Read all of this leaflet before you start using this medicine:
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others.
- It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Bupivacaine hydrochloride 0.5% is and what it is used for
2. Before you use Bupivacaine hydrochloride 0.5%
3. How to use Bupivacaine hydrochloride 0.5%
4. Possible side effects
5. Storage of Bupivacaine hydrochloride 0.5%
6. Further information

1. **What Bupivacaine hydrochloride 0.5% is and what it is used for**
The medicine contains bupivacaine, which is a long-acting anaesthetic agent intended to produce local or regional anaesthesia in surgery, various diagnostic and therapeutic procedures and in obstetrics.

Bupivacaine hydrochloride 0.5% is used in the following indications, especially when a long duration of anaesthesia is required:
- infiltration anaesthesia,
- peripheral nerve blocks,
- epidural anaesthesia.

Bupivacaine hydrochloride 0.5% is particularly recommended for pain relief e.g. during labour, as its sensory nerve block is more marked than its motor block.
The indications, recommended dosages and solution concentration appropriate for anaesthesia are specified in the Table below in section 3.

2. **Before you use Bupivacaine hydrochloride 0.5%**

Do not use Bupivacaine hydrochloride 0.5%:
- if you are hypersensitive (allergic) to bupivacaine or to other local anaesthetics of the amide type,
- for intravenous regional anaesthesia (Bier's block),
Take special care with Bupivacaine hydrochloride 0.5% in patients:
- with cardiovascular insufficiency (especially when epidural anaesthesia is used) or with cardiac disorders, because these patients are particularly sensitive to toxic effects of bupivacaine. In these persons, the doctor will reduce bupivacaine doses.
- with hepatic diseases or with reduced hepatic perfusion.
- with reduced volume of circulating blood (resulting, for example, from dehydration, bleeding, in persons with impaired venous return caused by extensive ascites, a large tumour in the abdominal cavity, advanced pregnancy), especially during epidural anaesthesia, because blood pressure may markedly decrease and heart rate slowing may occur.

Anaesthesia should be administered by a doctor familiar with the anaesthetic technique and trained in diagnostics and treatment of bupivacaine overdose.

During the use of Bupivacaine hydrochloride 0.5%:
- access to the appropriate resuscitation equipment, oxygen and necessary medicines has to be assured;
- it is necessary to conduct continuous monitoring of heart function and respiration, consciousness and other vital functions;
- bupivacaine administration into a blood vessel should be absolutely avoided (e.g. while producing neural blocks in the head and neck regions or major nerve blocks), because acute systemic toxicity symptoms may occur (poisoning, convulsions, up to cardiac arrest);
- caution should be exercised in the case of regional block in the head and neck regions in view of an increased risk of inadvertent intravenous injection of the medicine;
- particular caution should be exercised with extensive peripheral nerve blocks, in view of the necessary use of large volumes of the medicine and good vascularisation of these areas, which increases the risk of inadvertent intravenous injection of the medicine;
- multiple administrations of bupivacaine may lead to its elevated concentration in tissues and blood serum and to the occurrence of toxic symptoms;
- allergic reactions cannot be ruled out. However, in persons who developed allergic reactions after the use of ester-type local anaesthetics (e.g. procaine, tetracaine), no allergic reactions have been observed after amide-type local anaesthetics (e.g. bupivacaine).
- for retrobulbar anaesthesia, cases of cardiac arrest have been described.

Using Bupivacaine hydrochloride 0.5% in children
The recommended dose in children is 2 mg/kg.

Using Bupivacaine hydrochloride 0.5% in patients with hepatic function impairment
The medicine should be used with caution and at a lower dose in view of the risk of excessive concentrations of the medicine in bodily fluids and of medicine accumulation (when multiple doses are used).

Using Bupivacaine hydrochloride 0.5% in elderly patients
In elderly and debilitated patients, drug doses should be reduced.

Pregnancy
The medicine should not be used in early pregnancy unless in the doctor’s opinion the benefits for the mother are considered to outweigh the risk to the foetus.
Breastfeeding
Bupivacaine is excreted into the mother's milk in quantities which do not affect the infant's condition.

Driving and using machines
Depending on dosage, local anaesthetics may have a mild effect on driving and using machines.

Using other medicines
Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

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, since the systemic toxic effects may be additive.
Specific interaction studies with bupivacaine and class III anti-arrhythmic drugs (e.g. amiodarone) have not been performed, but caution is advised during the use of such concomitant treatment.

3. **HOW TO USE BUPIVACAINE HYDROCHLORIDE 0.5%**
The product does not contain preservatives.
Epidural or perineural administration.

Adults and adolescents aged 12 years and more
The table below contains the recommendations for product dosing in the most commonly used anaesthesia techniques. The individual dose should be calculated while taking into account the physician's experience and the patient's general clinical condition.
In the case of administering prolonged anaesthesia by using a technique of continuous block or repeated doses, the risk of attaining a toxic concentration in the plasma or causing local nerve damage should be taken into account.

<table>
<thead>
<tr>
<th>Recommended dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration (mg/ml)</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Anaesthesia for surgery</td>
</tr>
<tr>
<td>Lumbar epidural anaesthesia for surgery¹</td>
</tr>
<tr>
<td>Lumbar epidural anaesthesia for caesarean section¹</td>
</tr>
</tbody>
</table>

Version 2011/01
<table>
<thead>
<tr>
<th>Anaesthesia Type</th>
<th>2.5</th>
<th>5.0</th>
<th>6-15</th>
<th>12.5-37.5</th>
<th>10-15</th>
<th>1.5-2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracic epidural anaesthesia for surgery</td>
<td></td>
<td></td>
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<tr>
<td>11</td>
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<td></td>
</tr>
<tr>
<td>Sacral epidural anaesthesia</td>
<td>2.5</td>
<td>5.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>11</td>
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<tr>
<td>Peripheral nerve block</td>
<td>5.0</td>
<td></td>
<td></td>
<td>50-200</td>
<td>15-30</td>
<td></td>
</tr>
<tr>
<td>(branchial, femoral, ischiadic plexus)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4-8</td>
</tr>
<tr>
<td>Infiltration anaesthesia, minor nerve blocks</td>
<td>2.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3</td>
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<tr>
<td>Treatment of acute pain</td>
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<tr>
<td>Lumbar epidural</td>
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<tr>
<td>Single dose (e.g. postoperative anaesthesia)</td>
<td>2.5</td>
<td></td>
<td>6-15</td>
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<td></td>
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<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td>the shortest interval between doses is 30 minutes</td>
<td>2-5</td>
<td>1-2</td>
</tr>
<tr>
<td>Continuous anaesthesia</td>
<td>1.25</td>
<td>2.5</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td>10-15/h</td>
<td>12.5-18.8/h</td>
<td>12.5-18.8/h</td>
</tr>
<tr>
<td>Continuous anaesthesia during labour</td>
<td>1.25</td>
<td></td>
<td>5-10/h</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td>6.25-12.5/h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thoracic epidural continuous anaesthesia</td>
<td>1.25</td>
<td>2.5</td>
<td></td>
<td>5-10/h</td>
<td>6.3-12.5/h</td>
<td>10-18.8/h</td>
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<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td>4-7.5/h</td>
<td></td>
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<tr>
<td>Intra-articular anaesthesia</td>
<td>2.5</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td>≤40</td>
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<td></td>
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<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td>≤100</td>
<td>5-10</td>
<td></td>
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<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2-4 hours after</td>
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</tr>
</tbody>
</table>
(e.g. anaesthesia for arthroscopy of the knee) |  |  |  | withdrawal

| Infiltration anaesthesia, minor nerve blocks | 2.5 | ≤60 | ≤150 | 1-3 | 3-4 |

1) The dose includes the test dose.
2) In the case of major nerve blocks, the dose should be adjusted to the site of administration and general clinical condition of the patient. Anaesthesia of intercostal nerves and brachial plexus from supraclavicular access is associated with an increased frequency of serious adverse effects, regardless of the anaesthetic used for local anaesthesia (see section 4.4).
3) Total dose ≤400 mg/24 hours.
4) This solution is commonly used in epidural anaesthesia for the treatment of pain in combination with an opioid medicine. Total dose ≤400 mg/24 hours.
5) If the patient receives concomitantly bupivacaine in other anaesthesia techniques, the total administered dose of bupivacaine should not exceed 150 mg.

The doses listed in the table are considered sufficient for obtaining anaesthesia in an adult patient. The onset and duration of action may be different in individual patients. The values indicated in the Table usually represent the required dosing range. Various factors which may affect the individual anaesthesia techniques and individual requirements of the patient should be taken into account.

Unnecessary use of high doses of local anaesthetics should be avoided. To obtain complete block of all nerve fibres in large nerves, higher concentrations of the medicine are necessary. It is recommended to use lower concentrations for complete blockade of smaller nerves or for lower depth anaesthesia (e.g. elimination of labour pain). The volume of the administered medicine is determinant for the size of the anaesthetised area.

Careful aspiration before and during drug administration is recommended to avoid intravascular administration. The main dose of bupivacaine must be injected slowly, at a rate of 25 mg to 50 mg/min or the drug must be administered in divided doses with continuous monitoring of vital signs and verbal contact being maintained.
Before administering the medicine into the epidural space, it is recommended to use a test dose of 3 to 5 ml of the solution of bupivacaine with adrenalin. Inadvertent intravascular injection may be recognised on the basis of a brief increase in heart rate, and inadvertent intrathecal injection can produce signs of a spinal block. If acute toxicity symptoms occur, the injection must be discontinued immediately.

The existing observations indicate that the daily dose of 400 mg is well tolerated by an average adult.
Children aged 1 to 12 years

Recommended dosage

<table>
<thead>
<tr>
<th></th>
<th>Concentration (mg/ml)</th>
<th>Volume (ml)</th>
<th>Dose (mg)</th>
<th>Onset of action (minutes)</th>
<th>Duration of action (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of acute pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(in the peri- and postoperative period)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Sacral epidural anaesthesia</td>
<td>2.5</td>
<td>0.6-0.8</td>
<td>1.5-2</td>
<td>20-30</td>
<td>2-6</td>
</tr>
<tr>
<td>Lumbar epidural anaesthesia</td>
<td>2.5</td>
<td>0.6-0.8</td>
<td>1.5-2</td>
<td>20-30</td>
<td>2-6</td>
</tr>
<tr>
<td>Thoracic epidural anaesthesia</td>
<td>2.5</td>
<td>0.6-0.8</td>
<td>1.5-2</td>
<td>20-30</td>
<td>2-6</td>
</tr>
</tbody>
</table>

The doses listed in the table are considered recommended for use in children. Individual patients may require different doses. It is necessary to reduce the dose in children with high bodyweight. The dose should be determined on the basis of the normal bodyweight. Various factors which may influence the individual anesthetic techniques and individual requirements of the patient should be taken into account.

The recommended dose in children is 2 mg/kg. To obtain a lower concentration of the product, 0.5% solution should be diluted in 0.9% NaCl solution or 5% glucose solution. After dilution, the solution obtained can be stored for not more than 24 hours at 2 °C to 8 °C (refrigerator).

If more Bupivacaine hydrochloride 0.5% than recommended is used

Overdose symptoms primarily involve the cardiovascular system and the central nervous system.

Inadvertent intravascular administration may cause immediate toxic symptoms (within several seconds to a few minutes after injection). In case of overdose, the signs of systemic toxicity occur later (15-60 minutes after injection) due to a slower increase in the concentration of local anaesthetic in the blood.

Central nervous system toxicity symptoms develop gradually. The first symptoms are usually oral and circumoral paraesthesia, numbness of the tongue, light-headedness, tinnitus, hyperaesthesia and visual disturbances. Difficulty in articulating and muscle twitching appear
later and may precede generalised convulsions. Unconsciousness and grand mal seizures may follow and may last from a few seconds to several minutes. Hypoxia and hypercapnia occur rapidly during the seizures due to the increased muscular activity and inadequate ventilation. In severe cases asphyxia may occur. Acidosis, hypokalaemia and hypoxia increase the toxic effects of local anaesthetics. Recovery is due to redistribution of the local anaesthetic away from the central nervous system, metabolism and excretion of the drug. This takes place rapidly unless very large amounts of the medicine have been injected.

Very rarely, serious cardiovascular toxicity symptoms may occur. They are usually preceded by signs of central nervous system toxicity, which can, however, be masked by general anaesthesia or high doses sedative agents. A fall in blood pressure, bradycardia, arrhythmia and even cardiac arrest can occur as a result of high systemic concentrations of bupivacaine. In rare cases, cardiac arrest occurred without preceding central nervous system toxicity symptoms.

In generally anesthetised children, early toxicity symptoms may be difficult to detect.

_Treatment of acute toxicity symptoms_

If acute toxicity symptoms appear, drug administration should be immediately discontinued.

Hypotension and bradycardia should be treated by intravenous administration of 5 to 10 mg of ephedrine, repeated after 2-3 minutes if required. Ephedrine dose used in children depends on the age and bodyweight. In the event of cardiac arrest, prolonged resuscitation may be necessary.

In the event of cardiac arrest, resuscitation should be initiated immediately. It is very important to maintain good blood oxygenation, ventilation and circulation.

The objective of the treatment in patients with convulsions is predominantly to maintain ventilation and appropriate oxygenation, to interrupt the seizure and to maintain circulation. Oxygen must be always given. If necessary, assisted or controlled ventilation (oxygen mask, ambu bag or intratracheal intubation) should be used. If the seizure does not resolve spontaneously within 15 to 20 seconds, intravenous administration of an antiepileptic drug is necessary. Thiopental administered intravenously at a dose of 1-3 mg/kg will abort the convulsions rapidly. Alternatively, diazepam at a dose of 0.1 mg/kg may be used, although its action is slower. Prolonged convulsions may cause respiratory depression and oxygenation impairment. In such a case, a muscle relaxant may be administered, e.g. succinylcholine at a dose of 1 mg/kg, which requires tracheal intubation and controlled ventilation.

4. **POSSIBLE SIDE EFFECTS**

Bupivacaine hydrochloride 0.5% can cause side effects, although not everybody gets them.

Side effects are presented by frequency categories (very common ≥10, common ≥1/100, <1/10; uncommon ≥1/1000, <1/100; rare ≥1/10 000, <1/1000; very rare <1/10 000).

_Vascular disorders_

Very common: hypotension
Common: hypertension
Gastrointestinal disorders
Very common: nausea
Common: vomiting

Nervous system disorders
Common: paraesthesia, dizziness
Uncommon: signs and symptoms of central nervous system toxicity (convulsions, sensation of numbness around the lips, numbness of the tongue, hyperacusis, visual disturbances, loss of consciousness, tremor, light headedness, tinnitus, impaired speech articulation).
Rare: neuropathy, peripheral nerve injury, arachnoiditis

Cardiac disorders
Common: bradycardia
Rare: cardiac arrest, arrhythmia

Immune system disorders
Rare: allergic reactions, anaphylactic shock

Respiratory, thoracic and mediastinal disorders
Rare: respiratory depression

Eye disorders
Rare: double vision

Renal and urinary disorders
Common: Urinary retention.

In some persons, other side effects may occur during the use of Bupivacaine hydrochloride 0.5%. If you notice any side effects, also those not mentioned in this leaflet, please inform your doctor.

5. HOW TO STORE BUPIVACAINE HYDROCHLORIDE 0.5%
Do not store above 25 °C.
Keep out of the reach and sight of children.
The medicine does not contain preservatives.
After dilution, the solution obtained can be stored for not more than 24 hours at 2°C to 8°C (refrigerator).
Do not use Bupivacaine hydrochloride 0.5% after the expiry date stated on the package.

This medicine is subject to medical prescription.

6. FURTHER INFORMATION

What Bupivacaine hydrochloride 0.5% contains
- The active substance is bupivacaine hydrochloride: 1 ml of the solution contains 5 mg of bupivacaine hydrochloride.
- The other ingredients are: sodium chloride, hydrochloric acid 10% (for pH adjustment), water for injections.
What Bupivacaine hydrochloride 0.5% looks like and contents of the pack:
Bupivacaine hydrochloride 0.5% solution for injection is a transparent colourless liquid.
The package contains 10 ampoules made of colourless glass, containing 10 ml of solution in cardboard box.

Marketing Authorisation Holder and Manufacturer:
Warsaw Pharmaceutical Works Polfa SA
Karolkowa 22/24 str., 01-207 Warsaw, Poland

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder
Warsaw Pharmaceutical Works Polfa SA
Karolkowa 22/24 str., 01-207 Warsaw, Poland