PACKAGE INSERT

SCHEDULING STATUS: S4

PROPRIETARY NAME AND DOSAGE FORM:

Pharma-Q Bupivacaine Spinal with Dextrose Injection (20 mg/4 ml) spinal injection

COMPOSITION:

Each 4 ml in 5 ml ampoule contains:

- A hyperbaric solution containing bupivacaine hydrochloride monohydrate equivalent to bupivacaine hydrochloride anhydrous 20 mg.
- Dextrose anhydrous 290,8 mg (as dextrose monohydrate 320 mg).

Therefore, each 1 ml contains:

- A hyperbaric solution containing bupivacaine hydrochloride monohydrate equivalent to bupivacaine hydrochloride anhydrous 5 mg.
- Dextrose anhydrous 72,7 mg as dextrose monohydrate 80 mg.

Excipients: sodium hydroxide and water for injections.

PHARMACOLOGICAL CLASSIFICATION:

A 4 Local anaesthetics

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Bupivacaine hydrochloride is a local anaesthetic of the amide type. It is a potent agent capable of producing prolonged anaesthesia due to its amide structure. Bupivacaine

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hydrochloride blocks conduction of nerve impulses by decreasing or preventing the large transient increase in the permeability of excitable membranes to Na^+ that is produced by a light depolarization of the neuronal membrane. It stabilizes the neuronal membrane, preventing initiation and transmission of nerve impulses, thereby acting as a local anaesthetic.

Pharmacokinetic properties:

Absorption:

The onset of action of bupivacaine hydrochloride is rapid and anaesthesia may last for several hours. The duration of action (up to 8 hours) is significantly longer than any other commonly used local anaesthetic. When used as a 5 % injection combined with dextrose, it has an onset of action of 10 to 15 minutes. The duration of analgesia in the T_{10} to T_{12} (thoracic) segments is 2 - 3 hours. This concentration of 5 % bupivacaine hydrochloride with dextrose produces a moderate muscle relaxation of the lower extremities lasting 2 to 2,5 hours. The motor blockade of the abdominal relaxation of the lower extremities lasting 2 to 2,5 hours. The motor blockade of the abdominal muscles lasts 45 to 60 minutes. The duration of motor blockade is shorter than the duration of sensory blockade.

Distribution:

Bupivacaine hydrochloride is about 95 % bound to plasma protein and has a half-life of 2,7 to 3,5 hours in adults.

Metabolism:

Bupivacaine hydrochloride is metabolised in the liver.

Elimination:

Bupivacaine hydrochloride is excreted in the urine principally as metabolites with only 5 % to 6 % as unchanged medicine. Bupivacaine hydrochloride also diffuses into the cerebrospinal fluid however, the concentration in this fluid decreases rapidly after injection as the medicine is

bound to tissue absorbed into the vascular system.

INDICATIONS:

Pharma-Q Bupivacaine Spinal with Dextrose Injection is indicated for:

Induction of spinal anesthesia for surgical procedures such as:

- urological and lower limb surgery (lasting 2 - 3 hours)
- abdominal surgery (lasting 45 - 60 minutes).

CONTRAINDICATIONS:

Pharma-Q Bupivacaine Spinal with Dextrose Injection is contraindicated for use in:

- patients with a known hypersensitivity to bupivacaine hydrochloride or to any other local anaesthetic agents of the amide-type
- patients with low plasma cholinesterase concentrations or those receiving anti-cholinesterases
- patients who are under twelve years of age (see **DOSAGE AND DIRECTIONS FOR USE**)
- patients who require intravenous regional anaesthesia
- patients who require paracervical block in obstetrics (see **PREGNANCY AND LACTATION**).
- patients with cerebrospinal diseases or altered coagulant status (Techniques such as epidural anaesthesia should not be employed in these patients)
- patients who are pregnant (other than in labour) or lactating as the safety in pregnancy and lactation has not been established. Bupivacaine hydrochloride may be excreted into breast milk in small quantities (see **PREGNANCY AND LACTATION**).

WARNINGS and SPECIAL PRECAUTIONS:

ALWAYS HAVE RESUSCITATION EQUIPMENT AND MEDICATION AT HAND WHEN ANY LOCAL ANAESTHETIC IS USED (see DOSAGE and DIRECTIONS FOR USE)

Pharma-Q Bupivacaine Spinal with Dextrose Injection:

- appears to be more cardiotoxic than other local anaesthetics
- fatalities have occurred since toxicity is difficult to treat
- the central nervous system and cardiac toxicity can be enhanced by hypoxia and acidosis.

Special precautions with local anaesthetics:

- hypotension often accompanies spinal and epidural anaesthesia
- inappropriate positioning of the patient may be a contributory factor for women in labour
- foetal intoxication may occur following the use of local anaesthetics in labour
- local anaesthetics should be given with caution to the elderly, debilitated patients (see **DOSAGE AND DIRECTIONS FOR USE**) as well to patients with epilepsy, impaired cardiac conduction or impaired and/or hepatic damage
- patients with myasthenia gravis may be particularly susceptible to the effects of local anaesthetics.

Also take special precautions with spinal anaesthetics:

- spinal anaesthetics should be used with caution in patients with impaired cardiovascular function such as severe disturbances of cardiac rhythm, shock, heart block or congestive heart failure
- there should be careful and constant monitoring of cardiovascular and respiratory (adequacy of ventilation) vital signs and the patient's state of consciousness after local anaesthetic

injection

- in addition, dose-related convulsions and cardiovascular collapse may result from diminished tolerance and rapid absorption from the injection site
- Neurologic effects following spinal anaesthesia may include:
    - impaired perineal sensation and sexual function
    - persistent anaesthesia, paraesthesia, weakness and paralysis of the lower extremities
    - loss of sphincter control (from which there may be slow, incomplete or no recovery) and urinary retention
    - faecal and urinary incontinence
    - hypotension, high or total spinal block, headache, backache, septic meningitis, meningismus and arachnoiditis
    - slowing of labour and increased incidence of forceps delivery. Shivering, cranial nerve palsies due to traction on nerves(from loss of cerebrospinal fluid)
    - spinal headache may occur as a sequel to sub-arachnoid injection.

Effects on the ability to drive and use machines:

Patients should be instructed that they should avoid potentially hazardous tasks such as driving and operating machinery until they know how **Pharma-Q Bupivacaine Spinal with Dextrose Injection** affects them.

INTERACTIONS:

None known.

PREGNANCY AND LACTATION:

Pharma-Q Bupivacaine Spinal with Dextrose Injection:

- is contra-indicated for use in pregnancy and lactation (see **CONTRAINDICATIONS**)
- safety in pregnancy and lactation (other than in labour) has not been established
- bupivacaine hydrochloride may be excreted into breast milk in small quantities (see **CONTRAINDICATIONS**)
- the use of local anaesthetics during pregnancy in the presence of foetal hypoxia or acidosis may be dangerous
- foetal bradycardia frequently follows paracervical block with some amide-type local anaesthetics and may be associated with foetal acidosis (see **CONTRAINDICATIONS**)
- added risk appears to be present in prematurity, toxaemia of pregnancy and foetal distress.

DOSAGE AND DIRECTIONS FOR USE:

Pharma-Q Bupivacaine Spinal with Dextrose Injection:

- hyperbaric solutions of bupivacaine may be used for spinal anaesthesia
- preparations containing 0,5 % are given in doses of 10 to 20 mg (2 to 4 ml)
- the spread of aneasthesia is dependent upon several factors, the most important being the volume of solution injected and the age and positioning of the patient
- the difference in spread of aneasthesia between a 10 mg and 20 mg dose is approximately two segments
- the larger dose gives a half to 1 hour longer duration of anaesthesia in the lumbar segments and a longer lasting motor blockade
- when injected into the sub-arachnoid space via the **L_3/L_4** (lumbar) interspace while the
- if the patient is in the supine horizontal position, the blockade spreads to between the **T_4**

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and T_7 segments

- before administration of the medicine, make sure that resuscitative equipment, such as equipment to maintain a free airway, oxygenation and circulation is immediately available (see **WARNINGS and SPECIAL PRECAUTIONS**)
- doses exceeding 20 mg should not be used as the safety has not been established
- this injection is not recommended for children younger than 12 years of age (see **CONTRAINDICATIONS**)
- doses should be reduced and given with caution to the elderly or debilitated patients (see **WARNINGS and SPECIAL PRECAUTIONS**)
- any unused portion of solution must be discarded accordingly
- solutions which are discoloured or which contain particulate matter should not be administered to the patient.

Different dosages of Pharma-Q Bupivacaine Spinal with Dextrose Injection:

- **Anesthesia of the lower extremities and perineal procedures:**

  7,5 mg (1,5 ml of 0,5 % solution).

- **Lower abdominal anaesthesia**

  12 mg (2,4 ml of a 0,5 % solution).

- **Spinal anesthesia in obstetrics:**
  - **For vaginal delivery:** 6 mg (1,2 ml of 0,5 % solution).
  - **For Caesarean section:** 7,5 to 10,5 mg (1,5 to 2,1 ml of a 0,5 % solution)
  - aspiration for blood should be performed before injection and injection should be made slowly.

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SIDE EFFECTS:

Pharma-Q Bupivacaine Spinal with Dextrose Injection may have side effects**:**

- side effects apparent after local anaesthesia may be due to the anaesthetic or to errors in technique or may be the result of blockade of the sympathetic nervous system
- local anaesthetics may have systemic adverse effects as a result of the raised plasma concentrations, which ensue when the rate of absorption into the circulation exceeds the rate of breakdown
- the systemic toxicity of local anaesthetics mainly involves the central nervous system and the cardiovascular system

The following side effects may occur and the frequencies are unknown:

Immune system disorders:

Frequency unknown:

Hypersensitivity reactions which are characterized by cutaneous lesions (e.g. urticaria), oedema and other manifestations of allergy.

Nervous system disorders:

Frequency unknown:

Excitation or depression. Excitation of the central nervous system may be manifested by restlessness, excitement, nervousness, dizziness, tinnitus, blurred vision, nausea and vomiting, muscle twitching, tremors, and convulsions.

Numbness of the tongue and perioral region may appear as an early sign of systemic toxicity. Excitation may be transient and followed by depression of the nervous system with drowsiness, respiratory failure and coma.

Cardio-vascular disorders:

Frequency unknown:

The most prominent adverse effects associated with spinal or epidural anesthesia involves the cardiovascular system. Sympathetic block results in venodilation, reduced venous return, decreased cardiac output (myocardial depression) and peripheral vasodilation resulting in hypotension, bradycardia, arrhythmias and cardiac arrest.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See **SIDE EFFECTS** and **WARNINGS and SPECIAL PRECAUTIONS**.

Pharma-Q Bupivacaine Spinal with Dextrose Injection:

- over dosage should be treated symptomatically and supportive measures should be taken
- when systemic reactions to local anaesthetics occur, steps should be taken to maintain the circulation, respiration and to control convulsions
- therefore, resuscitation equipment and medication should always be at hand for emergencies (see **Boxed warning** in the **WARNINGS and SPECIAL PRECAUTIONS** section)
- treatment of extensive spinal blockade consists of assuring and maintaining the patient's airway and supporting ventilation using oxygen, if necessary, by assisted or controlled ventilation
- in the case of inadvertent intravascular injection resulting in convulsions, this should be treated rapidly by intravenous injection, e.g. thiopentone mg 100 mg-200 or diazepam 5 mg-10 mg
- it should be remembered that anti-convulsant treatment may also depress respiration and the circulation a short acting neuromuscular blocking agent, together with endotracheal intubation and artificial respiration, may be used when convulsions persist
- the circulation should be maintained with the infusion of plasma or intravenous fluids

- vasopressor agents, where appropriate, (preferably one with inotropic activity, e.g. ephedrine15 mg-30 mg, given intravenously) may be used in the treatment of marked hypotension or circulatory depression although their use is accompanied by a risk of central nervous system circulatory excitation circulatory depression although their use is accompanied by a risk of central nervous system excitation
- vasopressor should not be given to patients receiving oxytocic medicines.

IDENTIFICATION:

A clear colourless to light yellow solution in 5 ml clear, colourless, type I ampoules containing 4 ml injection.

PRESENTATION:

A hyperbaric 0,5 % solution of bupivacaine hydrochloride. Packs of 10 x 4 ml in 3 ml clear, colourless, type I glass ampoules.

STORAGE INSTRUCTIONS:

Store at or below 25 °C.

Keep out of reach of children.

Protect from light.

REGISTRATION NUMBER[~~S~~]:

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NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

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