

For the use of a registered medical practitioner or a Hospital or a Laboratory only

## LIGNOCAINE HYDROCHLORIDE INJECTION IP

### LIGNONIR 2%™\*

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#### DESCRIPTION :

LIGNONIR®\* (Lignocaine HCl) injection is sterile, non-pyrogenic, clear, colourless isotonic solutions that contain a local anaesthetic agent. which is chemically designated as acetamide 2-(diethylamino)-N-(2,6-dimethylphenyl)-monohydrochloride and has the molecular wt. 270.8 The pH of this solution is 6.5 (5-7)

#### COMPOSITION :

Each ml contains:

Lignocaine Hydrochloride IP	21.3 mg
Sodium Chloride IP	6.0 mg
Methylparaben IP	1.0 mg
Water for Injections IP	q. s.

#### PHARMACOLOGY :

##### PHARMACODYNAMIC :

Lignocaine is a local anaesthetic of the amide group. It is used to provide local anaesthesia at various sites in the body and it acts by inhibiting the ionic reflexes required for the initiation and conduction of impulses, thereby stabilising the neuronal membrane. In addition to blocking conduction in nerve axons in the peripheral nervous system, Lignocaine has important effects on the central nervous system and cardiovascular system. After absorption, Lignocaine may cause stimulation of the CNS followed by depression. In the cardiovascular system, it acts primarily on the myocardium where it may produce decreases in electrical excitability, conduction rate and force of contraction.

##### PHARMACOKINETIC :

Lignocaine is absorbed from injection sites including muscle and its rate of absorption is determined by factors such as the site of administration and the tissue vascularity. Except for intravascular administration, the highest blood levels occur following intercostal nerve block and the lowest after subcutaneous administration. Lignocaine is bound to plasma proteins, including alpha-1-acid-glycoprotein. The drug crosses the blood-brain and placental barriers.

Lignocaine is metabolised 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 Lignocaine. Further metabolism occurs and metabolites are excreted in the urine with less than 10 % of unchanged Lignocaine.

##### THERAPEUTIC INDICATIONS :

Lignocaine Injection is used as a local anaesthetic.

When injected into the skin, it causes loss of feeling before or during surgery

**DOSAGE & ADMINISTRATION :**

Lignocaine Injection is used as a local anaesthetic when injected subcutaneously.

This solution is not intended for use intravenously. Solutions of Lignocaine, which contain preservatives, should not be used for spinal, epidural, caudal or intravenous regional anaesthesia.

The dosage should be adjusted according to the response of the patient and the site of administration.

The lowest concentration and the smallest dose producing the required effect should be given. The maximum dose for healthy adults should not exceed 200 mg corresponding to 20 mls.

Children and elderly or debilitated patients require smaller doses, commensurate with age and physical status. Dosages should be reduced in patients with cardiac and/or liver disease.

The injection may be used for infiltration in volumes of 1 ml to 60 ml.

**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 Lignocaine HCl should not exceed 75–100 mg (1.5 to 2 mg/lb).

The onset of anesthesia, the duration of anesthesia and the degree of muscular relaxation are proportional to the volume and concentration (ie, total dose) of local anesthetic used. Thus, an increase in volume and concentration of Lignocaine Injection will decrease the onset of anesthesia, prolong the duration of anesthesia, provide a greater degree of muscular relaxation and increase the segmental spread of anesthesia. Although the incidence of side effects with Lignocaine HCl is quite low, caution should be exercised when employing large volumes and concentrations, since the incidence of side effects is directly proportional to the total dose of local anesthetic agent injected.

**CONTRAINDICATIONS :**

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

**WARNINGS :**

Lidocaine injections for infiltration and nerve block should be employed only by clinicians who are well versed in diagnosis and management of dose-related toxicity and other acute emergencies that might arise from the block to be employed and then only after ensuring the immediate availability of oxygen, other resuscitative drugs, cardiopulmonary equipment, and the personnel needed for proper management of toxic reactions and related emergencies (see also adverse reactions and precautions). Delay in proper management of dose-related toxicity, underventilation from any cause and/or altered sensitivity may lead to the development of acidosis, cardiac arrest and possibly death.

To avoid intravascular injection, aspiration should be performed before the local anaesthetic solution is injected. The needle must be repositioned until no return of blood can be elicited by aspiration. Note, however, that the absence of blood in the syringe does not guarantee that intravascular injection has been avoided.

Lidocaine injection solutions contain methylparaben as a preservative. Local anaesthetic solutions containing antimicrobial preservatives (e.g. methylparaben) should not be used for epidural or spinal anaesthesia because the safety of these agents has not been established with regard to intrathecal

injection, either intentional or accidental.

**CONTRAINDICATIONS :**

Lignocaine Injection is contraindicated in

- Known hypersensitivity to Lignocaine or other anaesthetics of the amide type
- Complete heart block
- Hypovolaemia

**SPECIAL WARNINGS AND PRECAUTIONS :**

Solutions of Lignocaine, which contain preservatives, are not suitable for spinal, epidural or caudal anaesthesia. Adverse effects reported following unpreserved Lignocaine solutions administered by this route include hypotension and isolated cases of bradycardia and cardiac arrest.

As with other local anaesthetics, Lignocaine should be used with caution in patients with epilepsy, cardiac conduction disturbances, congestive cardiac failure, bradycardia, severe shock, impaired respiratory function or impaired renal function with a creatinine clearance of less than 10mL/minute.

Lignocaine is metabolised in the liver and it should be used with caution in patients with impaired hepatic function. Lignocaine should not be used in cases of acute porphyrias.

Patients with myasthenia gravis are particularly susceptible to the effects of local anaesthetics.

Lignocaine HCl should be used with caution in persons with known drug sensitivities. Patients allergic to para-aminobenzoic acid derivatives (procaine, tetracaine, benzocaine, etc) may not have cross-sensitivity to Lignocaine HCl.

Facilities for resuscitation should be available when administering local anaesthetics.

The effect of local anaesthetics may be reduced if the injection is made into an inflamed or infected area.

Certain local anaesthetic procedures may be associated with serious adverse reactions, regardless of the local anaesthetic drug used.

- Retrobulbar injections may rarely reach the cranial subarachnoid space, causing serious/severe reactions, including cardiovascular collapse, apnoea, convulsions and temporary blindness
- Retro- and peribulbar injections of local anaesthetics carry a low risk of persistent ocular motor dysfunction. The primary causes include trauma and/or local toxic effects on muscles and/or nerves.

The severity of such tissue reactions is related to the degree of trauma, the concentration of the local anaesthetic and the duration of exposure of the tissue to the local anaesthetic. For this reason, as with all local anaesthetics, the lowest effective concentration and dose of local anaesthetic should be used.

**LIGNOCAINE INJECTIONS FOR INFILTRATION AND NERVE BLOCK SHOULD BE EMPLOYED ONLY BY CLINICIANS WHO ARE WELL VERSED IN DIAGNOSIS AND MANAGEMENT OF DOSE-RELATED TOXICITY**

AND OTHER ACUTE EMERGENCIES THAT MIGHT ARISE FROM THE BLOCK TO BE EMPLOYED AND THEN ONLY AFTER ENSURING THE IMMEDIATE AVAILABILITY OF OXYGEN, OTHER RESUSCITATIVE DRUGS, CARDIOPULMONARY EQUIPMENT AND THE PERSONNEL NEEDED FOR PROPER MANAGEMENT OF TOXIC REACTIONS AND RELATED EMERGENCIES.

DELAY IN PROPER MANAGEMENT OF DOSE-RELATED TOXICITY, UNDERVENTILATION FROM ANY CAUSE AND/OR ALTERED SENSITIVITY MAY LEAD TO THE DEVELOPMENT OF ACIDOSIS, CARDIAC ARREST AND, POSSIBLY, DEATH.

Lignocaine Injection is not recommended for use in neonates. The optimum serum concentration of Lignocaine required to avoid toxicity, such as convulsions and cardiac arrhythmias, in this age group is not known.

Intra-articular infusions of local anesthetics following arthroscopic and other surgical procedures is an unapproved use, and there may be chances of chondrolysis in patients receiving such infusions. Chondrolysis mainly involve the shoulder joint; Gleno-humeral chondrolysis may occur in pediatric and adult patients following intra-articular infusions of local anesthetics for periods of 48 to 72 hours. There is insufficient information to determine whether shorter infusion periods are not associated with these findings. The time of onset of symptoms, such as joint pain, stiffness and loss of motion can be variable, but may begin as early as the 2nd month after surgery. Currently, there is no effective treatment for chondrolysis. patients who experienced chondrolysis have required additional diagnostic and therapeutic procedures and some required arthroplasty or shoulder replacement.

Careful and constant monitoring of cardiovascular and respiratory (adequacy of ventilation) vital signs and the patient's state of consciousness should be accomplished after each local anesthetic injection. It should be kept in mind at such times that restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors, depression or drowsiness may be early warning signs of central nervous system toxicity.

Since amide-type local anesthetics are metabolized by the liver, Lignocaine Injection should be used with caution in patients with severe hepatic disease, because of their inability to metabolize local anesthetics normally, are at greater risk of developing toxic plasma concentrations. Lignocaine 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. Since it is not known whether amide-type local anesthetics may trigger this reaction and since the need for supplemental general anesthesia cannot be predicted in advance, it is suggested that a standard protocol for the management of malignant hyperthermia should be available.

Early unexplained signs of tachycardia, tachypnea, labile blood pressure and metabolic acidosis may precede temperature elevation. Successful outcome is dependent on early diagnosis, prompt discontinuance of the suspect triggering agent(s) and institution of treatment, including oxygen therapy, indicated supportive measures and dantrolene (consult dantrolene sodium intravenous package insert before using).

### **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 may occur. 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 be constantly observed. Resuscitative equipment and personnel for treating adverse reactions should be immediately available. Dosage recommendations should not be exceeded.

### **PREGNANCY AND LACTATION :**

#### **Pregnancy**

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

Lignocaine given by local perineal infiltration prior to delivery crosses rapidly into the foetal circulation. Elevated Lignocaine 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 Lignocaine are secreted into breast milk and the possibility of an allergic reaction in the infant, albeit remote, should be borne in mind when using Lignocaine in nursing mothers.

### **DRUG INTERACTIONS :**

The clearance of Lignocaine may be reduced by beta-adrenoceptor blocking agents (e.g. propranolol) and by cimetidine, requiring a reduction in the dosage of Lignocaine. Increase in serum levels of Lignocaine may also occur with anti-viral agents (e.g. amprenavir, atazanavir, darunavir, lopinavir).

Lignocaine 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 Lignocaine and class III anti-arrhythmic drugs (e.g. amiodarone) have not been performed, but caution is advised. 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 5HT<sub>3</sub> antagonists (e.g. tropisetron, dolasetron).

Concomitant use of quinupristin/dalfopristin should be avoided.

There may be an increased risk of enhanced and prolonged neuromuscular blockade in patients treated concurrently with muscle relaxants (e.g. suxamethonium).

### **ADVERSE REACTIONS :**

In common with other local anaesthetics, adverse reactions to Lignocaine 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

#### *Immune system disorders*

Hypersensitivity reactions (allergic or anaphylactoid reactions, anaphylactic shock)

Skin testing for allergy to Lignocaine is not considered to be reliable.

#### *Nervous & Psychiatric disorders*

Neurological signs of systemic toxicity include dizziness or light-headedness, nervousness, tremor, circumoral paraesthesia, tongue numbness, drowsiness, convulsions, coma.

CNS reactions may be excitatory and/or depressant and may manifest as nervousness, tremor, blurred vision, nausea and vomiting, followed by drowsiness, convulsions, coma and possible respiratory arrest. The excitatory reactions may be brief or may not occur at all, so that the first signs of toxicity may be drowsiness, followed by coma and respiratory failure. Cardiovascular reactions are depressant and may manifest as hypotension, bradycardia, myocardial depression and possible cardiac arrest.

Allergic reactions are rare. They may be characterised by cutaneous lesions, urticaria, oedema or anaphylactoid reactions. Skin testing for allergy to lidocaine is not considered to be reliable.

#### *Eye disorders*

Blurred vision, diplopia and transient amaurosis may be signs of Lignocaine toxicity.

Bilateral amaurosis may also be a consequence of accidental injection of the optic nerve sheath during ocular procedures.

Orbital inflammation and diplopia may occur following retro- or peribulbar anaesthesia

#### *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

**OVERDOSE :**

Symptoms of acute systemic toxicity

Central nervous system toxicity presents with symptoms of increasing severity. Patients may present initially with circumoral paraesthesia, numbness of the tongue, light-headedness, hyperacusis and tinnitus. Visual disturbance and muscular tremors or muscle twitching are more serious and precede the onset of generalised convulsions. These signs must not be mistaken for neurotic behaviour. Unconsciousness and grand mal convulsions may follow, which may last from a few seconds to several minutes. Hypoxia and hypercapnia occur rapidly following convulsions due to increased muscular activity, together with the interference with normal respiration and loss of the airway. In severe cases, apnoea may occur. Acidosis increases the toxic effects of local anaesthetics.

Effects on the cardiovascular system may be seen in severe cases. Hypotension, bradycardia, arrhythmia and cardiac arrest may occur as a result of high systemic concentrations, with potentially fatal outcome.

Recovery occurs as a consequence of redistribution of the local anaesthetic drug from the central nervous system, and metabolism and may be rapid unless large amounts of the drug have been injected.

*Treatment of acute toxicity*

If signs of acute systemic toxicity appear, injection of the local anaesthetic should be stopped immediately.

Treatment will be required if convulsions and CNS depression occurs. The objectives of treatment are to maintain oxygenation, stop the convulsions and support the circulation.

A patent airway should be established and oxygen should be administered, together with assisted ventilation (mask and bag) if necessary. The circulation should be maintained with infusions of plasma or intravenous fluids. Where further supportive treatment of circulatory depression is required, use of a vasopressor agent may be considered although this involves a risk of central nervous system excitation.

If the convulsions do not stop spontaneously in 15-20 seconds, they may be controlled by the intravenous administration of diazepam or thiopentone sodium, bearing in mind that anti-convulsant drugs may also depress respiration and the circulation. If cardiac arrest should occur, standard cardiopulmonary resuscitation procedures should be instituted.

Dialysis is of negligible value in the treatment of acute overdosage with Lignocaine.

**INCOMPATIBILITIES :**

Lignocaine causes precipitation of amphotericin, methohexitone sodium and sulphadiazine sodium in glucose injection.

It is recommended that admixtures of Lignocaine and glyceryl trinitrate should be avoided

**STORAGE :**

Store in cool, dark place. Do not freeze.

**PRESENTATION :**

LIGNONIR 2%™\* is available in 20 mL, 30 mL, 50 mL vials

***aculife***®

Manufactured in India by:

Aculife Healthcare Pvt. Ltd.

Sachana, Gujarat 382150, India.

\* TM owners-Nirma Ltd.