**Package leaflet: Information for the user**

**Bupivacaine 0.5% w/v with glucose solution for injection**
bupivacaine hydrochloride

**Read all of this leaflet carefully before this medicine is given to you because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

**What is in this leaflet**:


## 1. What Bupivacaine with glucose solution for injection is and what it is used for

Bupivacaine contains a medicine called bupivacaine hydrochloride. It belongs to a group of medicines called local anaesthetics.

Bupivacaine is used to numb (anaesthetise) parts of the body during surgery in adults and children of all ages. It stops pain happening during surgery (operations).

## 2. What you need to know before Bupivacaine with glucose solution for injection is given to you

**You must not be given Bupivacaine injection:**
- If you are allergic to bupivacaine hydrochloride or any of the other ingredients of this medicine (listed in Section 6).
- If you are allergic to any other local anaesthetics of the same class (such as lidocaine or ropivacaine).
- If you have a skin infection near to where the injection will be given.
- If you have blood poisoning (septicaemia).
- If you have something called cardiogenic shock (a serious condition where the heart is unable to supply enough blood to the body).
- If you have something called hypovolaemic shock (very low blood pressure leading to collapse).
- If you have problems with clotting of your blood.
- If you have diseases of the brain or spine such as meningitis, polio or spondylitis.
- If you have a severe headache caused by bleeding inside the head (intracranial haemorrhage).
- If you have problems with your spinal cord due to anaemia.
- If you have had a recent trauma, tuberculosis or tumours of the spine.

You must not be given this medicine if any of the above apply to you. If you are not sure, talk to your doctor or nurse before you are given this medicine.

**Warnings and precautions**
Talk to your doctor or nurse before having Bupivacaine injection:
- If you have heart, liver or kidney problems. This is because your doctor may need to adjust the dose of Bupivacaine injection.
- If you have been told that you have decreased volumes of blood (hypovolaemia).
- If you have fluid in your lungs.

If you are not sure if any of the above apply to you, talk to your doctor or nurse before you are given this medicine.

**Other medicines and Bupivacaine with glucose solution for injection**
Tell your doctor if you are taking, have recently taken or might take any other medicines. This includes medicines that you buy without a prescription and herbal medicines. This is because Bupivacaine injection can affect the way some medicines work and some medicines can have an effect on Bupivacaine injection.

In particular, tell your doctor if you are taking any of the following medicines:
- Other local anaesthetics.
- Medicines used to treat an uneven heart beat (arrhythmia), such as amiodarone.

Your doctor needs to know about these medicines to be able to work out the correct dose of Bupivacaine injection for you.

**Pregnancy, breast-feeding and fertility**
If you are pregnant or breast-feeding, think that you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

**Driving and using machines**
Bupivacaine injection may make you feel sleepy and affect the speed of your reactions. After you have been given Bupivacaine injection, you should not drive or use tools or machines until the next day.

**Bupivacaine with glucose solution for injection contains sodium**
This medicinal product contains less than 1 mmol sodium (23 mg) per ampoule. This is considered essentially sodium free.

## 3. How Bupivacaine with glucose solution for injection is given to you

Bupivacaine injection will be given to you by a doctor, who will decide the correct dose. It will be given to you as an injection into the lower part of your spine.

**Use in children and adolescents**
Bupivacaine injection is injected slowly into the spinal channel (part of the spine) by a doctor experienced in paediatric anaesthetic techniques. Dosage depends on the age and weight of the patient and will be determined by the doctor.

When Bupivacaine injection is injected, it stops the nerves from being able to pass pain messages to the brain.

**If you have been given too much Bupivacaine with glucose solution for injection**
Serious side effects from getting too much Bupivacaine injection need special treatment and the doctor treating you is trained to deal with these situations. The first signs of being given too much Bupivacaine injection are usually as follows:
- Feeling dizzy or light-headed.
- Numbness of the lips and around the mouth.
- Numbness of the tongue.
- Hearing problems.
- Problems with your sight (vision).

To reduce the risk of serious side effects, your doctor will stop giving you Bupivacaine injection as soon as these signs appear. This means that if any of these happen to you, or you think you have received too much Bupivacaine injection, **tell your doctor immediately**.

More serious side effects from being given too much Bupivacaine injection include tremors, fits (seizures) and heart problems.

## 4. Possible side effects

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

**Severe allergic reactions** (rare, may affect up to 1 in 1,000 people)
If you have a severe allergic reaction, **tell your doctor immediately.** The signs may include sudden onset of:
- Swelling of your face, lips, tongue or throat. This may make it difficult to swallow.
- Severe or sudden swelling of your hands, feet and ankles.
- Difficulty breathing.
- Severe itching of the skin (with raised lumps).
- Very low blood pressure which can make you feel faint or collapse.

**Other possible side effects:**

**Very common (may affect more than 1 in 10 people)**
- Low blood pressure. This might make you feel dizzy or light-headed.
- Feeling sick (nausea).
- Slow heart beat.

**Common (may affect up to 1 in 10 people)**
- Headache.
- Being sick (vomiting).
- Difficulty in passing urine or being incontinent.

**Uncommon (may affect up to 1 in 100 people)**
- Itching, numbness, burning or tingling of the skin.
- Back pain.
- Muscle weakness for a short time.

**Rare (may affect up to 1 in 1,000 people)**
- Heart attack.
- Difficulty breathing.
- Weakness or loss of feeling or loss of movement in your lower body.
- Long-lasting pain in your back or legs.
- Reduced or strange sensation or feeling in the skin.

Some symptoms can happen if the injection was given in the wrong way by mistake, or if you have been given it with other local anaesthetics. These include fits (seizures), feeling dizzy or light-headed, trembling and numbness of the tongue.

**Possible side effects seen with other local anaesthetics which might also be caused by Bupivacaine** injection **include:**
- Damaged nerves. Rarely (affecting less than 1 in 1,000 people), this may cause permanent problems.
- If too much Bupivacaine injection is given into the spinal fluid, the whole body may become numbed (anaesthetised).

**Additional side effects in children and adolescents**
Side effects in children are similar to those in adults.

Do not be concerned by this list of possible side effects. You may not get any of them.

**Reporting of side effects**
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard. By reporting side effects you can help provide more information on the safety of this medicine.

## 5. How to store Bupivacaine with glucose solution for injection

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the container after EXP. The expiry date refers to the last day of that month.
- Do not store above 25˚C.
- Your doctor or the hospital will normally store Bupivacaine injection and they are responsible for the quality of the product when it has been opened if it is not used immediately. They are also responsible for disposing of any unused Bupivacaine injection correctly.

## 6. Contents of the pack and other information

**What Bupivacaine with glucose solution for injection contains**
The active ingredient is bupivacaine hydrochloride anhydrous. Each millilitre (ml) of solution contains 5 mg of bupivacaine hydrochloride anhydrous.

The other ingredients are glucose anhydrous and/or glucose monohydrate, sodium hydroxide and water for injections.

**What Bupivacaine with glucose solution for injection looks like and contents of the pack**
Bupivacaine injection is a clear, colourless solution for injection. It comes in glass ampoules containing 4 ml of solution.

**Marketing Authorisation Holder and Manufacturer**
Aspen Pharma Trading Limited, 3016 Lake Drive, Citywest Business Campus, Dublin 24, Ireland
Tel: +44 (0)1 748 828 391

Bupivacaine with glucose solution for injection is manufactured by Cenexi, 52 Rue Marcel et Jacques Gaucher, 94120 Fontenay sous Bois, France.

To listen to or request a copy of this leaflet in Braille, large print or audio please call, free of charge:

0800 198 5000 (UK only)

Please be ready to give the following information:

**Product name** Bupivacaine 0.5% w/v with glucose solution for injection
Reference number 39699/0077

This is a service provided by the Royal National Institute of Blind People.

**This leaflet was last revised in April 2022**.

# Medical Information Leaflet

**Bupivacaine 0.5% w/v with glucose solution for injection**
bupivacaine hydrochloride

## 1. Name of the Medicinal Product

Bupivacaine 0.5% w/v with glucose solution for injection .

## 2. Qualitative and Quantitative Composition

Bupivacaine Hydrochloride BP 5.28 mg/ml equivalent to 5 mg/ml bupivacaine hydrochloride anhydrous. For the full list of excipients, see section 6.1.

## 3. Pharmaceutical Form

Solution for injection. Clear, colourless solution.

## 4. Clinical Particulars

### 4.1 Therapeutic Indications

Bupivacaine 0.5% w/v with glucose solution for injection is indicated in adults and children of all ages for intrathecal (subarachnoid) spinal anaesthesia for surgery (urological and lower limb surgery lasting 2-3 hours, abdominal surgery lasting 45-60 minutes).

Bupivacaine is a long acting anaesthetic agent of the amide type. Bupivacaine injection has a rapid onset of action and long duration. The duration of analgesia in the $T_{10}$-$T_{12}$ segments is 2-3 hours.

Bupivacaine injection produces a moderate muscular relaxation of the lower extremities lasting 2-2.5 hours. The motor blockade of the abdominal muscles makes the solution suitable for performance of abdominal surgery lasting 45-60 minutes. The duration of the motor blockade does not exceed the duration of analgesia. The cardiovascular effects of bupivacaine injection are similar or less than those seen with other spinal agents. Bupivacaine 5 mg/ml with glucose 80 mg/ml is exceptionally well tolerated by all tissues with which it comes in contact.

### 4.2 Posology and Method of Administration

**Adults and children above 12 years of age**
The doses recommended below should be regarded as a guide for use in the average adult. The figures reflect the expected average dose range needed. Standard textbooks should be consulted for factors affecting specific block techniques and for individual patient requirements.

The clinician's experience and knowledge of the patient's physical status are of importance in calculating the required dose. The lowest dose required for adequate anaesthesia should be used. Individual variations in onset and duration occur, and the extent of the spread of anaesthesia may be difficult to predict, but will be affected by the volume of the drug used, especially with the isobaric (plain) solution.

**Dosage recommendations**
Intrathecal anaesthesia for surgery:
2-4 ml (10-20 mg bupivacaine hydrochloride).

The dose should be reduced in the elderly and in patients in the late stages of pregnancy, see Section 4.4.

**Neonates, infants and children up to 40 kg**
Bupivacaine injection may be used in children.

One of the differences between small children and adults is a relatively high CSF volume in infants and neonates, requiring a relatively larger dose/kg to produce the same level of block as compared to adults.

Paediatric regional anaesthesia procedures should be performed by qualified clinicians who are familiar with this population and the techniques.

The doses in the table should be regarded as guidelines for use in paediatric patients. Individual variations occur. Standard textbooks should be consulted for factors affecting specific block technique and for individual patient requirements. The lowest dose required for adequate anaesthesia should be used.

**Dosage recommendations in neonates, infants and children**

| **Body weight (kg)** | **Dose (mg/kg)** |
|---|---|
| <5 | 0.40-0.50 mg/kg |
| 5 to 15 | 0.30-0.40 mg/kg |
| 15 to 40 | 0.25-0.30 mg/kg |

The spread of anaesthesia obtained with bupivacaine injection depends on several factors including the volume of solution and the position of the patient during and following the injection.

When injected at the $L_3$-$L_4$ intervertebral space, with the patient in the sitting position, 3 ml of Bupivacaine injection spreads to the $T_7$-$T_{10}$ spinal segments. With the patient receiving the injection in the horizontal position and then turned supine, the blockade spreads to $T_4$-$T_7$ spinal segments. It should be understood that the level of spinal anaesthesia achieved with any local anaesthetic can be unpredictable in a given patient.
The recommended site of injection is below $L_3$.

The effects of injections of bupivacaine exceeding 4 ml have not yet been studied and such volumes can therefore not be recommended.

**Method of administration**
Route of administration: For intrathecal injection.

## 4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Hypersensitivity to local anaesthetics of the amide type.

Intrathecal anaesthesia, regardless of the local anaesthetic used, has its own contraindications, 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.

Spinal stenosis and active disease (e.g. spondylitis, tuberculosis, tumour) or recent trauma (e.g. fracture) in the vertebral column.

Septicaemia.

Pyogenic infection of the skin at or adjacent to the site of lumbar puncture.

Cardiogenic or hypovolaemic shock.

Coagulation disorders or ongoing anticoagulation treatment.

## 4.4 Special Warnings and Precautions for Use

Intrathecal anaesthesia should only be undertaken by clinicians with the necessary knowledge and experience.

Regional anaesthetic procedures should always be performed in a properly equipped and staffed area. Resuscitative equipment and drugs should be immediately available and the anaesthetist should remain in constant attendance.

Intravenous access, e.g. an i.v. infusion, should be in place before starting the intrathecal anaesthesia. The clinician responsible should take the necessary precautions to avoid intravascular injection and be appropriately trained and familiar with the diagnosis and treatment of side effects, systemic toxicity and other complications. If signs of acute systemic toxicity or total spinal block appear, injection of the local anaesthetic should be stopped immediately, see sections 4.8 & 4.9.

Like all local anaesthetic drugs, bupivacaine may cause acute toxicity effects on the central nervous and cardiovascular systems, if utilised for local anaesthetic procedures resulting in high blood concentrations of the drug. This is especially the case after unintentional intravascular administration or injection into highly vascular areas.

Ventricular arrhythmia, ventricular fibrillation, sudden cardiovascular collapse and death have been reported in connection with high systemic concentrations of bupivacaine. Should cardiac arrest occur, a successful outcome may require prolonged resuscitative efforts. High systemic concentrations are not expected with doses normally used for intrathecal anaesthesia.

There is an increased risk of high or total spinal blockade, resulting in cardiovascular and respiratory depression, in the elderly and in patients in the late stages of pregnancy. The dose should therefore be reduced in these patients.

Intrathecal anaesthesia can cause hypotension and bradycardia. The risk of such effects can be reduced, e.g., by injecting a vasopressor. If hypotension develops it should be treated promptly with a sympathomimetic intravenously, repeated as necessary. 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 intrathecal anaesthesia.

Intrathecal anaesthesia can cause intercostal paralysis and patients with pleural effusions may suffer respiratory embarrassment. Septicaemia can increase the risk of intraspinal abscess formation in the postoperative period.

Neurological injury is a rare consequence of intrathecal anaesthesia and may result in paraesthesia, anaesthesia, motor weakness and paralysis. Occasionally these are permanent.

Before treatment is instituted, consideration should be taken if the benefits outweigh the possible risks for the patient.

Patients in poor general condition due to ageing or other compromising factors such as partial or complete heart conduction block, advanced liver or renal dysfunction require special attention, although regional anaesthesia may be the optimal choice for surgery in these patients.

Patients treated with anti-arrhythmic drugs class III (e.g. amiodarone) should be kept under close surveillance and ECG monitoring considered, since cardiac effects may be additive (see section 4.5).

## 4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Bupivacaine should be used with caution in patients receiving other local anaesthetics or agents structurally related to amide-type local anaesthetics, e.g. certain anti-arrhythmics, such as lidocaine and mexiletine, since the systemic toxic effects are additive.

Specific interaction studies with bupivacaine and anti-arrhythmic drugs class III (e.g. amiodarone) have not been performed, but caution is advised (see also section 4.4).

## 4.6 Fertility, Pregnancy and Lactation

**Pregnancy**

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 injection is administered in pregnancy. Bupivacaine injection should not therefore be given in early pregnancy unless the benefits are considered to outweigh the risks.

It should be noted that the dose should be reduced in patients in the late stages of pregnancy, see section 4.4.

**Breast-feeding**

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

Besides the direct anaesthetic effect, local anaesthetics may have a very mild effect on mental function and coordination even in the absence of overt CNS toxicity and may temporarily impair locomotion and alertness.

## 4.8 Undesirable Effects

### 4.8.1 General

The adverse reaction profile for Bupivacaine injection is similar to those for other long acting local anaesthetics used for intrathecal anaesthesia. Frequencies are defined as very

common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to<1/1,000), or not known (cannot be estimated from the available data).

**Table of Adverse Drug Reactions**

| System Organ Class | Frequency Classification | Adverse Drug Reaction |
|---|---|---|
| Immune system disorders | Rare | Allergic reactions, anaphylactic shock |
| Nervous system disorders | Common | Postdural puncture headache |
| | Uncommon | Paraesthesia, paresis, dysaesthesia |
| | Rare | Total unintentional spinal block, paraplegia, paralysis, neuropathy, arachnoiditis |
| Cardiac disorders | Very Common | Hypotension, bradycardia |
| | Rare | Cardiac arrest |
| Respiratory, thoracic and mediastinal disorders | Rare | Respiratory depression |
| Gastrointestinal disorders | Very Common | Nausea |
| | Common | Vomiting |
| Musculoskeletal and connective tissue disorders | Uncommon | Muscle weakness, back pain |
| Renal and urinary disorders | Common | Urinary retention, urinary incontinence |

Adverse reactions caused by the drug *per se* are difficult to distinguish from the physiological effects of the nerve block (e.g. decrease in blood pressure, bradycardia, temporary urinary retention), events caused directly (e.g. spinal haematoma) or indirectly (e.g. meningitis, epidural abcess) by needle puncture or events associated to cerebrospinal leakage (e.g. postdural puncture headache).

### 4.8.2 Acute systemic toxicity

Bupivacaine injection, used as recommended, is not likely to cause blood levels high enough to cause systemic toxicity. However, if other local anaesthetics are concomitantly administered, toxic effects are additive and may cause systemic toxic reactions.

Systemic toxicity is rarely associated with spinal anaesthesia but might occur after accidental intravascular injection. Systemic adverse reactions are characterised by numbness of the tongue, light-headedness, dizziness and tremors, followed by convulsions and cardiovascular disorders.

### 4.8.3 Treatment of acute systemic toxicity:

No treatment is required for milder symptoms of systemic toxicity but if convulsions occur then it is important to ensure adequate oxygenation and to arrest the convulsions if they last more than 15-30 seconds. Oxygen should be given by face mask and the respiration assisted or controlled if necessary. Convulsions can be arrested by injection of thiopental 100-150 mg intravenously or with diazepam 5-10 mg intravenously. Alternatively, succinylcholine 50-100 mg intravenously may be given but only if the clinician has the ability to perform endotracheal intubation and to manage a totally paralysed patient.

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

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

**Paediatric population**

Adverse drug reactions in children are similar to those in adults, however, in children, early signs of local anaesthetic toxicity may be difficult to detect in cases where the block is given during sedation or general anaesthesia.

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 4.9 Overdose

Bupivacaine injection, used as recommended, is not likely to cause blood levels high enough to cause systemic toxicity. However, if other local anaesthetics are concomitantly administered, toxic effects are additive and may cause systemic toxic reactions.

# 5. Pharmacological Properties

## 5.1 Pharmacodynamic Properties

Pharmacotherapeutic group (ATC code): N01B B01

Bupivacaine is a long acting local anaesthetic agent of the amide type. Moderate muscular relaxation of lower extremities. Motor blockade of the abdominal muscles.

Bupivacaine injection is hyperbaric and its initial spread in the intrathecal space is affected by gravity.

### 5.2 Pharmacokinetic Properties

Rapid onset of action and long duration i.e. $T_{10}$-$T_{12}$ segments - duration 2-3 hours.

Muscular relaxation of lower extremities lasts 2-2.5 hours.

Blockade of the abdominal muscles lasts 45-60 minutes. The duration of motor blockade does not exceed duration of analgesia.

In children the pharmacokinetics are similar to that in adults.

### 5.3 Preclinical Safety Data

Bupivacaine hydrochloride is a well-established active ingredient.

## 6. Pharmaceutical Particulars

### 6.1 List of Excipients

Glucose anhydrous and/or glucose monohydrate, sodium hydroxide and water for injections.

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf Life

3 years.

### 6.4 Special Precautions for Storage

Do not store above 25ºC.

### 6.5 Nature and Contents of Container

4 ml sterile wrapped glass ampoules or One Point Cut ampoules. Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal and other handling

The solution should be used immediately after opening of the ampoule. Any remaining solution should be discarded. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## 7. Marketing Authorisation Holder

The Marketing Authorisation for Bupivacaine with glucose solution for injection is held by

Aspen Pharma Trading Limited,
3016 Lake Drive,
Citywest Business Campus,
Dublin 24, Ireland
Tel: +44 (0)1 748 828 391

## 8. Marketing Authorisation Number

PL 39699/0077

## This leaflet was last revised in April 2022