



SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Hyperbaric Bupivacaine Hydrochloride Injection 0.5% W/V.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains bupivacaine hydrochloride 5.28mg equivalent to anhydrous bupivacaine hydrochloride 5mg.

3. PHARMACEUTICAL FORM

Solution for Injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Route of administration: for injection into the spinal subarachnoid space.

The following recommended doses should be regarded as a guide for use in the average adult:

Spinal anaesthesia for surgery:

Adults only: 2 - 4ml (10 - 20mg bupivacaine hydrochloride anhydrous).

Pregnant women: 2 - 2.5 ml (10 - 12.5mg bupivacaine hydrochloride anhydrous).

The spread of anaesthesia obtained with hyperbaric bupivacaine solution 0.5% w/v depends on several factors, including the volume administered and the position of the patient during and after the injection. When injected at the L3 - L4 intervertebral space with the patient in the sitting position, a dose of 3ml spreads to the T7 - T10 spinal segments. If the patient receives the injection in the horizontal position and is then turned supine, the blockade spreads to the T4 - T7 spinal segments. It should be noted that the level of spinal anaesthesia achieved with any local anaesthetic can be unpredictable in a given patient. The effects of injecting volumes in excess of 4ml have not been studied and such volumes cannot, therefore, be recommended.

4.3 Contraindications

Known hypersensitivity to local anaesthetics of the amide type.

Injection into inflamed or infected areas.

Spinal anaesthesia, regardless of the local anaesthetic used, has its

Own contra-indications which include:

- Active disease of the central nervous system such as meningitis, poliomyelitis, intracranial haemorrhage, sub-acute combined degeneration of the cord due to pernicious anaemia and cerebral and spinal tumours.
- Tuberculosis of the spine.
- Pyogenic infection of the skin at or adjacent to the site of lumbar puncture.
- Cardiogenic or hypovolaemic shock.
- Coagulation disorders or ongoing anticoagulation therapy.

4.4 Special warnings and precautions for use

Spinal anaesthesia should only be performed by clinicians with the necessary expertise. Resuscitative drugs and equipment should be immediately available and the anaesthetist should remain in constant attendance. Spinal anaesthesia with any local anaesthetic agent can cause hypotension and bradycardia which should be anticipated and appropriate precautions taken. These may include pre-loading the circulation with crystalloid or colloid solution. If hypotension develops, it should be treated with a vasopressor such as ephedrine 10 - 15mg intravenously. Severe hypotension may result from hypovolaemia due to haemorrhage or dehydration, or aorto-caval occlusion in patients with massive ascites, large abdominal tumours or late pregnancy. Marked hypotension should be avoided in patients with cardiac decompensation.

Patients with hypovolaemia due to any cause can develop sudden and severe hypotension during spinal anaesthesia. Spinal anaesthesia can cause intercostal paralysis and patients with pleural effusion may suffer respiratory embarrassment. Septicaemia can increase the risk of intraspinal abscess formation in the post-operative period.

4.5 Interaction with other medicinal products and other forms of interaction

Bupivacaine should be used with care in patients receiving anti-arrhythmic drugs with local anaesthetic activity, as their toxic effects may be additive.

4.6 Pregnancy and lactation

There is no evidence of untoward effects in human pregnancy. In large doses there is evidence of decreased pup survival in rats and an embryological effect in rabbits if bupivacaine is administered in pregnancy. Bupivacaine should not, therefore, be given in early pregnancy unless the benefits are considered to outweigh the risks. Bupivacaine enters the mother's milk but in such small quantities that there is generally no risk of affecting the child at therapeutic dose levels.

4.7 Effects on ability to drive and use machines

Following spinal anaesthesia, sufficient time should be allowed for the return of full functions before driving or using machines.

4.8 Undesirable effects

The safety of bupivacaine 5mg/ml with dextrose 80mg/ml is comparable to that of other local anaesthetics used for spinal anaesthesia.

In rare cases, bupivacaine has been associated with allergic reactions and anaphylactic shock.

Spinal anaesthesia itself can cause adverse reactions regardless of the local anaesthetic used. These include hypotension and bradycardia due to sympathetic blockade and/or vasovagal fainting.

In severe cases cardiac arrest can occur.

High spinal anaesthesia may result in paralysis of all respiratory muscles.

A post-lumbar puncture headache can occur postoperatively.

Neurological damage is a rare but well recognised consequence of regional and particularly spinal anaesthesia. It may be due to several causes, e.g. Direct injury to the spinal cord or spinal nerves, anterior spinal artery syndrome, injection of an irritant substance, or injection of a non-sterile solution. These may result in localised areas of paraesthesia or anaesthesia, motor weakness, loss of sphincter control and paraplegia. Occasionally these are permanent.

Neurological complications of this type have been reported following the use of all local anaesthetics used for spinal anaesthesia.

Systemic toxicity is rarely associated with spinal anaesthesia but might occur after accidental intravascular injection. The systemic toxicity of bupivacaine mainly involves the central nervous system and the cardiovascular system. CNS reactions are characterised by numbness of the tongue, light-headedness, dizziness and tremors, followed by convulsions and cardiovascular disorders. CVS reactions are related to depression of the conduction system of the heart and myocardium and include hypotension, bradycardia and ventricular arrhythmias.

Hepatic dysfunction, with reversible increases of sgot, sgpt, alkaline phosphatase & bilirubin, has been observed following repeated injections or infusions of bupivacaine. If signs of hepatic dysfunction are observed during treatment with bupivacaine, the drug should be discontinued.

4.9 Overdose

High or total spinal blockade causing respiratory paralysis should be managed by ensuring and maintaining a patent airway and administering oxygen by assisted or controlled ventilation.

Hypotension should be treated by the use of vasopressor agents, e.g. Ephedrine 10 - 15mg intravenously and repeated until the desired level of arterial pressure is reached. Intravenous fluids, both electrolytes and colloids, given rapidly can also reverse hypotension.

In the event of systemic toxicity. No treatment is required if the symptoms are mild. If convulsions occur, it is important to ensure adequate oxygenation and to arrest the convulsions if they last for more than 15 -30 seconds. Oxygen should be administered by face mask and respiration should be assisted or controlled if necessary. Thiopentone 100 - 150 mg or diazepam 5 - 10 mg may be administered intravenously to control convulsions. Alternatively, succinylcholine 50 - 100mg may be administered intravenously, provided that the clinician has the necessary expertise to perform endotracheal intubation and to manage a fully paralysed patient.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Bupivacaine is a long-acting local anaesthetic of the amide type. As with other local anaesthetic agents, bupivacaine acts by preventing the generation and conduction of nerve impulses.

Hyperbaric bupivacaine solution 0.5% w/v produces a moderate muscular relaxation of the lower extremities lasting 2 - 2.5 hours. The motor blockade of abdominal muscles makes the solution suitable for performance of abdominal surgery lasting 45 - 60 minutes. The duration of motor

blockade does not exceed the duration of analgesia. Cardiovascular effects of are similar or less than those seen with other spinal agents and the solution has been shown to be well tolerated by all tissues with which it comes in contact.

5.2 Pharmacokinetic properties

Like other local anaesthetics, the rate of systemic absorption of bupivacaine is dependent upon the total dose and concentration of drug administered, the route of administration and vascularity of the tissue locally. Hyperbaric bupivacaine solution 0.5% w/v has a rapid onset of action and long duration. In the T10 - T12 segments, the duration of analgesia 152- 3 hours.

Following absorption, bupivacaine is distributed to some extent to all body tissues, with higher concentrations found in highly perfused organs such as the liver, lungs, heart and brain. The drug is about 95% bound to plasma proteins. Only the free, unbound drug is available for placental transfer and foetal concentrations of bupivacaine are lower than maternal concentrations.

Bupivacaine is metabolised in the liver and is excreted in the urine principally as metabolites with only 5 to 6% as unchanged drug.

5.3 Preclinical safety data

No further relevant information other than that which is included in other parts of the summary of product characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dextrose monohydrate
Sodium hydroxide
Water for injections

6.2 Incompatibilities

Hyperbaric bupivacaine hydrochloride injection should not be mixed with other drugs. The solution must not be stored in contact with metals e.g. needles or metal parts of syringes as dissolved metals ions cause swelling at the site of injection.

6.3 Shelf life

3 Years.

6.4 Special precautions for storage

Do not store above 25°C.
Keep the container in the outer carton.

6.5 Nature and contents of container

Translucent plastic ampoules made from polypropylene Ph.Eur packed in cardboard cartons to contain 5, 10 or 20 ampoules. Translucent plastic ampoules made from polypropylene Ph.Eur packed in individual thermoformed sterile polypropylene lidded trays, which are then packed in cardboard cartons to contain 5 or 10 ampoules.

6.6 Instructions for use/handling

Use as directed by the physician.
Keep out of reach of children.
If only part used, discard the remaining solution.

7. MARKETING AUTHORISATION HOLDER

Antigen International Ltd.,
Roscrea,
Co. Tipperary,
Ireland.

8. MARKETING AUTHORISATION NUMBER

PL 02848/0201.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29TH SEPTEMBER, 1999.

10. DATE OF REVISION OF TEXT

MAY, 2002.