SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lidocaine Hydrochloride Injection BP 2% w/v.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml of solution contains 20mg of Lidocaine Hydrochloride.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Lidocaine is a local anaesthetic of the amide group. Lidocaine Hydrochloride Injection BP is for use in infiltration anaesthesia, intravenous regional anaesthesia and nerve blocks.

4.2 Posology and method of administration

Posology

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 [or 500mg if given in solutions containing adrenaline (epinephrine)].

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

Method of administration

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

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

Known hypersensitivity to anaesthetics of the amide type; hypovolemia; complete heart block.

Solutions containing adrenaline (epinephrine) should not be used in areas of the body supplied by end arteries or otherwise having a compromised blood supply such as digits, nose, ear or penis. Solutions containing adrenaline (epinephrine) should not be given intravenously.

4.4 Special warnings and precautions for use

Lidocaine should only be used by people with skills in resuscitation.
Facilities and equipment 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, congestive cardiac 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.

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 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 foetal heart rate is necessary (see section 4.6).

Injections in the head and neck region 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 local anaesthetic. For this reason, as with all local anaesthetic, the lowest effective concentration and dose of local anaesthetic should be used.

Lidocaine Hydrochloride Injection 2% w/v is not recommended in subjects with a shallow anterior chamber or a history of acute narrow angle glaucoma.

Use of Lidocaine Hydrochloride Injection 2% w/v in patients with shallow anterior chamber, a history of acute narrow angle glaucoma and/or insufficient pupil dilation can increase the risk of both iridocele and floppy iris syndrome.

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.

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

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.

Dopamine and 5 hydroxytryptamine reduce the convulsant threshold to Lidocaine.

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 Lidocaine and increase the CNS depressant effect.

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. Ranitidine produces a small reduction in renal 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).

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

Lidocaine should be used with caution in patients receiving other local anaesthetics or agents related structurally 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).

4.6 Fertility, 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 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.

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.

Fertility:

No data available

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

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 overdose).

The undesirable effects are defined using the following convention:
Not known (cannot be estimated from the available data).

Blood and Lymphatic System Disorders

Lidocaine may also result in methaemoglobinaemia.

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 disorders

Nausea, vomiting.

Skin & subcutaneous tissue disorders

Rash, urticaria, angioedema, face oedema.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme,
website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

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 disturbances 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 usually follow, which may last from a few second to several minutes. Hypoxia and hypercapnia occur rapidly following convulsions due to increase 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. If 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 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

Pharmacotherapeutic group: local anaesthetic of the amide type, ATC code: N01BB02

Mechanism of action

It is used to provide local anaesthesia at various sites in the body and 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.

5.2 Pharmacokinetic properties

Absorption

Lidocaine 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.

Distribution

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

Biotransformation

Lidocaine 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 lidocaine. Further metabolism occurs and metabolites are excreted in the urine with less than 10% as unchanged lidocaine.

Elimination

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.

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 caused precipitation of amphotericin, methohexital sodium and sulfadiazine sodium in glucose injection. It is recommended that admixtures of lidocaine and glyceryltrinitrate should be avoided.

6.3 Shelf life

3 years (36 months).

6.4 Special precautions for storage

Do not store above 25ºC.

Keep the ampoule in the outer carton in order to protect from light.

6.5 Nature and contents of container

2ml, 5ml, 10ml & 20ml translucent plastic ampoules, polypropylene Ph. Eur., packed in cardboard cartons to contain 10, 20, 50 and 100 ampoules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

If only part used, discard the remaining solution.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 12762/0585

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