SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lidocaine 2% w/v solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of solution for injection contains 20 mg lidocaine hydrochloride.

Each 2 ml of solution for injection contains 40 mg lidocaine hydrochloride

Each 5 ml of solution for injection contains 100 mg lidocaine hydrochloride.

Each 10 ml of solution for injection contains 200 mg lidocaine hydrochloride.

Excipient(s) with known effect:

Each ml of solution for injection contains approximately 1.9 mg (0.08 mmol) sodium.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Lidocaine is a local anaesthetic of the amide group. Lidocaine solution for injection is indicated for use in infiltration anaesthesia, intravenous regional anaesthesia and nerve blocks.

4.2 Posology and method of administration

The method of administration of lidocaine varies according to the procedure (infiltration anaesthesia, intravenous regional anaesthesia or nerve block).

The dosage should be adjusted according to the response of the patient and the site of administration. The lowest concentration and smallest dose producing the required effect should be given. The maximum dose for healthy adults should not exceed 200 mg.

Children and elderly or debilitated patients require smaller doses, commensurate with age and physical status.

4.3 Contraindications

Known hypersensitivity to anaesthetics of the amide type

Complete heart block

Hypovolaemia

4.4 Special warnings and precautions for use

Lidocaine should be administered by persons with resuscitative skills and equipment.

Facilities for resuscitation should be available when administering local anaesthetics.

As with other local anaesthetics, lidocaine should be used with caution in patients with epilepsy, myasthenia gravis, impaired cardiac conduction, congestive cardiac failure, bradycardia or impaired respiratory function, 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, or if the dose or site of administration is likely to produce high blood levels. Lidocaine is metabolised in the liver and it should be used with caution in patients with impaired hepatic function.

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

Intramuscular Lidocaine may increase creatinine phosphokinase concentrations which can interfere with the diagnosis of acute myocardial infarction. Lidocaine has been shown to be porphyrinogenic in animals and should be avoided in persons suffering from porphyria.

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

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

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.

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 muscle 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.

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

Paracervical block can sometimes cause foetal bradycardia/tachycardia, and careful monitoring of the foetal heart rate is necessary (see section 4.6).

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

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.

Each 5 ml of Lidocaine 2% w/v solution for injection contains approximately 9.44 mg (0.41 mmol) sodium.

4.5 Interaction with other medicinal products and other forms of interaction

Cimetidine and propranolol depress microsomal enzyme activity, thus enhancing lidocaine toxicity during anti-arrhythmic infusions if concomitantly administered with these drugs, requiring a reduction in the dosage of lidocaine. Both drugs decrease hepatic blood flow. Also, cimetidine depresses microsomial 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).

Hypokalaemia caused by diuretics may antagonize the action of lidocaine if administered concomitantly (see section 4.4).

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), prenylamine, adrenaline (if accidently injected intravenously)) or 5HT3 antagonists (e.g. tropisetron, dolasetron).

Concomitant use of quinupristin/dalfopristin may increase lidocaine levels with a subsequent increased risk of ventricular arrhythmias and therefore 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).

Narcotics are probably proconvulsants and this would support the evidence that Lidocaine reduces the seizure threshold to fentanyl in man.

Opioid-antiemetic combination sometimes used for sedation in children could reduce the convulsant threshold to lignocaine and increase the CNS depressant effect.

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.

Cardiovascular collapse has been reported following the use of bupivacaine in patients on treatment with verapamil and timolol; lidocaine is closely related to bupivacaine.

4.6 Fertility, pregnancy and lactation

Pregnancy

Although animal studies have revealed no evidence of harm to the foetus, 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. The ratio of umbilical to maternal venous concentration is 0.5 to 0.6. The foetus appears to be capable of metabolising Lidocaine at term. The elimination half life in the newborn of the drug received in utero is about three hours, compared with 100 minutes in the adult. Elevated lidocaine levels may persist in the newborn for at least 48 hours after delivery. Foetal bradycardia or tachycardia (see section 4.4), 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.

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. Where major motor nerve block occurs e.g. Brachial plexus, epidural, spinal block. Where there is a loss of sensation resulting from nerve block to areas of muscle co-ordination or balance. Advice is that for general anaesthesia as sedative/hypnotic drugs are often used during nerve blockade.

4.8 Undesirable 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 (See also section 4.9).

Blood and Lymphatic System Disorders

Lidocaine may also produce methaemoglobinaemia.

Immune system disorders

Hypersensitivity reactions (allergic or anaphylactoid reactions, anaphylactic shock) – see also Skin & subcutaneous tissue disorders) are rare. They may be characterised by cutaneous lesions,

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

Localised nerve damage at the site of injection (very rare).

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.

CNS (central 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.

Psychotic reactions have been reported following infusion for the control of arrhythmia.

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)

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.

Profound hypotension may be associated with B blockade, widespread sympathetic block from spinal or epidural block, intercostal nerve block administration or supine hypotension in pregnancy.

The major adverse effects on the CNS and CVS are primarily due to the absorption of lidocaine into the systemic circulation.

Ventricular fibrillation occurs less frequently than that seen with bupivacaine.

Respiratory, thoracic or mediastinal disorders

Dyspnoea, bronchospasm and respiratory depression

Gastrointestinal

Nausea, vomiting.

Skin and subcutaneous tissue disorders

Rash, urticaria, oedema (including angioedema, face oedema)

Prolonged neural blockade following epidural may be due to delayed spread. Permanent neural blockade may be more likely associated with hypotension and cord ischaemia.

Following regional blockade as when lidocaine is injected intrathecally or extradurally, hypotension, hypoventilation, Horners Syndrome and hypoglycaemia may be seen. The degree of these effects will depend on the dose and the height of the block. Urinary retention may occur following sacral or lumbar epidural block. It should not outlast the duration of the block. Apnoea and coma followed by aphasia and hemiparesis may occur following stellate ganglion block. The probable cause is a direct injection of lidocaine into the vertebral or carotid arteries.

Profound lethargy and death have been reported following the injection of only 10 – 32 mg of lidocaine for dental blocks.

The initial CNS toxic effects are demonstrated by a gradual onset of drowsiness or inebriation similar to alcoholic intoxication. Balance is disturbed, dizziness or light-headedness, nervousness, circumoral pins and needles (circumoral paraesthesia), tongue numbness, tinnitus, hyperacusis, visual disturbances, restlessness and twitching may occur. Severe intoxication of rapid onset may immediately lead to convulsions followed by circulatory depression. Major overdosage may depress all systems simultaneously.

4.9 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 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 the 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code:N01BB02

Lidocaine is a local anaesthetic of the amide type. It is used to provide local anaesthesia by nerve blockade at various sites in the body and in the control of dysrhythmias. It acts by inhibiting the ionic refluxes 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. 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. The effect lasts about ten to twenty minutes and about sixty to ninety minutes following intravenous and intramuscular injection respectively.

5.2 Pharmacokinetic properties

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.

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. This is seen in the epidural space where Lidocaine is absorbed more rapidly than prilocaine.

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 (Betaphase) and to its metabolism and excretion (Gamma phase).

Lidocaine is distributed less rapidly than prilocaine (an amide drug of similar potency and duration of action) but equally as with mepivacaine. Its distribution is throughout

all body tissues. 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.

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.

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..

5.3 Preclinical safety data

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Chloride

Sodium Hydroxide

Hydrochloric Acid

Water for Injections

6.2 Incompatibilities

Lidocaine solution for injection should not be mixed with other preparations unless compatibility is known.

6.3 Shelf life

Unopened: 2 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

2mL clear red OPC with two yellow ring ampoules

5mL yellow snapoff white band ampoules

10mL yellow snapoff green band ampoules

Pack size:

For 2 mL: 10 x 2 ml and 20 x 2 ml ampoules

For 5 mL: 10 x 5 ml and 20 x 5 ml ampoules

For 10 mL: 10 x 10 ml and 20 x 10 ml ampoules

6.6 Special precautions for disposal

For single use only.

Use immediately after opening.

If only part of an ampoule is used, discard the remaining solution.

The injection should not be used if particles are present.

7 MARKETING AUTHORISATION HOLDER

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