

LYCAN INJECTION 1% W/V

Active Ingredient:

Lidocaine Hydrochloride10mg/ml

Product Description:

A clear and colourless solution.

Pharmacodynamics:

1. Lidocaine is used to provide anaesthesia by nerve blockade at various sites in the body and in the control of dysrhythmias.
2. It has a rapid onset of action (about one minute following intravenous injection and fifteen minutes following intramuscular injection) and rapidly spreads through the surrounding tissues.
3. The effect lasts about ten to twenty minutes and about sixty to ninety minutes following intravenous and intramuscular injection respectively.

Pharmacotherapeutic group:

Anaesthetics, local, amides

Pharmacokinetics:

The concentration of Lidocaine in the blood will be determined by its rate of absorption from the site of injection, the rate of tissue distribution and the rate of metabolism and excretion.

Absorption

The systemic absorption of Lidocaine is determined by the site of injection, the dosage and its pharmacological profile. The maximum blood concentration occurs following intercostal nerve blockade followed in order of decreasing concentration, the lumbar epidural space, brachial plexus site and subcutaneous tissue. The total dose injected regardless of the site is the primary determinant of the absorption rate and blood levels achieved. There is a linear relationship between the amount of Lidocaine injected and the resultant peak anaesthetic blood levels. The lipid solubility and vasodilator activity will also influence its rate of absorption.

Distribution

Lidocaine is distributed throughout the total body water. Its rate of disappearance from the blood can be described by a two or three compartment model. There is a rapid disappearance (Alpha phase) which is believed to be related to uptake by rapidly equilibrating tissues (i.e. tissues with a high vascular perfusion). The slower phase is related to distribution, to slowly equilibrating tissues (Beta phase) and to its metabolism and excretion (Gamma phase). In general, the more highly perfused organs will show higher concentrations of Lidocaine. The highest percentage of this drug will be found in skeletal muscle. This is because of the mass of muscle rather than an affinity.

Biotransformation

Lidocaine undergoes enzymatic degradation primarily in the liver. Some degradation may take in tissues other than liver. The main pathway involves oxidative de-ethylation to monoethylglycinexylidide followed by a subsequent hydrolysis to xylidine.

Elimination

The excretion occurs via the kidney with less than 5% in the unchanged form appearing in the urine. The renal clearance is inversely related to its protein binding affinity and the pH of the urine. This suggests by the latter that excretion of Lidocaine occurs by non-ionic diffusion.

Indication(s):

Lidocaine is intended for the production of local or regional anaesthesia by nerve block, infiltration injection, caudal or other epidural blocks.

Treatment or prophylaxis of life-threatening ventricular arrhythmias, including those associated with myocardial infarction, general anaesthesia in patients predisposed to ventricular arrhythmias, digitalis intoxication, or following resuscitation from cardiac arrest.

Dosage and Administration:

Lidocaine Injection is for one dose in one patient only, discard any remaining contents.

As a local anaesthetic for infiltration and nerve block:

The dosage varies and depends upon the area to be anaesthetised, vascularity of the tissues, number of neuronal segments to be blocked, individual tolerance and the technique of anaesthesia. The lowest dose needed to provide effective anaesthesia should be administered. For specific techniques and procedures, refer to standard textbooks.

It is recommended that the dose of lidocaine at any one time should not exceed 3mg/kg. However, the dose administered must be tailored to the individual patient and procedure, and the maximum doses here quoted should be used as a guide only.

Adult

The normal recommended dosage of lidocaine for various anaesthetic procedures in average, healthy 70kg adult patients are as follows:

Procedure	Concentration (%)	Volume (ml)	Dose (mg)
Infiltration	1.0	20	200
Peripheral Nerve Blocks			
Paravertebral	1.0	3-5	30-50
Pudendal (each side)	1.0	10	100
Paracervical	1.0	10	100
Sympathetic Nerve Blocks			
Cervical (stellate ganglion)	1.0	5	50
Lumbar	1.0	10	100
Epidural Blocks (2-3ml per segment)			
Thoracic	1.0	10-20	100-200
Lumbar-analgesia	1.0	10-20	100-200
Lumbar - anaesthesia	2.0	5-10	100-200
Caudal-obstetric analgesia	1.0	10-20	100-200

The doses suggested above are only a guide. Toxic levels vary widely between patients so doses should be individualised and blood levels should be monitored.

Epidural injections should be administered slowly with frequent aspirations. Subarachnoid and intravascular injections are two of the most serious complications of this technique. If blood or spinal fluid becomes manifest during aspiration, the needle must be withdrawn and relocated.

The technique of epidural anaesthesia should only be attempted by physicians skilled in this area and readiness for emergencies must be ensured. During spinal anaesthesia the positioning of the patient is very important and the patient's pulse and blood pressure should be monitored. 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.

For continuous epidural or caudal anaesthesia and paracervical block for obstetric analgesia the maximum dose should not be repeated at intervals of less than 1.5 hours.

Adults: The dose should not exceed 200mg. For spinal anaesthesia, the dose should not exceed 100mg.

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. Early signs of local anaesthetic toxicity may be difficult to detect in cases where the block is given during general anaesthesia. The dose should not exceed 3mg/kg.

For intravenous use in cardiac arrhythmias:

Patients with congestive heart failure or cardiogenic shock may require smaller bolus doses.

Adults: The usual dose is lidocaine 50 to 100mg administered intravenously under ECG monitoring. The dose may be injected at a rate of approximately 25 to 50 mg (2.5 to 5.0 mL of the lidocaine 1% solution) per minute. A sufficient period of time should be allowed to enable a slow circulation to carry the drug to the site of action. If the initial dose of 50 to 100mg does not produce the desired response, a second dose may be given after five minutes. No more than 200 to 300mg of lidocaine should be administered during a one hour period.

Following a single injection in those patients in whom arrhythmia tends to recur and who are incapable of receiving oral antiarrhythmic therapy, intravenous infusions of lidocaine may be administered at a rate of 1 to 4mg/minute (20 to 50 mcg/kg/minute). Intravenous infusions must be given under ECG monitoring to avoid potential overdosage and toxicity. The infusion should be terminated as soon as the patient's cardiac rhythm appears to be stable or at the earliest signs of toxicity. It should rarely be necessary to continue the infusion beyond 24 hours. As soon as possible, patients should be changed to an oral antiarrhythmic agent for maintenance therapy.

Paediatrics: For children, a reduced dose based on body weight or surface area should be used. Experience with lidocaine is limited. A suggested paediatric dose is a loading dose of 0.5 to 1mg/kg repeated if necessary up to 3-5mg/kg, followed by continuous infusions of 10 to 50 micrograms/kg/min.

Use in elderly

A reduction in dosage may be necessary for elderly patients especially those with compromised cardiovascular and/or hepatic function.

Impaired hepatic function

Although lidocaine is metabolised by the liver, dosage reduction for local anaesthesia is probably not warranted. However, caution should be exercised with repeated doses.

Impaired renal function

Impairment of renal function is unlikely to affect lidocaine clearance in short term (24 hours). However, toxicity due to accumulation may develop with prolonged or repeated administration.

Route of Administration:

Subcutaneous (SC), Intramuscular (IM) or Intravenous (IV) injection

Contraindication(s):

1. Hypersensitivity to the active substance, to anaesthetics of the amide type or to any of the excipients.
2. Lidocaine is contraindicated in patients with complete heart block and hypovolaemia.
3. Inflammation or sepsis at the proposed site of injection and in the presence of septicaemia.
4. Patients with myasthenia gravis, severe shock or impaired cardiac conduction.
5. Epidural or spinal anaesthesia in patients with
 - uncorrected hypotension or
 - coagulation disorders or receiving anticoagulants or
 - serious diseases of the central nervous system or spinal cord such as meningitis, spinal fluid block, cranial or spinal haemorrhage, tumours, poliomyelitis, syphilis, tuberculosis or metastatic lesions of the spinal cord.
6. Antiarrhythmic use in patients with
 - supraventricular arrhythmia or
 - Stokes - Adams syndrome or severe degrees of sinoatrial, atrioventricular or intraventricular block unless the patient has an artificial pacemaker.
7. Lidocaine suppresses ventricular pacemaker activity and may cause ventricular standstill in such patients.
8. General contraindications related to epidural anaesthesia, regardless of the local anaesthetic used, should be taken into account.

Warning(s) and Precaution(s):

1. Lidocaine should be administered by persons with resuscitative skills and equipment. Facilities for resuscitation should be available when administering local anaesthetics.
2. It should be used with caution in patients with myasthenia gravis, epilepsy, congestive heart failure, bradycardia or respiratory depression, including where agents are known to interact with lidocaine either to increase its availability or additive effects e.g. phenytoin or prolong its elimination e.g. hepatic or end renal insufficiency where the metabolites of lidocaine may accumulate.
3. Intramuscular lidocaine may increase creatinine phosphokinase concentrations which can interfere with the diagnosis of acute myocardial infarction.
4. The effect of lidocaine may be reduced if it is injected into inflamed or infected areas.
5. Hypokalaemia, hypoxia and disorder of acid-base balance should be corrected before treatment with intravenous lidocaine begins.
6. Certain local anaesthetic procedures may be associated with serious adverse reactions, regardless of local anaesthetic drug used.
7. 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.
8. 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.
9. Paracervical block can sometimes cause foetal bradycardia or tachycardia and careful monitoring of the foetal heart rate is necessary.
10. Injections in the head and neck regions may be made inadvertently into an artery causing cerebral symptoms even at low doses.
11. Retrobulbar injections may rarely reach the cranial subarachnoid space, causing serious/severe reactions including cardiovascular collapse, apnoea, convulsions and temporary blindness.
12. 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.
13. 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 local anaesthetic. For this reason, as with all local anaesthetic, the lowest effective concentration and dose of local anaesthetic should be used.
14. Paediatric population: 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.

Interactions with Other Medicaments:

1. Lidocaine toxicity is enhanced, by the co-administration of cimetidine and propranolol requiring a reduction in the dosage of lidocaine. Both drugs decrease hepatic blood flow. Also, cimetidine depresses microsomal activity. Ranitidine produces a small reduction in lidocaine clearance. Increase in serum levels of lidocaine may also occur with anti-viral agents (e.g. amprenavir, atazanavir, darunavir, lopinavir).
2. Hypokalaemia caused by diuretics may antagonize the action of lidocaine if administered concomitantly.
3. 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.
4. 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), prenylamine, adrenaline (if accidentally injected intravenously) or 5-HT₃ antagonists (e.g. tropisetron, dolasetron).

5. Concomitant use of quinupristin/dalfopristin may increase lidocaine levels with a subsequent increased risk of ventricular arrhythmias and therefore should be avoided.
6. There may be an increased risk of enhanced and prolonged neuromuscular blockade in patients treated concurrently with muscle relaxants (e.g. suxamethonium).
7. Cardiovascular collapse has been reported following the use of bupivacaine in patients on treatment with verapamil and timolol.
8. Dopamine and 5-hydroxytryptamine reduce the convulsant threshold to lidocaine.
9. Narcotics are probably proconvulsants and this would support the evidence that lidocaine reduces the seizure threshold to fentanyl in man.
10. Opioid-antiemetic combination sometimes used for sedation in children could reduce the convulsant threshold to lidocaine and increase the CNS depressant effect.
11. While adrenaline when used in conjunction with lidocaine might decrease vascular absorption, it greatly increases the danger of ventricular tachycardia and fibrillation if accidentally injected intravenously.

Pregnancy and lactation:

Pregnancy

Lidocaine should not be administered during early pregnancy unless the benefits are considered to outweigh the risks. Lidocaine readily crosses the placental barrier after epidural or intravenous administration to the mother. Foetal bradycardia or tachycardia, neonatal bradycardia, hypotonia or respiratory depression may occur.

Breast-feeding

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.

Side Effects:

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. 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 Lidocaine is not considered to be reliable.

Nervous and psychiatric disorder

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.

Blood and lymphatic system disorders

Lidocaine may also result in methaemoglobinaemia.

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.

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 anesthesia. Isolated cases of bradycardia and cardiac arrest have also been reported.

Respiratory, thoracic or mediastinal disorders

Dyspnoea, bronchospasm, respiratory depression, respiratory arrest.

Gastrointestinal disorders

Nausea, vomiting.

Skin and subcutaneous tissue disorders

Rash, urticaria, angioedema, face oedema.

Effects on Ability to Drive and Use Machine:

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

Overdose and Treatment:

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 CNS excitation. Convulsions may be controlled by the intravenous administration of Diazepam or Thiopentone Sodium, bearing in mind that anti-convulsant drugs may also depress respiration and circulation. Prolonged convulsions may jeopardize 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.

Instruction for use:

For single use only.

Incompatibilities:

Lidocaine has been found to be incompatible when mixed with amphotericin, methohexitone and glyceryl trinitrate.

Storage Conditions:

Store at temperature below 30°C.

The product is for single use only. Use immediately after opening. Discard unused portion.

Dosage forms and packaging available:

5mlx10 ampoules, 5mlx50 ampoules

Shelf Life:

3 years from the manufacturing date.



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