SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. NAME OF FINISHED PHARMACEUTICAL PRODUCT:

PIVAC (Bupivacaine Hydrochloride in Dextrose Injection USP)

1.1 Strength

5 mg/ml

1.2 Pharmaceutical form

Clear colourless liquid Injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Sr. No.	Ingredients	Specification	Quantity per ml	Activity
1.	Bupivacaine Hydrochloride eq to Bupivacaine Hydrochloride Anhydrous	USP	5.0 mg	Active Ingredient
2.	Dextrose	USP	80.0 mg	Active Ingredient
3.	Disodium edetate	USP	1 mg	Chelating agent
4.	Sodium Hydroxide	USP	--	pH adjusting agent
5.	Hydrochloric acid	USP	--	pH adjusting agent
6.	Water for Injection	USP	q.s	Vehicle

3. PHARMACEUTICAL FORM:

Liquid Injection.

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications

Bupivacaine Hydrochloride in Dextrose Injection USP (Bupivacaine hydrochloride in dextrose Injection USP) 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 Hydrochloride In Dextrose Injection USP has a rapid onset of action and long duration. The duration of analgesia in the T10–T12m segments is 2–3 hours.

4.2 Posology and method of administration

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.

Neonates, infants and children up to 40 kg:

Bupivacaine Hydrochloride In Dextrose Injection USP 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 Hydrochloride In Dextrose Injection USP depends on several factors including the volume of solution and the position of the patient during and following the injection.

When injected at the L3–L4 intervertebral space, with the patient in the sitting position, 3 ml of Bupivacaine Hydrochloride In Dextrose Injection USP spreads to the T7–T10 spinal segments.

With the patient receiving 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 anaesthesia achieved with any local anaesthetic can be unpredictable in a given patient.
The recommended site of injection is below L3.

The effects of injections of Bupivacaine Hydrochloride In Dextrose Injection USP exceeding 4 ml have not yet been studied and such volumes can therefore not be recommended.

4.3 Method of administration

Intrathecal route

4.4 Contraindications

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.

4.5 Special warning 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.

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 with any local anaesthetic can cause hypotension and bradycardia which should be anticipated and appropriate precautions taken.

These may include preloading the circulation with crystalloid or colloid solution. If hypotension develops, it should be treated with a vasopressor such as ephedrine 10–15 mg 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 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, 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.

4.6 Paediatric population

Not applicable.

4.7 Interactions with other FPPs and other forms of interactions

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.

4.8 Additional information on special populations

Not available.

4.9 Paediatric population

Not available.

4.10 Fertility, Pregnancy and Lactation

Fertility

Not available.

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 PIVAC is administered in pregnancy. PIVAC 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.

Lactation

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.

4.11 Effects on ability to drive and use machines

Bupivacaine Hydrochloride has minor influence on the ability to drive and use machines. Besides the direct anaesthetic effect, local anaesthetics may have a very mild effect on mental function and co-ordination even in the absence of overt CNS toxicity and may temporarily impair locomotion and alertness.

4.12 Undesirable effects

Tabulated list of adverse reactions

The adverse reaction profile for Bupivacaine Hydrochloride 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), very rare (<1/10,000) 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).

4.13 Overdose

Bupivacaine 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)

Pharmacotherapeutic Group: Local Anaesthetic

ATC code: Bupivacaine Hydrochloride N01BB01.

Dextrose: B05CX01

Mechanism of action

Bupivacaine hydrochloride is a long acting local anaesthetic of the amide type with both anaesthetic and analgesic effects. At high doses it produces surgical anaesthesia, while at lower doses it produces sensory block (analgesia) with less pronounced motor block.

Onset and duration of the local anaesthetic effect of bupivacaine depends on the dose and site of administration.

Bupivacaine, like other local anaesthetics, causes a reversible blockade of impulse propagation along nerve fibres by preventing the inward movement of sodium ions through the cell membrane of the nerve fibres. The sodium channels of the nerve membrane are considered a receptor for local anaesthetic molecules.

Local anaesthetics may have similar effects on other excitable membranes e.g. in the brain and myocardium. If excessive amounts of drug reach the systemic circulation, symptoms and signs of toxicity may appear, emanating from the central nervous and cardiovascular systems.

5.2. Pharmacokinetic properties

Rapid onset of action and long duration i.e. T10-T12 segments-duration 2 to 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

Not available

6. PHARMACEUTICAL PARTICULARS:

6.1 List of Excipients

Following excipients are used in the formulation of PIVAC.

Disodium EDTA

Sodium Hydroxide

Hydrochloric Acid

Water for Injection

6.2 Incompatibilities

NA

6.3 Shelf life

36 Months from the date of manufacture.

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

Each filled and sealed 4ml flint glass ampoule USP Type I containing 4ml clear colourless liquid is labeled. 10 such ampoules are placed in plastic tray and such a tray is packed in a monocarton along with insert.

6.6 Special precaution for disposal and other handling

Keep out of reach of children.

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESS:

Manufactured By:

KILITCH DRUGS (INDIA) LTD.

Plot no- C-301/2, M.I.D.C, T.T.C Industrial Area, Pawane, Navi Mumbai - 400705, Maharashtra, India.

8. MARKETING AUTHORIZATION NUMBERS:

FDA-HMP-MA-0828

9. DATE OF FIRST REGISTRATION/ RENEWAL OF THE REGISTRATION:

Date of first registration: 09/02/2024

10. DATE OF REVISION OF THE TEXT:

14/02/2024

11. DOSIMETRY (IF APPLICABLE)

Not Applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE)

Not Applicable.

The Summary of Product Characteristics (SPC) is satisfactory.