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2. Trade Name:
   • Lidocaine Hydrochloride Pharmacell injection 2%

3. Generic Name
   • Lidocaine Hydrochloride injection 2%.

4. COMPOSITION
   • Lidocaine Hydrochloride Pharmacell 20 ml vial solution for injection contains 400 mg lidocaine hydrochloride.
   • Lidocaine Hydrochloride Pharmacell 50 ml vial solution for injection contains 1000 mg lidocaine hydrochloride.

5. PHARMACEUTICAL FORM
   Vial Contains solution for injection through infiltration anaesthesia by injection, intravenous regional anaesthesia & nerve blocks.

6. Pharmacological action
   Lidocaine Hydrochloride Pharmacell is a local anaesthetic of the amide type. 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, Lidocaine has important effects on the central nervous system and cardiovascular system. After absorption Lidocaine may cause stimulation of the CNS followed by depression and in the cardiovascular system, it acts primarily on the myocardium where it may produce decreases in electrical excitability, conduction rate and force of contraction.

7. Pharmacokinetic properties
   Lidocaine Hydrochloride Pharmacell 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. Lidocaine is bound to plasma proteins, including alpha-1-acid-glycoprotein. The drug crosses the blood brain and placental barriers.

   Lidocaine Hydrochloride Pharmacell is metabolised in the liver and about 90% of a given dose undergoes N-dealkylation to form monoethylglycinexylidide and glycineyxlidide, 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.

8. Indications
   Suppression of ventricular extrasystoles and ventricular tachycardia, especially after an acute myocardial infarction. Local anaesthesia by surface infiltration, regional, epidural and caudal routes, dental anaesthesia, either alone or in combination with adrenaline.

   Lidocaine Hydrochloride Pharmacell may also be administered by subcutaneous, intramuscular or intravenous injection.

   Not intended for use in the eye.

9. Dosage and administration
   The usual adult I.V. bolus dose is 50-100 mg administered at a rate of approximately 25-50 mg per minute. If the desired response is not achieved, a second dose may be administered 5 minutes after completion of the first injection. Not more than 200-300 mg should be administered during a one hour period. Elderly patients and those with congestive heart failure or cardiogenic shock may require smaller bolus doses.
In ventricular arrhythmias

Maintenance infusion of a 0.2 or 0.4% solution in 5% glucose.
Adults: 20-50 micrograms/kg/minute (1-4 mg/minute in an average 70 kg adult).
Slower infusion rates should be used in patients with congestive heart failure or liver disease; no dosing modification appears necessary in patients with renal failure. When arrhythmias reappear during a constant infusion of Lidocaine, a small bolus may be given to rapidly increase plasma concentration of the drug; the infusion rate is increased simultaneously. The infusion should be terminated as soon as the patient's basic cardiac rhythm appears to be stable or at the earliest sign of toxicity.
Infants and children may be given an initial I.V. bolus of 0.5-1 mg/kg. This dose may be repeated according to the response of the patient, but the total dose should not exceed 3-5 mg/kg. A maintenance I.V. infusion of 10-50 micrograms/kg per minute may be given via an infusion pump.
For advanced cardiac life support in children, the recommended dosage is an initial I.V. bolus of 1 mg/kg. If ventricular tachycardia or ventricular fibrillation is not corrected following defibrillation and an initial bolus, an I.V. infusion should be started at a rate of 20-50 mcg/kg per minute.
Constant ECG monitoring is recommended during therapy with Lidocaine Hydrochloride, however if this equipment is not available and a ventricular arrhythmia is suspected, a single I.M. dose may be administered if bradycardia is not present. The deltoid muscle is the preferred site for I.M. injection.

In Local Anaesthesia

Usual doses should generally be reduced in children and in elderly or debilitated patients. To minimise the possibility of toxic reactions, children should be given Lidocaine Hydrochloride solutions in concentrations of 0.5% or 1%.
Single doses of Lidocaine (for anaesthesia other than spinal) should not exceed 4.5 mg/kg (or 200 mg) in adults or children. For spinal anaesthesia, up to 100 mg of the drug may be given. For continuous epidural or caudal anaesthesia, the maximum dose should not be repeated at intervals of less than 1.5 hours. For paracervical block for obstetric analgesia (including abortion) the maximum recommended dosage (200 mg) should not be repeated at intervals of less than 1.5 hours. For I.V. regional anaesthesia in adults using a 0.5% solution, the dose administered should not exceed 4 mg/kg.
Solutions of 1% Lidocaine Hydrochloride (without preservative) are used for epidural or caudal anaesthesia. To prevent intravascular or subarachnoid injection of a large epidural dose of Lidocaine, a test dose of 2-5 mls should be injected at least 5 minutes prior to administering the total dose.
In epidural anaesthesia 2-3 mls of 1% solution is usually required for each dermatone to be anaesthetised. In caudal block for production of obstetric analgesia or in epidural thoracic block, 20-30 mls of a 1% solution (200-300 mg) of the drug may be used.
For epidural lumbar anaesthesia, the dose is 25-30 mls (250-300 mg) of a 1% solution. For intercostal nerve block: 3 mls of a 1% solution (30 mg).
For paravertebral nerve block: 3-5 mls of a 1% solution (30-50 mg).
For pudendal nerve block (each side): 10 mls of a 1% solution (100 mg).
For paracervical nerve block (each side) for obstetric analgesia: 10 mls of a 1% solution (100 mg). For sympathetic nerve blocks: Cervical (stellate ganglion) nerve block: 5 mls of a 1% solution (50 mg). Lumbar nerve block: 5-10 mls of a 1% solution (50-100Mg).
For percutaneous infiltration anaesthesia: 1-60 mls of a 0.5-1% solution (5-300 mg).
For I.V. regional anaesthesia: 10-60 mls of 0.5% solution (50-300 mg).

10. Contraindications

Known hypersensitivity to lidocaine or other anaesthetics of the amide type.
In ventricular arrhythmia
- Sino-atrial disorders
- All grades of atrioventricular block
- Severe myocardial depression
- Porphyria (use with caution in local anaesthesia)
Local anaesthesia
- Complete heart block
- Hypovolaemia
11. Side Effect
In common with other local anaesthetics, 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. Systematic toxicity mainly involves the central nervous system and/or the cardiovascular system.

Immune system disorders:
Hypersensitivity reactions (allergic or anaphylactoid reactions, anaphylactic shock) – see also Skin & subcutaneous tissue disorders
Skin testing for allergy to Lidocaine 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.
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.
Hypotension may accompany spinal and epidural anaesthesia. Isolated cases of bradycardia and cardiac arrest have also been reported.
Respiratory, thoracic or mediastinal disorders
Dyspnoea, bronchospasm, respiratory depression, respiratory arrest

Gastrointestinal:
Nausea, vomiting

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

12. 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 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. Prolonged convulsions may jeopardise the patient's ventilation and oxygenation and early endotracheal intubation should be considered. If cardiac arrest should occur, standard cardiopulmonary resuscitation procedures should be instituted. Continual optimal oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance. Dialysis is of negligible value in the treatment of acute overdosage with Lidocaine.

13. Drug interaction
The clearance of Lidocaine may be reduced by beta-adrenoceptor blocking agents (e.g. propranolol) and 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). 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 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. There may be an increased risk of enhanced and prolonged neuromuscular blockade in patients treated concurrently with muscle relaxants (e.g. suxamethonium).

14. Pregnancy and lactation

Pregnancy
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 Hydrochloride Pharmacell** given by epidural or paracervical block, especially in large doses, or 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.

15. Precaution and warning effects
As with other local anaesthetics, Lidocaine should be used with caution in patients with epilepsy, myasthenia gravis, cardiac conduction disturbances (see also section 4.3), congestive heart failure, bradycardia, severe shock, impaired respiratory function or impaired renal function with a creatinine clearance of less than 10mL/minute. **Lidocaine Hydrochloride Pharmacell** is metabolised in the liver and it should be used with caution in patients with impaired hepatic function. Lower doses should be used in congestive cardiac failure and following cardiac surgery (See 4.2 Posology).

Hypokalaemia, hypoxia and disorders of acid-base balance should be corrected before treatment with intravenous lidocaine begins.

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.

- Central nerve blocks may cause cardiovascular depression, especially in the presence of hypovolaemia, and therefore epidural anaesthesia should be used with caution in patients with impaired cardiovascular function.
- Epidural anaesthesia may lead to hypotension and bradycardia. This risk can be reduced by preloading the circulation with crystalloidal or colloidal solutions. Hypotension should be treated promptly.
• Paracervical block can sometimes cause foetal bradycardia or tachycardia, and careful monitoring of the foetal heart rate is necessary.

• Injections in the head and neck regions may be made inadvertently into an artery, causing cerebral symptoms even at low doses.

• 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.

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

16. Package & Storage
Protect from light and store at less than 25° C. Lidocaine Hydrochloride Pharmacell vial solution for injection will be supplied in clear Type I European Pharmacopeia glass vials (20 ml or 50ml) sealed with rubber closure and flip off cap in a carton box with inner leaflet. The rubber stopper of the vials does not contain latex.

17. Instruction to Patient
Before you receive your medicine
Lidocaine hydrochloride Pharmacell should not be used in patients who are allergic to lidocaine hydrochloride, or to one or more of the ingredients of Lidocaine Hydrochloride Pharmacell Injection 2%. Tell your doctor if you ever had an allergic or bad reaction, for example, skin rash or breathlessness, to any local anaesthetic medicines. Before you receive this medicine, you should also tell your doctor if:
• you suffer from heart, lung or breathing disorder
• you have kidney or liver disease
• you are feeling unwell or run down for any reason
• you suffer from epilepsy or have fits
• you are pregnant or breast-feeding
• you have inflammation or infection in the area to be injected.
You should also tell your doctor if you are taking any other medication, in particular any of the following:
• cimetidine (for stomach ulcer or heartburn)
• beta-blockers, for example, propranolol, (for angina, high blood pressure or other heart problems).

Driving and Operating Machinery: Depending on where and how lidocaine hydrochloride is used, it may affect your ability to drive or operate machinery. Ask your doctor about when it would be safe to drive or operate machines.

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