# BUPIVACAINE hydrochloride in DEXTROSE

## REGIVELL®

**5 mg/mL (0.5% w/v) Solution for Injection (Spinal)**

**Local Anesthetic**

**FORMULATION :**
Each mL contains :
Bupivacaine hydrochloride, BP..... 5 mg
Dextrose monohydrate, BP..... 80 mg

**INDICATIONS :**
It is mainly used for infiltration anesthesia and regional nerve blocks, particularly epidural block and in peripheral nerve block. It is also used in epidural analgesia in labor and delivery.

**MECHANISM OF ACTION :**
Pharmacology : Bupivacaine is a long-acting local anesthetic agent of the amide type. It has rapid onset of action and long duration. The duration of analgesia in the T10-T12 segments is 2-3 hrs. Bupivacaine produces a moderate muscular relaxation of the lower extremities lasting 2-2.5 hrs. The motor blockade of the abdominal muscles makes the solution suitable for performance of abdominal surgery lasting for 45-60 min. The duration of motor blockade does not exceed the duration of analgesia.
Bupivacaine is hyperbaric and its initial spread in the subarachnoid space is considerably affected by gravity. Moreover, it spreads cephalad more extensively than the isobaric solutions, even in the horizontal position when the effect of gravity is minimal. Due to the larger intrathecal distribution and the consequently lower mean concentration, the duration of anesthesia tends to be shorter. Thus, the solution without added dextrose produce a lower level of block, but of longer duration than the hyperbaric solution.
Bupivacaine, like other local anesthetics, causes a reversible blockade of impulse propagation along nerve fibers by preventing the inward movement of sodium ions through the nerve membrane. Local anesthetics of the amide type are thought to act within the sodium channels of the nerve membrane.
**Pharmacokinetics :** Absorption from the subarachnoid space is relatively slow and this, together with the small dose required for spinal anesthesia, limits the maximum plasma concentration, which is approximately 0.4 mg/mL for every 100 mg injected. This means that the maximum recommended dose (20 mg) would result in plasma clearance of 0.58 L/min, a volume of distribution at steady state of 73 L, an elimination t½ of 2.7 hrs and hepatic extraction ratio of 0.4. Clearance of bupivacaine is almost entirely due to liver metabolism and depends upon both liver blood flow and the activity of the metabolizing enzymes. Bupivacaine readily crosses the placenta and equilibrium in regards to free drug will be reached. Because the degree of protein-binding in the fetus is less than in the mother, the total plasma concentration will be the same. Bupivacaine is excreted in breast milk, but in such small quantities that there is no risk to the child.

**DOSAGE RECOMMENDATIONS :**
Adults : Spinal Anesthesia for Surgery : 1.5-3 mL (bupivacaine HCl 7.5-15 mg) and 2-4 mL (10-20 mg).
The dosage in the table are those thought to be necessary for the production of a successful block and should be regarded as a guideline for use in the average adult. Regarding spread and duration times, there are wide individual variations and it is impossible to be precise.

| Upper level of anaesthesia (Bupivacaine 5 mg/mL) | % | Site of Injection | Position of Patient | Dosage | | Onset (min) | Duration (hrs) | Indication |
|---|---|---|---|---|---|---|---|---|
| | | | | mg | ml | | | |
| L1 | 0.5 | L3/4/5 | Sitting | 1.5-3 | 7.5-15 | 5-8 | 2-3 | Lower limb, urological and perineal surgery. Note : The patient should be laid horizontally 2-3 min after injection or if he/she complains of faintness |
| T5 | | L2/3/4 | Horizontal | 3-4<br>2-4 | 15-20<br>10-20 | 5-8 | 1.5-2 | Lower abdominal operations (including Caesarian action) |

The spread of Anesthesia is dependent of several factors including the volume of solution and the position of the patient during and following injection.
When injected at the sitting position, 3 mL of bupivacaine spreads to the T7-T10 spinal segments.
With the patient supine, the injection in the horizontal position and then turned supine, the blockade spreads to T4-T7 spinal segments. It should be understood that the level of spinal Anesthesia achieved with any local Anesthesia can be unpredictable in a given patient.
Children : One of the differences between small children and adults is a relatively high cerebrospinal fluid (CSF) volume in infants and neonates, requiring a relatively larger dose/kg to produce the same level of block as compared to adult.
Recommended Dose : Children >15 kg body weight: 0.25-0.3 mg/kg; 5-15 kg body weight : 0.3-0.4 mg/kg. Infants ≤ 5 kg body weight : 0.4-0.5 mg/kg.
Spinal injections should only be made after the subarachnoid space has been clearly identified by lumbar puncture. No drug should be injected until clear CSF is seen to escape from the spinal needle or it is detected by aspiration.

**DRUG INTERACTIONS :**
Bupivacaine should be used with care in patients receiving antiarrhythmic drugs due to an increased risk of myocardial depression. Increased risk of bupivacaine HCl toxicity with propranolol.

**CONTRAINDICATIONS :**
Known hypersensitivity to local anaesthetic of the amide type.
Acute active diseases of the central nervous system eg, meningitis, poliomyelitis, intracranial hemorrhage, demyelinating, increased intracranial pressure, cerebral and spinal tumors; spinal stenosis and active disease (eg, spondylitis, tumor) or recent trauma (eg, fracture) in the vertebral column; tuberculosis of the spine; pyrogenic infection of the skin at or adjacent to the site of lumbar puncture; septicemia; pernicious anemia with subacute combined degeneration of the spinal cord; coagulation disorders or ongoing anticoagulation treatment; uncorrected hypotension, cardiogenic or hypovolemic shock; obstetric paracervical block, IV regional anaesthesia (Bier's block) and all IV infusions.

**ADVERSE DRUG REACTIONS :**
In general, almost all the adverse effects seen with spinal anaesthesia are due to the nerve blockade itself and not to the drug used. These effects include hypotension, bradycardia and postdural puncture headache. High or Total Spinal Blockade : Severe adverse reactions following spinal anaesthesia are rare, but may occur in connection with extensive (total) spinal blockade.
Total spinal blockade will result in cardiovascular and respiratory depression. The cardiovascular depression is caused by an extensive sympathetic blockade which may result in profound hypotension and bradycardia, or even cardiac arrest. Ventilatory depression is caused by blockade of the innervation of the respiratory muscles, including the diaphragm.
Neurological Reactions : Neurological damage is rare, though recognized, consequence of regional and particularly spinal anaesthesia. It may be due to several causes eg, direct injury to the spinal cord or nerves, anterior spinal artery syndrome, injection of an irritant substance and nonsterile solution or the development of a space occupying lesion (hematoma or abscess) within the spinal canal. These may result in localized areas of paresthesia or anaesthesia, motor weakness, loss of sphincter control or paraplegia. Occasionally, these are permanent.
Neurological complications of this type have been reported with all local anaesthetics used for spinal anaesthesia.
Allergic Reactions : Allergy to amide type local anesthetics is very rare but may be present as allergic dermatitis, bronchospasm or anaphylaxis.
Acute Systemic Toxicity : Like all local anesthetic drugs, bupivacaine may have acute toxic effects on the central nervous and cardiovascular systems if given in high doses. The first manifestation of CNS toxicity is drowsiness merging into unconsciousness and respiratory arrest. The cardiovascular reactions are depressant and may be characterized by hypotension, myocardial depression, bradycardia and possibly cardiac arrest. In view of the low dosage employed, systemic adverse reactions are rarely associated with spinal anesthesia, but may occur after accidental intravascular injection. Systemic adverse reactions are characterized by numbness of the tongue, lightheadedness, dizziness and tremors, followed by convulsions and cardiovascular disorders.

**PRECAUTION :**
The safety and effectiveness of bupivacaine depend on proper dosage, correct technique and adequate precautions. Standard textbooks should be consulted for specific techniques and precautions for spinal anaesthetic procedures. If signs of acute systemic toxicity or total spinal block appear, injection of the local anaesthetic should be stopped immediately.
Injection should always be made slowly with frequent aspirations to avoid inadvertent intravascular injection which can produce toxic effects.
Bupivacaine should be used with caution in patients with cardiac block, impaired liver function and cardiovascular disturbances.
Besides the direct anesthetic effect, local anesthetics 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.
When any local anaesthetic agent is used, resuscitative equipment and agents, including oxygen, should be immediately available in order to manage possible adverse reactions involving the cardiovascular, respiratory or central nervous system.
Spinal anaesthesia can cause intercostal paralysis and patients with pleural effusions may suffer respiratory embarrassment.
The possibility of hypotension and bradycardia following epidural or subarachnoid blockade should be anticipated and appropriate precautions taken, including the prior establishment of an IV line and the availability of vasopressor agents and oxygen. Hypotension is common in patients with hypovolemia due to hemorrhage or dehydration and in those with aortocaval occlusion due to abdominal tumors or the pregnant uterus in late pregnancy. Hypotension is poorly tolerated by patients with coronary or cerebrovascular disease.
Bupivacaine should be used with caution in patients with genetic predisposition to malignant hyperthermia as the safety of amide local anaesthetic agents in these patients has not been fully established. A standard protocol for the management of malignant hyperthermia should be available.
Spinal anaesthesia can be unpredictable and very high blocks are sometimes encountered with paralysis of the intercostal muscles, and even the diaphragm, especially in pregnancy. On rare occasions, it will be necessary to assist or control ventilation.
There is an increased risk for high or total spinal blockade in the elderly and in patients in the late stages of pregnancy. The dose should therefore be reduced in these patients.
Use in pregnancy & lactation : Bupivacaine should be used with caution during pregnancy and lactation.

**STORAGE CONDITION :**
Store at temperatures not exceeding 30°C.

**PACKAGING PRESENTATION :**
USP Type I Glass Ampoule x 4 mL (Box of 5's)

**CAUTION :**
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

**ADR REPORTING :**
For suspected adverse drug reaction, report to the FDA : www.fda.gov.ph

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**NAME AND ADDRESS OF MANUFACTURER :**

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