Prescribing Information (Summary of Product Characteristics)

1. Name of the medicinal Product
Bupivacaine Hydrochloride Injection USP 0.5 % w/v

2. Qualitative and Quantitative Composition
Bupivacaine Hydrochloride USP

Excipient(s) with known effect:
Each ml of the solution contains approx. 0.14 mmol (3.2 mg) of Sodium.

For the full list of excipients, see section 6.1

3. Pharmaceutical Form
Injection
A clear colourless solution

4. Clinical Particulars

1. Therapeutic Indications
It is indicated for the relief of surgical operations, including obstetric operations such as caesarean section, acute pain relief, including labour or postoperative pain, diagnosis and treatment of chronic pain, e.g. sympathetic nerve blocks. It is also indicated in treatment of different anaesthetic techniques including local infiltration, minor and major nerve blocks and epidural blockade. Surgical anaesthesia in adults and children above 12 years of age. Acute pain management in adults, infants and children above 1 year of age.

2. Posology and Method of Administration

	Conc. (mg/ml)	**Volume /Rate (ml)**	**Dose (mg)**	**Onset (min)**	**Duration (hours)** [7)]
SURGICAL ANAESTHESIA					
Lumbar Epidural Administration					
Surgery & Caesarean Section	5.0	15-30	75-150	15-30	2-3
Thoracic Epidural Administration					
Surgery	2.5	5-15	12.5-37.5	10-15	1.5-2
	5.0	5-10	25-50	10-15	2-3
Caudal Epidural Block					
	2.5	20-30	50-75	20-30	1-2
	5.0	20-30	100-150	15-30	2-3
Major Nerve Block (e.g. brachial plexus, femoral, sciatic)	5.0	10-35	50-175	15-30	4-8
Field block (e.g. minor nerve blocks and infiltration)	2.5	<60	<150	1-3	3-4
	5.0	≤30	≤150	1-10	3-8

Acute Pain Management					
Lumbar Epidural Administration					
Intermittent injections [3] (e.g. post-operative pain relief)	2.5	6-15; min interval 30 min	15-37.5; min interval 30 min	2-5	1-2
Continuous infusion [4]	1.25	10-15/h	12.5-18.8/h		
Continuous infusion, labour pain relief [4]	2.5	5-7.5/h	12.5-18.8/h	-	-
Thoracic Epidural Administration					
Continuous infusion	2.5	4-7.5/h	10-18.8/h	-	-
	1.25	5-10/h	6.3-12.5/h	-	-
Intra-Articular Block [6] *(e.g., following knee arthroscopy)*	2.5	<40	<100[5]	5-10	2-4 h after wash out
Field Block *(e.g. minor nerve blocks and infiltration)*	2.5	<60	<150	1-3	3-4

Paediatric patients 1 to 12 years of age: The lowest dose required for adequate analgesia should be used. In children the dosage should be calculated on a weight basis up to 2 mg/kg.

	Conc. mg/ml	**Volume ml/kg**	**Dose mg/kg**	**Onset min**	**Duration hours**
Acute Pain Management (pre- and Postoperative)					
Caudal Epidural Administration	2.5	0.6-0.8	1.5-2	20-30	2-6
Lumbar Epidural Administration	2.5	0.6-0.8	1.5-2	20-30	2-6
Thoracic Epidural Administration[b]	2.5	0.6-0.8	1.5-2	20-30	2-6
Field Block (e.g. minor nerve blocks and infiltration)	2.5 5.0		0.5-2.0 0.5-2.0		

Peripheral Nerve Blocks (e.g. ilioinguinal – iliohypogastric)	2.5 5.0		0.5 - 2.0 0.5 - 2.0	a) a)	

a) The onset and duration of peripheral nerve blocks depend on the type ofblock and the dose administered.
b) Thoracic epidural blocks need to be given by incremental dosage until the desired level of anaesthesia is achieved.

3. Contraindications

It is contra-indicated in patients with a known hypersensitivity to local anaesthetic agents of the amide group or to other components or to any of the other excipients. It also contra-indicated for intravenous regional anaesthesia (Bier's block) and obstetrical paracervical block. Injection of adrenaline containing bupivacaine in areas of end arteries (e.g. penile block, Oberst block) may cause ischemic tissue necrosis. Epidural anaesthesia, regardless of the local anaesthetic used, has its own contraindications which include: meningitis, poliomyelitis, intracranial haemorrhage, subacute combined degeneration of the cord due to pernicious anaemia, and cerebral or spinal tumors, 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 anticoagulant therapy. Epidural anaesthesia is contraindicated in patients with an expanding cerebral lesion, a tumor, cyst or abscess.

4. Special Warnings and Special Precautions for Use

Bupivacaine may cause acute toxicity effects on the central nervous and cardiovascular systems ventricular arrhythmia, ventricular fibrillation, sudden cardiovascular collapse, cardiac arrest and death. Before any nerve block is attempted, intravenous access for resuscitation purposes should be established. Some patients require special attention to reduce the risk of side effects:

The elderly and patients in poor general condition should be given reduced doses commensurate with their physical status. Patients with impaired cardiovascular function, partial or complete heart block, advanced liver disease or severe renal dysfunction. Patients treated with anti-arrhythmic medicinal products class III (e.g. amiodarone) should be under close surveillance and ECG monitoring. Epidural anaesthesia should be avoided or used with caution in patients with untreated hypovolaemia or significantly impaired venous return.

Retrobulbar injections may very rarely reach the cranial subarachnoid space causing temporary blindness, cardiovascular collapse, apnoea, convulsions. Retro- and peribulbar injections of local anaesthetics carry a low risk of persistent ocular muscle dysfunction. Vasoconstrictors may aggravate tissue reactions. Small doses of local anaesthetics injected into the head and neck, including retrobulbar, dental and stellate ganglion blocks, may produce systemic toxicity. The safety and efficacy of bupivacaine hydrochloride in children < 1 year of age have not been established.

Pregnancy: It should not be given in early pregnancy unless the benefits are considered to outweigh the risks.

Lactation: It enters the mother's milk, but in such small quantities that there is no risk of affecting the child at therapeutic dose levels.

4.5 Interaction with other medicinal products and other forms of interaction

Bupivacaine Hydrochloride 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.

4.6 Fertility, Pregnancy and Lactation

Pregnancy: Bupivacaine Hydrochloride should not be given in early pregnancy unless the benefits are considered to outweigh the risks.

Lactation: Bupivacaine Hydrochloride enters the mother's milk, but in such small quantities that there is no risk of affecting the child at therapeutic dose levels.

7. Effects on ability To Drive and use Machines
Not Applicable

4.8 Undesirable Effects
Accidental sub-arachnoid injection can lead to very high spinal anaesthesia poss ibly with apnoea and severe hypotension. Neurological damage is a rare but well recognised consequence of regional and particularly epidural and spinal anaesthesia. These may result in localised areas of paraesthesia or anaesthesia, motor weakness, loss of sphincter control and paraplegia. Hepatic dysfunction, with reversible increases of SGOT, SGPT, alkaline phosphates and bi lirubin, has been observed following repeated injections or Jong-tenn infusions of bupivacaine. Other common drug reactions are paraesthesia, dizziness, Bradycardia, Hypertension, Nausea, Vomiting and Urinary retention.

4.9 Overdose
Accidental intmvascular injections of local anaesthetics may cause immediate (within seconds to a few minutes) systemic toxic reactions. In the event of overdose, system toxicity appears later (15-60 minutes after injection) due to slower increase in local anaesthetic blood concentration.

5. Pharmacological Properties

1. Pharmacodynamics Properties
Pharmacotherapeutic group: Anesthetics, local; Amides
ATC Code: N01BB01
Bupivacaine Hydrochloride interferes with the function of all organs in which conduction or transmission of impulses occurs. These include effects on the C.N.S, the autonomic ganglia, the neuromuscular junction and all forms of muscle fibres. At high doses it produces surgical anaesthesia, while at lower doses it produces sensory block with less pronounced motor block. Following absorption, Bupivacaine Hydrochloride may cause stimulation of the C.N.S followed by depression and, in the cardiovascular system.

5.2 Pharmacokinetic Properties
The rate of systemic absorption of Bupivacainc Hydrochloride is dependent upon the total dose and concentration administered, the route of administration and the vascularity of the tissue locally. Bupivacaine Hydrochloride is about 95% bound to plasma proteins, mainly to alpha-1-acid glycoprotein at low concentrations and to albumin at high concentrations. In adults, the terminal half-life of Bupivacainc Hydrochloride is 2.7 hours. In neonates and some young infants, terminal elimination half-lives could be as long as 8 to 12 hours. Local anaesthetics arc distributed to some extent to all body tissues, with higher concentrations found in highly perfused organs such as liver, heart and brain.Bupivacainc Hydrochloride is metabolised in the liver and is excreted in the urine mainly as metabolites, with only 5 to 6% as unchanged drug.

3. Preclinical Safety Data
Not Applicable

6. Pharmaceutical Particulars
1. List of Excipients
Sodium Chloride (Inj. Grade) BP
Hydrochloric acid (AR Grade) BP
Sodium Hydroxide BP
Water for Injection BP

2. Incompatibilities
Not applicable

3. Shelf Life
24 months
After first opening from a microbiological point of view the product should be used immediately.

4. Special Precautions for Storage

Do not Store above 30°C. Protect from light. Do not refrigerate or freeze.

5. Nature and Contents of Container
A 20 ml clear glass USP type-I vial having 20 mm grey butyl rubber stopper & 20 mm green F/O seal. Such 5 labelled vials packed in printed carton with packaging insert.

6. Special precaution for disposal and other handling
For single use only.
Any unused solution should be discarded.

7. Marketing Authorization Holder And Manufacturing Site Addresses
a. Name and Address of Marketing Authorization Holder
Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, **India.**
Telephone no.: +91-79-41078096
Fax: +91-79-41078062
E-mail: hiren@lincolnpharma.com
Website: www.lincolnpharma.com

b. Name and Address of manufacturing site(s)
Lincoln Parentral Limited
11, Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, **India.**
Telephone no.: +91-79-41078096
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8. Marketing Authorization Number
TAN 22 HM 0138

9. Date of First <Registration> / Renewal of The <Registration>
13/04/2022

10.Date of Revision of the Text