

**Important Safety Information on
Importation of Danish-authorized Marcain–Adrenalin, 5 mg/mL and 5
mcg/mL
due to the Current Shortage of Canadian-authorized SENSORCAINE with
Epinephrine, 5 mg/mL and 5 mcg/mL**



2024/08/13

Audience

Healthcare professionals including pharmacists, anesthesiologists, critical care physicians, emergency physicians and those involved with administering anesthesia.

Key messages

- **Due to a critical shortage of SENSORCAINE with Epinephrine (bupivacaine hydrochloride, 5 mg/mL and epinephrine (epinephrine bitartrate), 5 mcg/mL) in Canada and given the medical importance of this local anesthetic, Health Canada has permitted the exceptional, temporary importation and sale of Danish-authorized Marcain-Adrenalin (bupivacaine hydrochloride, 5 mg/mL and adrenaline (adrenaline tartrate), 5 mcg/mL) with Danish-only labels by Aspen Pharmacare Canada Inc.**
- **Healthcare professionals are advised to:**
 - **Be aware that there are important differences in product labelling between the Danish-authorized product and the Canadian-authorized product (see Information for healthcare professionals section and Table 1).**
 - **Refer to the Canadian Product Monograph for SENSORCAINE with Epinephrine (bupivacaine hydrochloride, 5 mg/mL and epinephrine (epinephrine bitartrate), 5 mcg/mL) by Aspen Pharmacare Canada Inc., available in English and French on [Health Canada's Drug Product Database](#), for information on proper use.**

What is the issue?

Given the critical shortage of SENSORCAINE with Epinephrine (bupivacaine hydrochloride, 5 mg/mL and epinephrine (epinephrine bitartrate), 5 mcg/mL), and to maintain continuity of supply in Canada, Health Canada has authorized the exceptional, temporary importation and sale of Danish-authorized Marcain-

Adrenalin (bupivacaine hydrochloride, 5 mg/mL and adrenaline (adrenaline tartrate), 5 mcg/mL) with Danish-only labels by Aspen Pharmacare Canada Inc.

Products affected

Product Brand Name	Dosage Form, Strength, and Packaging Format	Country of Authorization and Identifying Code	Manufacturer	Importer in Canada
Marcaïn – Adrenalin (bupivacaine hydrochloride and adrenaline [adrenaline tartrate])	Solution for injection 5 mg/mL and 5 mcg/mL 20 mL single use vials preservative-free	Denmark 10213	Aspen Pharma Trading Limited, Ireland	Aspen Pharmacare Canada Inc.

Background information

In Canada, SENSORCAINE with Epinephrine (bupivacaine hydrochloride and epinephrine) is indicated for the production of local or regional anesthesia 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.

Information for healthcare professionals

This product should be administered by appropriately trained healthcare professionals, familiar with its actions, characteristics, and hazards.

The Danish-authorized product has the same active ingredients, concentration and dosage form as the Canadian-authorized SENSORCAINE with Epinephrine (bupivacaine hydrochloride, 5 mg/mL and epinephrine (epinephrine bitartrate), 5 mcg/mL). Both the Danish-authorized product and the Canadian-authorized product are packaged in the same single-use vials of 20 mL (see Appendix 1). However, there are differences in labelling between the Danish-authorized product and Canadian-authorized product, including product naming and differences in expression of strength, which may pose a risk for significant patient harm if dosing

or product selection errors occur.

- The product labels and information for the Danish-authorized product use the term “adrenaline tartrate” for one of the active ingredients, whereas “epinephrine bitartrate” is used in the Canadian product labelling.

Epinephrine bitartrate and adrenaline tartrate are identical

substances; the only difference is in the naming convention used.

- Despite having the same concentration, the expression of strength for bupivacaine is listed differently on the labels of the Danish-authorized product. There is no percentage expression of strength (i.e., 0.5%) or total quantity per total volume (i.e., 100 mg/20 mL) on the Danish-authorized labels.
- On the labels of the Danish-authorized product, adrenaline (epinephrine) is listed in mikrog/ml, rather than in mcg/mL and the ratio (i.e., 1: 200, 000) is absent.
- The Danish-authorized product labels do not identify that the product is a **sterile single use vial**.
- The precautionary statement, “Do not use if solution is coloured or contains a precipitate”, which appears on the label of the Canadian-authorized product, is not found on the label of the Danish-authorized product.

The Danish-authorized product does not have a Drug Identification Number (DIN) or a barcode that scans in medication management systems in Canada. A facility-generated sticker is recommended to enable barcode scanning and allow proper identification of the product being dispensed and administered.

Table 1: Labelling differences between Danish-authorized Marcain – Adrenalin and Canadian-authorized SENSORCAINE with Epinephrine

	Drug product for importation	Canadian drug product
Product Brand Name	Marcain – Adrenalin	SENSORCAINE with Epinephrine
Dosage Form	Solution for injection	Solution for Block/Infiltration, Epidural
Expression of Strength	bupivacaine hydrochloride, 5 mg/mL adrenaline (adrenaline tartrate), 5 mikrog/mL	0.5% bupivacaine hydrochloride 100 mg/20mL (5 mg/mL) epinephrine (epinephrine bitartrate) 1:200,000, 100

mcg/20 mL (5 mcg/mL)

Identifying Code	10213	DIN 01976206
Package size	5 x 20 mL vials	10 x 20 mL single use vials
Labelling Language	Danish	English/French

Healthcare professionals are advised that:

- The Danish-authorized product should be used in the same manner as the Canadian-authorized product.
- The Canadian Product Monograph for SENSORCAINE with Epinephrine (bupivacaine hydrochloride, 5 mg/mL and epinephrine (epinephrine bitartrate), 5 mcg/mL), by Aspen Pharmacare Canada Inc., available in English and French on [Health Canada's Drug Product Database](#), should be consulted for information on proper use.
- Additional information on the Danish-authorized product can be found in Aspen's English and French translation of the Summary of Product Characteristics for Marcain – Adrenalin, available at www.aspenpharma.ca.

Action taken by Health Canada

To help mitigate the critical shortage of SENSORCAINE with Epinephrine (bupivacaine hydrochloride and epinephrine) in Canada, Health Canada has permitted the exceptional, temporary importation and sale of Danish-authorized Marcain – Adrenalin (bupivacaine hydrochloride and adrenaline) by Aspen Pharmacare Canada Inc. and added this product to the [List of Drug for Exceptional Importation and Sale](#).

Health Canada has worked with Aspen Pharmacare Canada Inc. to prepare this alert for SENSORCAINE with Epinephrine. Health Canada is communicating this important safety information to healthcare professionals and Canadians via the [Recalls and Safety Alerts Database](#) on the Healthy Canadians Web Site. This communication update will be further distributed through the MedEffect™ e-Notice email notification system.

Report health or safety concerns

Managing marketed health product-related side effects depends on healthcare professionals and consumers reporting them. Any case of serious or unexpected side effects in patients receiving Marcain – Adrenalin should be reported to Aspen Pharmacare Canada Inc. or Health Canada.

Aspen Pharmacare Canada Inc.
Unit 8, 1155 North Service Road W.
Oakville, ON, L6M 3E3

Telephone: 1-844-330-1213
Fax: 1-437-800-4554

To correct your mailing address or fax number, contact Aspen Pharmacare Canada Inc.

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

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on [Adverse Reaction Reporting](http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Regulatory Operations and Enforcement Branch
E-mail: hpce-cpsal@hc-sc.gc.ca
Telephone: 1-800-267-9675

Mike Egli

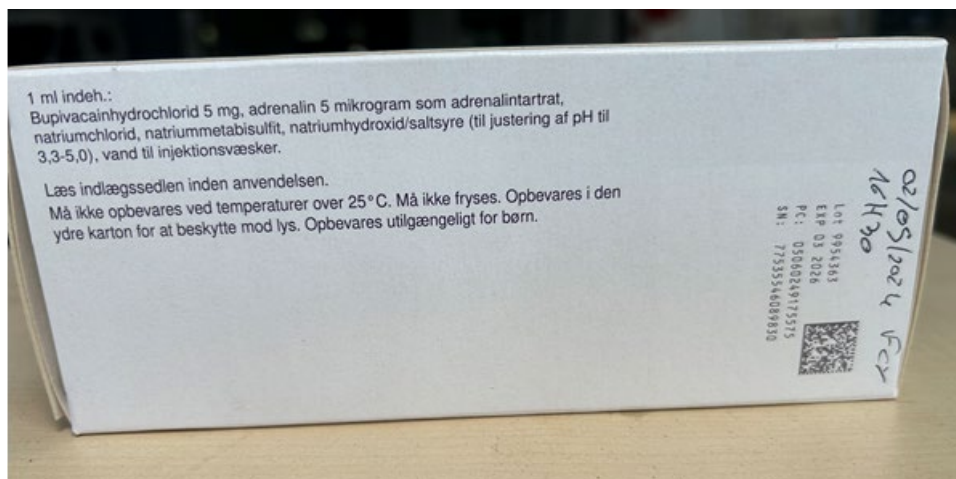
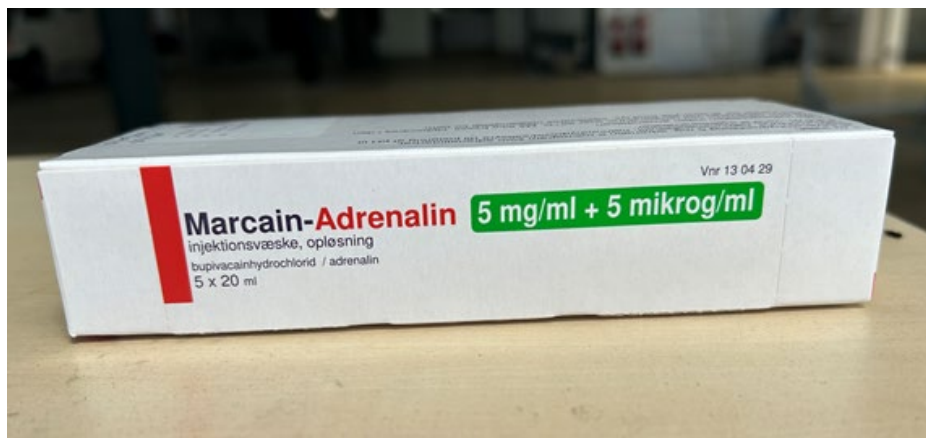
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Reason: This electronic signature confirms that, on
this date, I have reviewed and approved the
contents of this document.
Date: Aug 13, 2024 06:35 EDT

Original signed by
Mike Egli
General Manager
Aspen Pharmacare Canada Inc.

Appendix 1.

A. Image(s) of Marcain-Adrenalin with Danish-only labelling

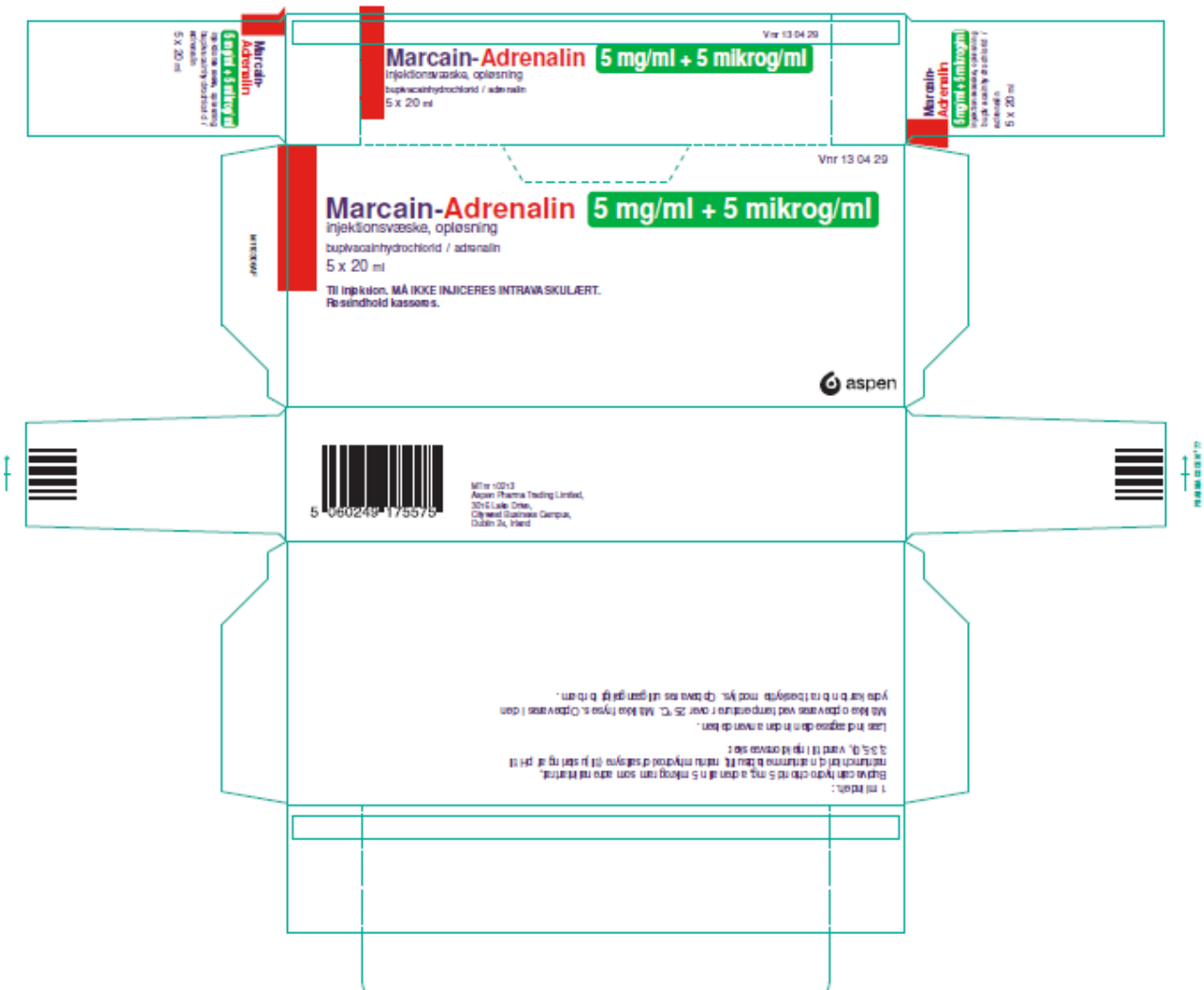




B. Marcain – Adrenalin vial label



C. Marcaïn – Adrenalin carton label



D. Marcaïn – Adrenalin leaflet mock up (EN-translated):

Package leaflet: Information for the user

Marcaine-Adrenaline 2.5 mg/ml + 5 micrograms/ml solution for injection**Marcaine-Adrenaline 5 mg/ml + 5 micrograms/ml solution for injection**

Bupivacaine and adrenaline

Please read this package leaflet carefully before you are given this medicine as it contains important information.

- Keep this package leaflet. You may need to read it again.
- Ask your doctor or healthcare professional if there is anything else you want to know.
- Contact your doctor or healthcare professional if you experience any side effects, including side effects that are not listed here. See Section 4.

See the latest package leaflet at

www.indlaegsseddel.dk.

What is in this package leaflet

1. What Marcaine-Adrenaline is and what it is used for
2. What you need to know before you are given Marcaine-Adrenaline
3. How you will be treated with Marcaine-Adrenaline
4. Side effects
5. How to store Marcaine-Adrenaline
6. Pack sizes and additional information

1. What Marcaine-Adrenaline is and what it is used for

Marcaine-Adrenaline is an anaesthetic (local anaesthetic) that is used to numb parts of the body. Anaesthetic is used to prevent pain from occurring or to provide pain relief.

Marcaine-Adrenaline 2.5 mg/ml

+ 5 micrograms/ml is used:

- As anaesthetic in surgery for adults and children over 12 years of age.
- For acute onset of pain in adults and children over 1 year of age.

Marcaine-Adrenaline 5 mg/ml

+ 5 micrograms/ml is used:

- As anaesthetic in surgery for adults and children over 12 years of age.
- For acute onset of pain in adults and children over 12 years of age.

Marcaine-Adrenaline is used as an injection in one of the following ways:

- by injecting the medicine into the tissue that is to undergo surgery.
- by injecting the medicine into a nerve or a group of nerves that lead to the part of the body that is to undergo surgery, e.g., by injection into the armpit, if the arm or hand is to undergo surgery.
- by injecting the medicine into an area around the bone marrow where the anaesthesia will work.

Marcaine works by temporarily preventing the nerves in the anaesthetised area from feeling pain, heat or cold. However, the feeling of pressure and touch will still be noticed. In this way, the nerves are numbed in the part of the body that is to undergo surgery. In many cases, this means that the nerves to the muscles in the area will also be blocked, which causes temporary weakness or paralysis.

Adrenaline works by decreasing the diameter of the blood vessel and by decreasing blood flow. In this way, Marcaine-Adrenaline remains in the tissue for longer instead of being transported further and the numbness/effect of the anaesthesia can be extended accordingly. In a similar way, adrenaline can reduce surgical bleeding from the injected tissues.

2. What you need to know before you are given Marcaine-Adrenaline

You should not be given Marcaine-Adrenaline:

- if you are allergic to bupivacaine or other amide-type local anaesthetics, adrenaline or any of the other ingredients in Marcaine-Adrenaline, e.g., sodium metabisulfite (listed in section 6).
- in some cases, the doctor will not use Marcaine-Adrenaline at all (e.g., in Bier's blockade, penile block and Oberst block, as well as in epidural blockade in connection with delivery of a baby).
- if you have untreated, reduced blood volume.

The doctor may have prescribed use other than that mentioned in this information. Instructions from the doctor must be followed.

Your doctor or nurse will take extra care when treating you with Marcaine-Adrenaline

Talk to your doctor or healthcare professional before you are given Marcaine-Adrenaline:

- if you have heart rhythm disorders (AV block) or other heart disease in general
- if you have high blood pressure
- if you have advanced liver disease. Problems with your liver enzymes may occur, especially if you receive long-term treatment with this medicine (see section 4).
- if you have impaired kidney function;
- if you have metabolic disease
- if you have diabetes mellitus (diabetes)
- if you are older or if your general condition is poor
- if you are pregnant and are near the end of your pregnancy.

Children and adolescents

The safety and efficacy of Marcaine-Adrenaline 2.5 mg/ml + 5 micrograms/ml in children under 1 year of age are not documented. The safety and efficacy of Marcaine-Adrenaline 5 mg/ml + 5 micrograms/ml in children under 12 years of age are not documented.

Use of other medication at the same time as Marcaine-Adrenaline

Always tell your doctor if you are taking other medicines or have done so recently. This includes medication bought without a prescription.

Tell your doctor:

- if you are taking other pain medication that acts locally
- if you are taking propofol (short-acting anaesthetic)
- if you are taking medication for heart rhythm disorders, e.g., lidocaine or amiodarone
- if you are taking verapamil (medicine to treat heart rhythm disorders and heart cramps)
- if you are taking ACE inhibitors (medicine for high blood pressure)
- if you are taking non-selective beta blockers, e.g., propranolol (medication to treat high blood pressure and other conditions, for prevention of angina pectoris and migraine)
- if you are taking medication for depression, such as tricyclic antidepressants
- if you are taking antipsychotic medications, such as phenothiazines
- if you are taking medication for migraines, such as ergotamine
- if you are taking cimetidine (medicine for too much stomach acid).

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or plan to become pregnant, ask your doctor for advice before being given this medication.

Marcaine-Adrenaline can be used during pregnancy and breastfeeding.

Driving and operating machines

Do not drive or operate machines on the day of surgery as Marcaine-Adrenaline may temporarily affect your motor skills and responsiveness.

Marcaine-Adrenaline contains sodium

This medication contains 3.3 mg sodium (main component of cooking/table salt) per 1 ml. This is equivalent to 0.2% of the recommended maximum daily intake of sodium for an adult.

Marcaine-Adrenaline contains sodium metabisulfite

In rare cases, may cause hypersensitivity reactions and difficulty breathing.

3. How you will be treated with Marcaine-Adrenaline

Your doctor can tell you which dose you will be taking and how often you should take it. If in doubt, ask your doctor or healthcare professional. Only the doctor can change the dose.

The doctor calculates the dose for each patient. Your dose depends on your disease and health condition. Marcaine-Adrenaline will be given to you by an anaesthesiologist.

Use for children and adolescents

Marcaine-Adrenaline is given as a slow injection, either epidural (brain/spinal cord membrane) or other places in the body by an anaesthetist who has experience with anaesthesia for children. Dose depends on age and weight and will be determined by the anaesthesiologist.

If you have been given too much Marcaine-Adrenaline

Serious side effects associated with overdoses are extremely rare. The doctor is trained to handle such situations.

The first signs of overdose with bupivacaine in Marcaine-Adrenaline will be confusion, numbness of the lips and around the mouth, numbness of the tongue and visual and hearing disturbances. Tell your doctor immediately if you notice any of these signs.

Speech disturbances, muscle contractions, or muscle cramps are more serious signs.

In the event of severe overdose or incorrect injection, tremors, convulsions or unconsciousness may occur.

Signs of adrenaline overdose will be cardiovascular symptoms such as a sensation of warmth, sweating, palpitations, migraine-like headache, blood pressure increase, angina pectoris, rapid palpitations and cardiac arrest. Tell your doctor immediately if you notice any of these signs.

The risk of serious side effects decreases rapidly when Marcaine-Adrenaline treatment is stopped as soon as possible when early signs of overdose occur.

Ask your doctor or healthcare professional if there is anything else you are in doubt about.

Contact your doctor, emergency department or pharmacist if you think you have taken more Marcaine-Adrenaline than your doctor has prescribed and you feel unwell.

4. Side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects that you or your relatives must respond to immediately:

Uncommon (may occur in between 1 and 10 out of 1,000 people treated):

- Symptoms of central nervous system poisoning such as convulsions, pins and needles or tingling sensation or numbness around the mouth, numbness of the tongue, impaired hearing, visual disturbances, loss of consciousness, tremor, confusion, ringing in the ears (tinnitus), speech disturbances in connection with pronunciation of words.

Rare side effects (may occur in between 1 and 10 out of 10,000 people treated):

- Cardiac arrest.
- Irregular pulse. Can be or may become serious. Contact your doctor.
- Pain and sensory disturbances due to nerve inflammation.
- Nerve damage. Symptoms of nerve damage can be: pain, numbness, itching and a tingling, crawling or pins and needles sensation in the hands and feet.
- Inflammation of the spinal cord (arachnoiditis). Symptoms of inflammation of the spinal cord may include: drowsiness, pain in joints, sensory disturbances, fever, rapid breathing.
- Paralysis or weakness (paresis).
- Paralysis on both sides, most often in the lower half of the body or in both legs (paraplegia).
- Impaired breathing. Lips and nails turning a blue colour. Call 112 (in UK, 999).
- Sudden skin rash and fainting (within minutes to hours) due to hypersensitivity (anaphylactic shock), may be life-threatening, call 112 (In UK, 999).

Unknown (incidence cannot be estimated from available data)

- Liver injury due to medication

Other side effects

Very common side effects (may occur in more than 1 in 10 people treated):

- Dizziness, possible fainting due to low blood pressure.
- Nausea.

Common side effects (may occur in between 1 and 10 out of 100 people treated):

- Pins and needles, tingling sensations or numbness of the skin.
- Dizziness.
- Vomiting.
- Difficulty urinating.
- High blood pressure. Contact your doctor. High blood pressure should be treated. Very high blood pressure is serious.
- Slow pulse. May become serious. If you experience a very slow and irregular pulse or feel unwell or faint, contact your doctor. Call 112 (in UK, 999).

Rare side effects (may occur in between 1 and 10 out of 10,000 people treated):

- Double vision.
- Allergic reactions.

Unknown (incidence cannot be estimated from available data)

- Liver problems that may appear in your blood tests

Side effects in children and adolescents:

Side effects in children are similar to those seen in adults.

Reporting of side effects

If you experience any side effects, you should talk to your doctor, nurse or pharmacist. This also applies to possible side effects that are not listed in this package leaflet. You can also report side effects directly to the Danish Medicines Agency, Axel Heides Gade 1 DK-2300 Copenhagen S. Website: www.meldenbivirkning.dk

By reporting side effects, you can help provide more information about the safety of this medicine.

5. How to store Marcaine-Adrenaline

Do not store above 25°C. Do not freeze. Store in the outer box in order to protect from light.

Keep the medicine out of reach of children.

Do not use the medication after the expiry date, which is stated on the package. The expiry date refers to the last day of that month.

Ask your pharmacist how to dispose of any unused medicine. Do not throw any medicines away via wastewater, down the toilet or in household rubbish.

6. Pack sizes and additional information

Marcaine-Adrenaline solution for injection contains:

- Active substances: Bupivacaine hydrochloride and adrenaline tartrate
- Other ingredients: Sodium hydroxide and/or hydrochloric acid for adjustment of pH (acidity), sodium chloride, sodium metabisulfite and water for injections.

What Marcaine-Adrenaline looks like and contents of the pack

Marcaine-Adrenaline injection fluid contains a solution: Marcaine-Adrenaline is available in 2 strengths: 2.5 mg/ml + 5 micrograms/ml and 5 mg/ml + 5 micrograms/ml. Marcaine-Adrenaline injection is available in vials of 20 ml.

Marketing Authorisation Holder and Manufacturer

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Manufacturer
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