1.6.1

Prescribing Information (Summary of Product Characteristics)

1.6.1.1 Name of the medicinal Product

Lidocaine Injection BP 2%

1.6.1.1.1 strength

2% w/v

1.6.1.1.2 Pharmaceutical Form

Solution for Injection

1.6.1.2 Qualitative and Quantitative Composition

1.6.1.2.1 Qualitative declaration

Lidocaine hydrochloride BP

1.6.1.2.2 Quantitative declaration

Sr. No.	Ingredients Chemical Name	Specification	Standard Quantity/Tablet (mg)	Reason for Inclusion
01	Lidocaine Hydrochloride (A)	BP	21. 30	Local anesthetic
02	Disodium Edetate	BP	0.500	Chelating agent
03	Sodium Chloride	BP	6.000	Tonicity agent.
04	Sodium Bisulphite	BP	1.250	Antioxidant
05	Sodium Hydroxide	BP	0.425	Buffering agent
06.	Methyl Hydroxybenzoate	BP	1.000	Preservative
07	Water For Injections	BP	Q.S	Sterile vehicle

1.6.1.3 Pharmaceutical Form

Solution for Injection

A clear colourless liquid filled in glass vial.

1.6.1.4 Clinical Particulars

1.6.1.4.1 Therapeutic Indications

Symptoms of depression (especially where sedation is required).

Nocturnal enuresis where organic pathology is excluded.

1.6.1.4.2 Posology and Method of Administration

The lowest dosage that results in effective anaesthesia should be used and should be based on the status of the patient and the type of regional anaesthesia intended.

Adults weighing an Average of 70 kg: Various Anaesthetic Procedures: Recommended Dosage: Infiltration: 10 ml.

Epidural Blocks: Lumbar Anaesthesia: 5-10 ml. The dose is determined by the number of segments to be anaesthetised (2-3 ml/segment).

Note: Recommended Dosage: The previously-suggested concentrations and volumes serve only as a guide. Toxic doses vary widely between patients and toxic effects may occur after any local anaesthetic procedure. Careful observation of the patient must therefore be maintained. It is recommended that the dose of Lidocaine at any one time should not exceed 3 mg/kg.

However, the dose administered must be tailored to the individual patient and procedure, and the maximum doses given should be used as a guide only.

Only single dose containers should be used for epidural and IV regional anaesthesia and for peripheral nerve block.

Hypotension: During thoracic, lumbar and caudal epidural anaesthesia, a marked fall in blood pressure and/or intercostal paralysis may be seen, possibly due to the use of excessive doses, improper positioning of the patient or accidental disposition of the anaesthetic within the subarachnoid space. Hypotension and bradycardia may occur as a result of sympathetic blockade.

Children: For children, a reduced dosage based on body weight or surface area should be used. The dosage should be calculated for each patient individually and modified in accordance with the physician's experience and knowledge of the patient.

In order to minimize the possibility of toxic effects, the use of Lidocaine Injection 0.5% or 1% solutions is recommended for most anaesthetic procedures involving paediatric patients.

Elderly: A reduction in dosage may be necessary for elderly patients especially those with compromised cardiovascular and/or hepatic function. In epidural anaesthesia, a smaller dose may provide adequate anaesthesia.

Impaired Hepatic function: In epidural anaesthesia, a smaller dose may provide adequate anaesthesia.

Impaired Renal Function: Impairment of renal function is unlikely to affect Lidocaine clearance in the short-term (24 hrs).

However, toxicity due to accumulation may develop with prolonged or repeated administration.

1.6.1.4.3 Contraindications

Allergy or hypersensitivity to amide-type local anesthetics or other components of the injection solution which may be present. Detection of suspected hypersensitivity by skin testing is of limited value.

Local anaesthetics arc contraindicated for epidural and spinal anaesthesia in patients with uncorrected hypotension and in those with coagulation disorders or receiving anticoagulation treatment.

Local anaesthetic techniques must not be used when there is inflammation and/or sepsis in the region of the proposed injection and in the presence of septicaemia.

1.6.1.4.4 Special Warnings and Special Precautions for Use

When any local anaesthetic agent is used, resuscitative equipment and drugs, including oxygen, should be immediately available in order to manage possible adverse reactions involving the cardiovascular, respiratory or central nervous systems. Injection should always be made slowly with frequent aspirations to avoid inadvertent intravascular injection, which can produce toxic effects. The safety and effectiveness of Lidocaine depend on proper dosage, correct technique and adequate precautions. Standard textbooks should be consulted regarding specific techniques and precautions for various regional anaesthetic procedures. The lowest dosage that results in effective anaesthesia should be used. Repeated injection of Lidocaine Injection may cause accumulation of Lidocaine or its metabolites and result in toxic effects. Debilitated, elderly or acutely ill patients should be given reduced doses commensurate with their age and physical status. Local anaesthetic should be given with great caution to patients with pre-existing abnormal neurological conditions. The possibility of hypotension and bradycardia following epidural or subarachnoid blockade should be anticipated and precautions taken, including the prior establishment of an IV line and the availability of vasopressor drugs and oxygen. Since Lidocaine is metabolised in the liver and excreted via the kidneys, the possibility of drug accumulation should be considered in patients with hepatic and/or renal impairment. Lidocaine should be given with caution is

patients with known drug sensitivities. Patients allergic to ester derivatives of para-aminobenzoic acid (procaine, tetracaine, benzocaine, etc) have not shown cross-sensitivity to agents of the amide type. Lidocaine 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. Lidocaine should be given with great caution to patients with severe bradycardia, cardiac conduction disturbances or severe digitalis intoxication. Inadvertent intravascular or subarachnoid injection of small doses of local anaesthetics injected into the head and neck area, including retrobulbar, dental and stellate ganglion blocks, may produce adverse reactions similar to systemic toxicity seen with unintentional intravascular injections of larger doses. Clinicians who perform retrobulbar blocks should be aware that there have been reports of respiratory arrest following the use of local anaesthetic injections for re trobulbar block. Prior to retrobulbar block, necessary equipment, drugs and personnel should be immediately available as with all other regional procedures.

Use in pregnancy: the safe use of lidocaine during pregnancy has not been established. Lidocaine has, however, been used extensively for surgical procedures during pregnancy with no reports of Ill effects to mother or foetus. Lidocaine has been effectively used for obstetrical analgesia and adverse effects on the course of labour or delivery arc rare. After epidural administration of Lidocaine to women in labour, Lidocaine crosses the placental barrier. However, concentrations in umbilical veins arc lower than those found in the maternal circulation. Adrenaline-free solutions should be used during labour for paracervical or pudendal blocks. Note: Paracervical blocks may be associated with foetal bradycardia. Foetal bradycardia frequently follows paracervical block and may be associated with foetal acidosis and hypoxia. Occasional cases of perinatal morbidity and mortality have been reported. When the recommended dose is exceeded the risk of foetal bradycardia increases.

Use in lactation: Lidocaine passes into breast milk. The amount of Lidocaine appearing in breast milk from a nursing mother receiving parenteral lidocaine is unlikely to lead to a significant accumulation of the parent drug in the breastfed infant. The remote possibility of an idiosyncratic or allergic reaction in the breastfed infant from Lidocaine remains to be determined.

1.6.1.4.5 Interaction with other medicinal products and other forms of interaction

Antiarrhythmic Drugs: Local anaesthetics of the amide type, e.g. Lidocaine, should be used with caution in patients receiving antiarrhythmic drugs since potentiation of cardiac effects may occur.

Beta-Adrenoreceptor Antagonists: Propranolol and metoprolol reduce the metabolism of IV administered Lidocaine and the possibility of this effect with other -adrenergic blockers should be kept in mind.

Cimetidine: Cimetidine reduces the clearance of IV administered Lidocaine and toxic effects due to high serum Lidocaine levels have been reported when these 2 drugs have been administered concurrently.

Anticonvulsive Agents: Diphenylhydantoin and other antiepileptic drugs, e.g. phenobarbitone, primidone and carbamazepine appear to enhance the metabolism of Lidocaine but the significance of this effect is not known. Diphenylhydantoin and Lidocaine have additive cardiac depressant effects.

1.6.1.4.6 Fertility, Pregnancy and Lactation

Pregnancy: Category B. Although animal studies have revealed no evidence of harm to the foetus, Lidocaine crosses the placenta and should not be administered during early pregnancy unless the benefits are considered to outweigh the risks.

Lidocaine given by local perineal infiltration prior to delivery crosses rapidly into the foetal circulation. Elevated lidocaine levels may persist in the newborn for at least 48 hours after delivery. Foetal bradycardia or neonatal bradycardia, hypotonia or respiratory depression may occur.

Lactation: Small amounts of lidocaine are secreted into breast milk and the possibility of an allergic reaction in the infant, albeit remote, should be borne in mind when using lidocaine in nursing mothers.

1.6.1.4.7 Effects on ability To Drive and use Machines

Where outpatient anesthesia affects areas of the body involved in driving or operating machinery, patients should be advised to avoid these activities until normal function is fully restored.

1.6.1.4.8 Undesirable Effects

In common with other local anesthetics, adverse reactions to lidocaine are rare and are usually the result of raised plasma concentrations due to accidental intravascular injection, excessive dosage or rapid absorption from highly vascular areas, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. Systemic toxicity mainly involves the central nervous system and/or the cardiovascular system.

Adverse effects reported following unpreserved lidocaine solutions administered by this route include hypotension and isolated cases of bradycardia and cardiac arrest.

Immune system disorders: Hypersensitivity reactions (allergic or anaphylactoid reactions, anaphylactic shock) – see also Skin & subcutaneous tissue disorders)

Nervous & Psychiatric disorders: Neurological signs of systemic toxicity include dizziness or light-headedness, nervousness, tremor, circumoral paraesthesia, tongue numbness, drowsiness, convulsions, coma

Nervous system reactions may be excitatory and or depressant. Signs of CNS stimulation may be brief, or may not occur at all, so that the first signs of toxicity may be confusion and drowsiness, followed by coma and respiratory failure.

Neurological complications of spinal anaesthesia include transient neurological symptoms such as pain of the lower back, buttock and legs. These symptoms usually develop within twenty-four hours of anaesthesia and resolve within a few days. Isolated cases of arachnoiditis or cauda equina syndrome, with persistent paraesthesia, bowel and urinary dysfunction, or lower limb paralysis have been reported following spinal anaesthesia with lidocaine and other similar agents. The majority of cases have been associated with hyperbaric concentrations of lidocaine or prolonged spinal infusion.

Eye disorders: Blurred vision, diplopia and transient amaurosis may be signs of lidocaine toxicity. Bilateral amaurosis may also be a consequence of accidental injection of the optic nerve sheath during ocular procedures. Orbital inflammation and diplopia have been reported following retro- or peribulbar anaesthesia (see section 4.4 Special warnings and precautions for use)

Ear and labyrinth disorders: Tinnitus, hyperacusis

Cardiac and vascular disorders: Cardiovascular reactions are depressant and may manifest as hypotension, bradycardia, myocardial depression, cardiac arrhythmias and possibly cardiac arrest or circulatory collapse.

Respiratory, thoracic or mediastinal disorders: Dyspnoea, bronchospasm, respiratory depression, respiratory arrest

Gastrointestinal: Nausea, vomiting

Skin & subcutaneous tissue disorders: Rash, urticaria, angioedema, face oedema.

1.6.1.4.9 Overdose

Overdosage of Lidocaine HCl usually results in signs of central nervous system or cardiovascular toxicity. May develop convulsions or signs of respiratory depression and arrest, the patency of the airway and adequacy of ventilation must be assured immediately. Convulsions may persist despite ventilatory therapy with oxygen; small increments of anticonvulsive agents may be given intravenously. Examples of such agents include a benzodiazepine (e.g., diazepam), an ultrashort-acting barbiturate (e.g., thiopental or thiamylal) or a short-acting barbiturate (e.g., pentobarbital or secobarbital). If the patient is under general anesthesia, a short-acting muscle relaxant (e.g., succinylcholine) may be administered. Should circulatory depression occur, vasopressors may be used. If cardiac arrest occurs, standard CPR procedures should be instituted. Dialysis is of negligible value in the treatment of acute overdosage from lidocaine HCl.

1.6.1.5 Pharmacological Properties

1.6.1.5.1 Pharmacodynamics Properties

Lidocaine works as local anesthetics. It blocks both the initiation and conduction of nerve impulses by decreasing the neuronal membrane's permeability to sodium ions, which results in inhibition of depolarization with resultant blockade of conduction.

1.6.1.5.2 Pharmacokinetic Properties

Except for intravascular administration, the highest blood levels occur following intercostal nerve block and the lowest after subcutaneous administration. Lidocaine is bound to plasma

proteins, including alpha-1-acid-glycoprotein. The drug crosses the blood-brain and placental barriers.

Lidocaine is metabolized in the liver and about 90 % of a given dose undergoes N-dealkylation to form monoethylglycinexylidide and glycinexylidide, both of which may contribute to the therapeutic and toxic effects of lidocaine. Further metabolism occurs and metabolites are excreted in the urine with less than 10 % of unchanged lidocaine. The elimination half-life of lidocaine following an intravenous bolus injection is one to two hours, but this may be prolonged in patients with hepatic dysfunction.

1.6.1.5.3 Preclinical Safety Data

No further information other than that which is included in the Summary of Product Characteristics.

1.6.1.6 Pharmaceutical Particulars

1.6.1.6.1 List of Excipients

Disodium Edetate BP
Sodium Chloride BP
Sodium Bisulphite IHS
Sodium Hydroxide BP
Methyl Hydroxybenzoate BP
Water For Injections BP

1.6.1.6.2 Incompatibilities

Lidocaine causes precipitation of amphotericin, methohexitone sodium and sulphadiazine sodium in glucose injection. It is recommended that admixtures of lidocaine and glyceryl trinitrate should be avoided.

1.6.1.6.3 Shelf Life

36 months

1.6.1.6.4 Special Precautions for Storage

Do not store above 30°C. Protect from light.

1.6.1.6.5 Nature and Contents of Container

A clear colourless liquid filled in 30 ml clear glass (TYPE-III) vial, such 25 vial is packed in a printed carton with packaging insert.

1.6.1.6.6 Special precaution for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

1.6.1.7 Marketing Authorization Holder And Manufacturing Site Addresses

1.6.1.7.1 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
Email: hiren@lincolnpharma.com
Website: www.lincolnpharma.com

1.6.1.7.2 Name and Address of manufacturing site(s)

Lincoln Pharmaceuticals Limited
Trimul Estate, Khatraj, Taluka: Kalol,
District: Gandhinagar Gujarat, India.
Telephone no.: +91-79-41078096
Fax: +91-79-41078062
Email: hiren@lincolnpharma.com
Website: www.lincolnpharma.com

1.6.1.8 Marketing Authorization Number

To be included after obtaining first registration.

1.6.1.9 Date of First <Registration> / Renewal of The <Registration>

It will be applicable after registration of this product.

1.6.1.10 **Date of Revision of the Text**

1.6.1.11 Dosimetry (If Applicable)

Not Applicable

1.6.1.12 Instructions for preparation of radiopharmaceuticals (if Applicable)

Not Applicable