonged up to eight hours. In children between 1 to 7 years the pharmacokinetics are similar to those in adults. Intercostal blocks give the highest peak plasma concentration due to a rapid absorption (maximum plasma concentrations in the order of 1-4 mg/L after a 400 mg dose), while subcutaneous abdominal injections give the lowest plasma concentration. Epidural and major plexus blocks are intermediate. In children, rapid absorption and high plasma concentrations (in the order of 1-1.5 mg/L after a dose of 3 mg/kg) are seen with caudal block.

Bupivacaine shows complete, biphasic absorption from the epidural space with plasma half-lives in the order of seven minutes after initial administration, slowing to six hours over time. The slow absorption is rate-limiting in the elimination of bupivacaine, which explains why the apparent elimination half-life after epidural administration is longer than after intravenous administration.

Distribution:

Bupivacaine has a total plasma clearance of 0.58 L/min a volume of distribution at steady state of 73 L.

Bupivacaine readily crosses the placenta and equilibrium in regard to the unbound concentration is rapidly reached. The degree of plasma protein binding in the foetus is less than in the mother, which results in lower total plasma concentrations in the foetus than in the mother. The free concentration, however, is the same in both mother and foetus.

In adults the protein-binding capacity of bupivacaine is high at 96%. Generally, the lower the plasma concentration of drug, the higher the percentage of drug bound to plasma proteins.

Bupivacaine is mainly bound to alpha-1-acid glycoprotein.

An increase in total plasma concentration has been observed during continuous epidural infusion for postoperative pain relief. This is related to a postoperative increase in alpha-1-acid glycoprotein. The unbound, i.e. pharmacologically active, concentration is similar before and after surgery.

The pK_a of bupivacaine (8.1) is similar to that of lidocaine. However, bupivacaine possesses a greater degree of lipid solubility and is protein bound (95%) to a greater extent than lidocaine (64%).

Metabolism:

Bupivacaine is extensively metabolized in the liver predominantly by aromatic hydroxylation to 4-hydroxy-bupivacaine and N-dealkylation to 2,6-pipecoloxylidine (PPX), both mediated by cytochrome P450 3A4. The metabolites have a pharmacological activity that is less than that of bupivacaine. Bupivacaine and the metabolites are excreted mainly via the kidneys**.**

Elimination:

The terminal half-life of bupivacaine in adults is 2.7 hours, and in neonates it is prolonged up to eight hours. Bupivacaine has an intermediate hepatic extraction ratio of 0.38 after i.v. administration. In children, the pharmacokinetics are similar to those in adults. The elderly may have a prolonged half-life.

The kidney is the main excretory organ for most local anaesthetics and their metabolites. About 1% of bupivacaine is excreted in the urine as unchanged drug in 24 h and approximately 5% as PPX. The plasma concentrations of PPX and 4-hydroxy-bupivacaine during and after continuous administration of bupivacaine are low as compared to the parent drug.

Clearance of bupivacaine is almost entirely due to liver metabolism and more sensitive to changes in intrinsic hepatic enzyme function than to liver perfusion.

11 STORAGE, STABILITY AND DISPOSAL

Store SENSORCAINE (bupivacaine hydrochloride) and SENSORCAINE with Epinephrine at 15-25°C. Do not freeze. Protect SENSORCAINE with Epinephrine from light. Do not use if solution is coloured or contains a precipitate.

12 SPECIAL HANDLING INSTRUCTIONS

Due to the nature of the Polyamp® system, the plastic ampoules must not be autoclaved.

Due to the heat sensitivity of epinephrine, products containing epinephrine must not be autoclaved.

SENSORCAINE/SENSORCAINE with Epinephrine are without preservative and are for single use only. Discard unused portion.

Adequate precautions should be taken to avoid prolonged contact between local anaesthetic solutions containing epinephrine (low pH) and metal surfaces (e.g., needles or metal parts of syringes), since dissolved metal ions, particularly copper ions, may cause severe local irritation (swelling, oedema) at the site of injection and accelerate the degradation of epinephrine.

The solubility of bupivacaine is limited at pH > 6.5. This must be taken into consideration when alkaline solutions, i.e., carbonates, are added since precipitation might occur. In the case of epinephrine-containing solutions, mixing with alkaline solutions may cause rapid degradation of epinephrine.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

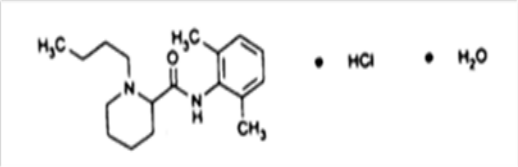
Bupivacaine Hydrochloride

Proper name: bupivacaine hydrochloride

Chemical name: 2-piperidinecarboxamide,1-butyl-N-(2,6- dimethylphenyl), monohydrochloride, monohydrate

Molecular formula and molecular mass: $C_{18}H_{28}N_2O \bullet HCl \bullet H_2O$ and 342.91

Structural formula:



Physicochemical properties: White, odourless, crystalline powder. Freely soluble in water and in alcohol. Slightly soluble in chloroform and in acetone. Melting point approximately 248°F, with decomposition.

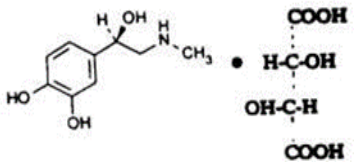
Epinephrine

Proper name: epinephrine bitartrate

Chemical name: 1,2-benzenediol,4-[1-hydroxy-2- (methylamino)ethyl]-,(R)-,[R- (R*,R*)]-2,3-dihydroxybutanedioate(1:1) salt

Molecular formula and molecular mass: $C_9H_{13}NO_3 \bullet C_4H_6O_6$ and 333.3

Structural formula:



Physicochemical properties: White or greyish white or light brownish grey, odourless crystalline powder, which slowly darkens on exposure to light. Freely soluble in water. Slightly soluble in alcohol. Practically insoluble in chloroform and in ether. Solutions are acidic, with pH approximately 3.5.

14 CLINICAL TRIALS

The clinical trial data on which the original indication was authorized is not available

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology:

Acute toxicity (LD_{50}) after single intravenous and subcutaneous administration in mice and rats and after intraperitoneal administration in mice are shown in Table 5. Lethal doses after intravenous injection in rabbits and dogs are shown in Table 6.

Table 5 -Lethal toxicity in mice and rats after single administration of bupivacaine

Animals	No.	Route of Administration	LD_{50} (mg/kg) and Standard Error
Mice (NMRI)	36	i.v.	7.3 ± 1.0
	31	s.c.	53 ± 5
Rats (Sprague-Dawley)	36	i.v.	5.6 ± 0.2
	40	s.c.	48 ± 3
Mice (Charles River)	41	i.p.	58.7 ± 2.0

Table 6 -Lethal toxicity in rabbits and dogs after administration of bupivacaine.

Animals	No.	Route of Administration	LD_{50} (mg/kg) and Standard Error
Rabbits	8	i.v.	6.9 ± 0.7
Dogs	5	i.p.	20.4a ± 2.4

[a]cumulative dose

Seizure threshold for bupivacaine in Rhesus monkeys was found to be 4.4 mg/kg with a mean arterial plasma concentration of 4.5 µg/mL.

Some tissue irritation has been seen in rabbits after intracutaneous administration of bupivacaine (0.2-1%). Muscular atrophy appeared after repeated intramuscular injection into one and the same muscle. However, three weeks after administration, the regeneration of the affected muscle appeared to be almost complete.

Epidural injections of bupivacaine (0.25-1%) to cats did not reveal any morphological changes of the spinal cords. Spinal subarachnoid injections of bupivacaine (0.5%) in the cynomolgus monkey did not demonstrate any treatment-related damage.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

SENSORCAINE®
Bupivacaine hydrochloride Solution

SENSORCAINE® with Epinephrine
Bupivacaine hydrochloride and Epinephrine Solution

Read this carefully before you start taking **SENSORCAINE** and **SENSORCAINE with Epinephrine** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **SENSORCAINE a**nd **SENSORCAINE with Epinephrine**.

What is SENSORCAINE and SENSORCAINE with Epinephrine used for?

SENSORCAINE / SENSORCAINE with Epinephrine are used to numb (anaesthetise) part of the body during surgery and also for pain relief. SENSORCAINE / SENSORCAINE with Epinephrine can be used to:

- numb the area of the body where surgery is to be performed.
- provide pain relief in labour.
- provide pain relief after surgery.
- provide pain relief after an injury.

How does SENSORCAINE and SENSORCAINE with Epinephrine work?

SENSORCAINE / SENSORCAINE with Epinephrine work by temporarily blocking the nerves in the area it is injected so you do not feel pain, heat or cold. This makes the area numb and relieves pain. You may still feel pressure and touch. In many cases the nerves to the muscles in the area will also be blocked. This can cause temporary weakness or paralysis.

What are the ingredients in SENSORCAINE and SENSORCAINE with Epinephrine?

Medicinal ingredients:

SENSORCAINE: bupivacaine hydrochloride.
SENSORCAINE with Epinephrine: bupivacaine hydrochloride, epinephrine bitartrate.

Non-medicinal ingredients:

SENSORCAINE contains sodium chloride, sodium hydroxide and/or hydrochloric acid and water for injection.
SENSORCAINE with Epinephrine contains sodium chloride, sodium hydroxide and/or hydrochloric acid, sodium metabisulphite and water for injection.

SENSORCAINE and SENSORCAINE with Epinephrine comes in the following dosage forms:

SENSORCAINE is available as a solution: 0.25% (2.5 mg/mL) and 0.5% (5 mg/mL).

SENSORCAINE with Epinephrine is available as SENSORCAINE 0.25% (2.5 mg/mL) or 0.5% (5 mg/mL) with epinephrine (as bitartrate) 5 mcg/mL (1:200,000).

Do not use SENSORCAINE and SENSORCAINE with Epinephrine if you are allergic(hypersensitive) to:

- bupivacaine hydrochloride
- epinephrine bitartrate
- any other "-caine" type anaesthetics
- sodium metabisulfite
- any of the non-medicinal ingredients in the product, or component of the container (see above)

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take SENSORCAINE and SENSORCAINE with Epinephrine. Talk about any health conditions or problems you may have, including if you:

- have heart problems
- have high blood pressure
- have problems with the blood flow to your brain
- have Peripheral Vascular Disease or problems with your blood circulation
- have thyroid problems
- have diabetes
- have liver problems
- have kidney problems
- have asthma
- are pregnant
- are breastfeeding or planning to breastfeed

Other warnings you should know about:

Driving and Using Machines: SENSORCAINE / SENSORCAINE with Epinephrine can affect your level of alertness, your reactions and your coordination. You should use caution driving and when operating tools or machinery on the day you receive SENSORCAINE / SENSORCAINE with Epinephrine.

Liver Injury: Serious cases of liver injury including drug-induced liver injury (DILI), liver failure and increased liver enzymes have been reported in people being treated with bupivacaine, the medicinal ingredient in SENSORCAINE / SENSORCAINE with Epinephrine. This is more likely to happen in people being treated with SENSORCAINE / SENSORCAINE with Epinephrine repeatedly or for a long time. These side effects happened in people with and without a history of previous liver problems. For more information and this and other serious side effects, see the **Serious side effects and what to do about them** table, below.

Joint Damage: Because of the potential for irreversible joint damage, SENSORCAINE should not be used to treat pain following joint surgery.

Use in Children:

- SENSORCAINE / SENSORCAINE with Epinephrine is not to be used in children under 2 years of age.
- It is not known if SENSORCAINE / SENSORCAINE with Epinephrine is safe and effective in children 2 - 12 years of age. SEONSORCAINE / SEONSORCAINE with Epinephrine should only be used in this age group if the benefit outweighs the risk.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with SENSORCAINE and SENSORCAINE with Epinephrine:

- other local anaesthetics, such as lidocaine, ropivacaine, mepivacaine, prilocaine, chloroprocaine
- medicines used to treat heartburn, such as cimetidine and ranitidine
- sedatives

Additional medicines that may interact with SENSORCAINE with Epinephrine include:

- medicines used to treat depression such as monoamine oxidase (MAO) inhibitors, triptyline, imipramine
- ergot-type medicines used to treat migraines
- phenothiazines used to treat mental health problems
- medicines used to treat high blood pressure, such as propranolol

How to take SENSORCAINE and SENSORCAINE with Epinephrine:

Usual dose:

Your healthcare professional will decide how much SENSORCAINE / SENSORCAINE with Epinephrine to give you.

Overdose:

If you think you, or a person you are caring for, have been given too much SENSORCAINE or SENSORCAINE with Epinephrine contact a healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

The first signs that too much SENSORCAINE / SENSORCAINE with Epinephrine has been given are: lightheadedness, numbness of the lips and around the mouth, numbness of the tongue, hearing disturbances, ringing in the ears, and visual disturbances. Symptoms that are more serious include speech problems, muscle twitching and tremors. Tell your healthcare professional immediately if you notice any of these symptoms.

In the case of a serious overdose or a misplaced injection, trembling, seizures or unconsciousness may occur

What are possible side effects from using SENSORCAINE and SENSORCAINE with Epinephrine?

These are not all the possible side effects you may have when taking SENSORCAINE / SENSORCAINE with Epinephrine. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

•feeling sick, nausea
•vomiting
•dizziness

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON **Low Blood Pressure:** dizziness, fainting, lightheadedness May occur when you go from lying or sitting to standing up.		**X**	
COMMON Slow heart beat		**X**	
Trouble urinating, unable to pass urine		**X**	
High Blood Pressure: headache, fatigue, vision problems, irregular heart beat		**X**	
RARE **Allergic Reaction:** rash, hives, itching, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing, fast heart rate, sneezing, nausea, vomiting, fainting, sweating			**X**
Double vision		**X**	
Irregular heart beat or heart skips a beat (heart palpitations)			**X**
Nerve Problems: nerve injury, paralysis, numbness or tingling of the extremities, weakness		**X**	
Central Nervous System Problems: restlessness, anxiety, dizziness, ringing in the ears, blurred vision, tremors, seizures or fits			**X**

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Heart Attack or Cardiovascular Collapse: chest pain or tightness, pain spreading to the neck, jaw or back, nausea, indigestion, shortness of breath, cold sweat, fatigue, lightheadedness, fast heart beat, fainting			**X**
Liver Injury (including Drug Induced Liver Injury, liver failure): yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite			**X**

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Your healthcare professional or the hospital will store SENSORCAINE / SENSORCAINE with Epinephrine.

Keep out of reach and sight of children.

If you want more information about SENSORCAINE / SENSORCAINE with Epinephrine:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website (www.aspenpharma.ca), or by calling 1-844-330-1213.

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