SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT:

LOX 2%

Lidocaine Injection BP

Strength:

21.3 mg/ml – 50 ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION :

Sr. No.	Particulars	Grade	Qty./ml	Function
1.	Lidocaine Hydrochloride	BP	21.3 mg	Active

For full list of Excipients, see section 6.1.

3. PHARMACEUTICAL FORM :

Solution for Injection.

A clear, colourless solution.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

LOX (Lidocaine HCl) Injections are indicated for production of local or regional anesthesia by infiltration techniques such as intravenous regional anesthesia by peripheral nerve block techniques such as brachial plexus and intercostal and by central neural techniques such as lumbar and caudal epidural blocks.

4.2 Dosage and method of administration:

Recommended Dosages summarizes the recommended volumes and concentrations of Lidocaine Injection for various types of anesthetic procedures. The dosages suggested in this table are for normal healthy adults and refer to the use of epinephrine free solutions.

When larger volumes are required, only solutions containing epinephrine should be used except in those cases where vasopressor drugs may be contraindicated.

MAXIMUM RECOMMENDED DOSAGES:

Adults:

For normal healthy adults, the individual maximum recommended dose of Lidocaine HCl with epinephrine should not exceed 7 mg/kg (3.5 mg/lb) of body weight, and in general it is recommended that the maximum total dose not exceed 500 mg. When used without epinephrine the maximum individual dose should not exceed 4.5 mg/kg (2mg/lb) of body weight, and in general it is recommended that the maximum total dose does not exceed 300 mg.

For continuous epidural or caudal anesthesia, the maximum recommended dosage should not be administered at intervals of less than 90 minutes. When continuous lumbar or caudal epidural anesthesia is used for non-obstetrical procedures, more drugs may be administered if required to produce adequate anesthesia.

The maximum recommended dose per 90 minute period of Lidocaine hydrochloride for paracervical block in obstetrical patients and non-obstetrical patients is 200 mg total. One half of the total dose is usually administered to each side. Inject slowly, five minutes between sides. For intravenous regional anesthesia, the dose administered should not exceed 4 mg/kg in adults.

Children:

It is difficult to recommend a maximum dose of any drug for children, since this varies as a function of age and weight.

For children over 3 years of age who have a normal lean body mass and normal body development, the maximum dose is determined by the child's age and weight. For example, in a child of 5 years weighing 50 lbs the dose of Lidocaine HCl should not exceed 75 to 100 mg (1.5 to 2 mg/lb). The use of even more dilute solutions (i.e., 0.25 to 0.5%) and total dosages not to exceed 3 mg/kg (1.4 mg/lb) are recommended for induction of intravenous regional anesthesia in children.
In order to guard against systemic toxicity, the lowest effective concentration and lowest effective dose should be used at all times. In some cases it will be necessary to dilute available concentrations with 0.9% w/v sodium chloride injection in order to obtain the required final concentration.

NOTE: Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever the solution and container permit. The Injection is not to be used if its color is pinkish or darker than slightly yellow or if it contains a precipitate.

Procedure	**Lidocaine hydrochloride Injection (without Epinephrine)**		
	Conc. (%)	**Vol. (mL)**	**Total Dose (mg)**
Infiltration			
Peripheral Nerve Blocks, e.g.			
Dental	2	1 to 5	20 to 100
Intercostal	1	3	30
Paravertebral	1	3 to 5	30 to 50
Pudendal (each side)	1	10	100
Paracervical			
Obstetrical analgesia (each side)	1	10	100
Cervical (stellate ganglion)	1	5	50
Lumbar	1	5 to 10	50 to 100
Central Neural Blocks			
Epidural*			
Thoracic	1	20 to 30	200 to 300
Lumbar			
Analgesia	1	25 to 30	250 to 300
	2	10 to 15	200 to 300
Obstetrical analgesia	1	20 to 30	200 to 300

***Dose d determined by number of dermatomes to be anesthetized (2 to 3 mL/dermatome).**
The Above Suggested Concentrations and volumes serve only as a Guide. Other Volumes and Concentrations May Be Used Provided the Total Maximum Recommended Dose is Not Exceeded.

Route of Administration: Local Anaesthetic

4.3 Contraindications:

Lidocaine is contraindicated in patients with a known history of hypersensitivity to local anesthetics of the amide type.

4.4 Special warnings and precautions for use:

Intra-articular in fusions of local anesthetics following arthroscopic and other surgical procedures is an unapproved use, and there have been post-marketing reports of chondrolysis in patients receiving such with reference to literature infusions. The majority of reported cases of chondrolysis have involved the shoulder joint.

Local anesthetic solutions containing antimicrobial preservatives (e.g., methyl paraben) should not be used for epidural or spinal anesthesia because the safety of these agents has not been established with regard to intrathecal injection, either intentional or accidental.

LOX with sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.

Precautions: General:

The lowest dosage that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. During the administration of epidural anesthesia, it is recommended that a test dose be administered initially and that the patient be monitored for central nervous system toxicity and cardiovascular toxicity, as well as for signs of unintended intrathecal administration, before proceeding.

When clinical conditions permit, consideration should be given to employing local anesthetic solutions that contain epinephrine for the test dose because circulatory changes compatible with epinephrine may also serve as a warning sign of unintended intravascular injection. An intravascular injection is still possible even if aspirations for blood are negative.

Repeated doses of Lidocaine may cause significant increases in blood levels with each repeated dose because of slow accumulation of the drug or its metabolites. Debilitated, elderly patients, acutely ill patients, and children should be given reduced doses commensurate with their age and physical condition. Lidocaine should also be used with caution in patients with severe shock or heart block. Lumbar and caudal epidural anesthesia should be used with extreme caution in persons with the following conditions: existing neurological disease, spinal deformities, septicemia, and severe hypertension.

LOX Injection should be used with caution in patients with hepatic disease with severe hepatic disease because of their inability to metabolize local anesthetics normally, are at greater risk of developing toxic plasma concentrations. LOX Injection should also be used with caution in patients with impaired cardiovascular function since they may be less able to compensate for functional changes associated with the prolongation of A. V conduction produced by these drugs. Many drugs used during the conduct of anesthesia are considered potential triggering agents for familial malignant hyperthermia.

Use in the Head and Neck Area:

Small doses of local anesthetics 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. Confusion, convulsions, respiratory depression and/or respiratory arrest, and cardiovascular stimulation or depression have been reported.

These reactions may be due to intra-arterial injection of the local anesthetic with retrograde flow to the cerebral circulation. Patients receiving these blocks should have their circulation and respiration monitored and is constantly observed. Dosage recommendations should not be exceeded.

Information for Patients:

When appropriate, patients should be informed in advance that they may experience temporary loss of sensation and motor activity, usually in the lower half of the body, following proper administration of epidural anesthesia.

Drug/Laboratory Test Interactions:

The intramuscular injection of Lidocaine may result in an increase in creatine phosphokinase levels. Thus, the use of this enzyme determination, without isoenzyme separation, as a diagnostic test for the presence of acute myocardial infarction may be compromised by the intramuscular injection of Lidocaine.

Labor and Delivery:
Local anesthetics rapidly cross the placenta and when used for epidural, paracervical, pudendal or caudal block anesthesia, can cause varying degrees of maternal, fetal and neonatal toxicity. Adverse reactions in the parturient, fetus and neonate involve alterations of the central nervous system, peripheral vascular tone and cardiac function.
Maternal hypotension has resulted from regional anesthesia. Local anesthetics produce vasodilation by blocking sympathetic nerves. Epidural, spinal, paracervical, or pudendal anesthesia may alter the forces of parturition through changes in uterine contractility or maternal expulsive efforts. Fetal bradycardia may occur in 20 to 30 percent of patients receiving paracervical nerve block anesthesia with the amide-type local anesthetics and may be associated with fetal acidosis. Fetal heart rate should always be monitored during paracervical anesthesia. Babies so affected present with unexplained neonatal depression at birth, which correlates with high local anesthetic serum levels, and often manifest seizures within six hours. Prompt use of supportive measures combined with forced urinary excretion of the local anesthetic has been used successfully to manage this complication.
Pediatric Use:
Dosages in children should be reduced, commensurate with age, body weight and physical condition.

4.5 Interaction with other medicinal products and other forms of interaction:
Effects of Lidocaine on other medicinal products:
Lidocaine should be used with caution in patients receiving other local anaesthetics or agents structurally related to amide-type local anaesthetics (e.g. anti-arrhythmics, such as mexiletine), since the systemic toxic effects are additive. Specific interaction studies with Lidocaine and class III anti-arrhythmic drugs (e.g. amiodarone) have not been performed, but caution is advised.
There may be an increased risk of enhanced and prolonged neuromuscular blockade in patients treated concurrently with muscle relaxants (e.g. suxamethonium).

Effects of other medicinal products on Lidocaine:
There may be an increased risk of ventricular arrhythmia in patients treated concurrently with antipsychotics which prolong or may prolong the QT interval (e.g. pimozide, sertindole, olanzapine, quetiapine, zotepine), or 5HT3 antagonists (e.g. tropisetron, dolasetron). Concomitant use of quinupristin/dalfopristin should be avoided.
Hypokalaemia produced by acetazolamide, loop diuretics and thiazides antagonises the effect of Lidocaine.
The clearance of Lidocaine may be reduced by beta-adrenoceptor blocking agents (e.g. propranolol) and by cimetidine, requiring a reduction in the dosage of Lidocaine.
Increase in serum levels of Lidocaine may also occur with anti-viral agents (e.g. amprenavir, atazanavir, darunavir, lopinavir).
Cardiovascular collapse has been reported following the use of bupivacaine in patients on treatment with verapamil and timolol; Lidocaine is closely related to bupivacaine.
While adrenaline (epinephrine) when used in conjunction with Lidocaine might decrease vascular absorption, it greatly increases the danger of ventricular tachycardia and fibrillation if accidentally injected intravenously.

4.6 Fertility, pregnancy and lactation:

Pregnancy:

Teratogenic Effects: Pregnancy Category B:

General consideration should be given to this fact before administering Lidocaine to women of childbearing potential, especially during early pregnancy when maximum organogenesis takes place.

Nursing Mothers:

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Lidocaine is administered to a nursing woman.

4.7 Effects on ability to drive and use machines:

Where outpatient anaesthesia 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.

4.8 Undesirable effects:

Systemic:

These adverse experiences are, in general, dose-related and may result from high plasma levels caused by excessive dosage, rapid absorption or inadvertent intravascular injection, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. Serious adverse experiences are generally systemic in nature as following types, those most commonly reported.

Central Nervous System:

CNS manifestations are excitatory and/or depressant and may be characterized by lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred or double vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest.

Cardiovascular System:

Cardiovascular manifestations are usually depressant and are characterized by bradycardia, hypotension, and cardiovascular collapse, which may lead to cardiac arrest.

Allergic:

Allergic reactions are characterized by cutaneous lesions, urticaria, edema or anaphylactoid reactions and may occur as a result of sensitivity either to local anesthetic agents or to the methylparaben used as a preservative in the multiple dose vials.

Neurologic:

With reference to literature caudal or lumbar epidural block, occasional unintentional penetration of the subarachnoid space by the catheter may occur. Subsequent adverse effects may depend partially on the amount of drug administered subdurally. These may include spinal block of varying magnitude (including total spinal block), hypotension secondary to spinal block, loss of bladder and bowel control, and loss of perineal sensation and sexual function.

Persistent motor, sensory and/or autonomic (sphincter control) deficit of some lower spinal segments with slow recovery (several months) or incomplete recovery have been reported in rare instances when caudal or lumbar epidural block has been attempted. Backache and headache have also been noted following use of these anesthetic procedures.

4.9 Overdose:

Acute emergencies from local anesthetics are generally related to high plasma levels encountered during therapeutic use of local anesthetics or to unintended subarachnoid injection of local anesthetic solution.

Management of Local Anesthetic Emergencies:

The first consideration is prevention, best accomplished by careful and constant monitoring of cardiovascular and respiratory vital signs and the patient's state of consciousness after each local anesthetic injection. At the first sign of change, oxygen should be administered. The first step in the management of convulsions, as well as under ventilation or apnea due to unintended subarachnoid injection of drug solution, consists of immediate attention to the maintenance of a patent airway and assisted or controlled ventilation with oxygen and a delivery system capable of permitting immediate positive airway pressure by mask. The clinician should be familiar, prior to the use of local anesthetics, with these anticonvulsant drugs. Supportive treatment of circulatory depression may require administration of intravenous fluids and, when appropriate, a vasopressor as directed by the clinical situation (e.g., ephedrine).

5. PHARMACOLOGICAL PROPERTIES :

5.1 Pharmacodynamic properties :

Mechanism of Action:

Lidocaine stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of impulses thereby effecting local anesthetic action.

Hemodynamics:

Excessive blood levels may cause changes in cardiac output, total peripheral resistance, and mean arterial pressure. With central neural blockade these changes may be attributable to block of autonomic fibers, a direct depressant effect of the local anesthetic agent on various components of the cardiovascular system, and/or the beta-adrenergic receptor stimulating action of epinephrine when present. The net effect is normally a modest hypotension when the recommended dosages are not exceeded.

5.2 Pharmacokinetic properties :

Lidocaine is completely absorbed following parenteral administration, its rate of absorption depending, upon various factors such as the site of administration and the presence or absence of a vasoconstrictor agent. The plasma binding of Lidocaine is dependent on drug concentration, and the fraction bound decreases with increasing concentration.

At concentrations of 1 to 4 mcg of free base per mL 60 to 80 percent of Lidocaine is protein bound. Lidocaine is metabolized rapidly by the liver, and metabolites and unchanged drug are excreted by the kidneys. The pharmacological/ toxicological actions of these metabolites are similar to, but less potent than, those of Lidocaine. The elimination half-life of Lidocaine following an intravenous bolus injection is typically 1.5 to 2 hours. Because of the rapid rate at which Lidocaine is metabolized, any condition that affects liver function may alter Lidocaine kinetics.

The half-life may be prolonged two fold or more in patients with liver dysfunction. Renal dysfunction does not affect Lidocaine kinetics but may increase the accumulation of metabolites.

5.3 Pre-clinical Safety Data:

No further relevant information available.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of Excipients:

Sodium Chloride BP
Sodium Hydroxide BP
Methyl Paraben BP
Water for Injection BP (Bulk)

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.

6.3 Shelf – life:

24 Months

6.4 Special precautions for storage:

Store below 30°C., protected from light. Do not freeze

6.5 Nature and contents of container:

50 ml flint USP type - I Victory vial, stoppered with 20 mm grey bromo butyl rubber stopper & sealed with 20 mm green flip off lacquered "NEON" embossed aluminum seal.

6.6 Special Precautions for Handling and Disposal:

Use as directed by a physician.

7. MARKETING AUTHORIZATION HOLDER:

M/s. NEON LABORATORIES LIMITED
140, Damji Shamji Industrial Complex,
28, Mahal Indl. Estate, Mahakali Caves Road,
Andheri (East), Mumbai - 400 093

8. MARKETING AUTHORIZATION NUMBER :

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