1.17 **Summary Product Characteristics (SPC)**

1. **NAME OF THE MEDICINAL PRODUCT**

Lidocaine Injection BP 2%w/v, 30ml

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

QUALITATIVE COMPOSITION

Each ml contains:

Lidocaine Hydrochloride BP..... 20mg

QUANTITATIVE COMPOSITION

Each ml contains:

Sodium Chloride BP ..... 6 mg.

Methyl Paraben BP .....1 mg

(As Preservative)

Water for Injections BP..... Q.s.

3. **PHARMACEUTICAL FORM**

Solution for Infusion

4. **CLINICAL PARTICULARS**

4.1 Therapeutic indications

Suppression of ventricular extrasystoles and ventricular tachycardia, especially after an acute myocardial infarction.

Local anesthesia by surface infiltration, regional, epidural and caudal routes, dental anesthesia, either alone or in combination with adrenaline. Lidocaine may also be administered by subcutaneous, intramuscular or intravenous injection.

Not intended for use in the eye.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

In ventricular arrhythmias

The usual adult IV 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.

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 IV 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 IV 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 IV bolus of 1 mg/kg. If ventricular tachycardia or ventricular fibrillation is not corrected following defibrillation and an initial bolus, an IV 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 IM dose may be administered if bradycardia is not present. The deltoid muscle is the preferred site for IM 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 12 – 18 years of age. Lidocaine by local infiltration for children under the age of 12 years should not exceed 3mg/kg, repeated not more often than every 4 hours.

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 IV 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 dermatome 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% solution or 0.5 to 30ml of a 1% solution (5-300mg).
For IV regional anaesthesia: 10-60 mls of 0.5% solution (50-300 mg).

4.3 CONTRAINDICATIONS

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

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

As with other local anaesthetics, lidocaine should be used with caution in patients with epilepsy, cardiac conduction disturbances, (see also section Contraindications) congestive cardiac failure, bradycardia, severe shock, impaired respiratory function or impaired renal function with a creatinine clearance of less than 10ml/minute. Lidocaine is metabolized in the liver and it should be used with caution in patients with impaired hepatic function. Lidocaine should not be used in cases of acute porphyrias.
Patients with myasthenia gravis are particularly susceptible to the effects of local anaesthetics.
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 en treating patients for more than a few days; abrupt discontinuation should be avoided and the dose reduced gradually.

Abuse of diazepam has been reported.

- 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. 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.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Effects of Lidocaine on other medicinal products

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 antiarrhythmic drugs (e.g. amiodarone) have not been performed, but caution is advised.

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

Effects of other medicinal products on Lidocaine

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). Page **10** of **29** Concomitant use of quinupristin/dalfopristin should be avoided.

4.6 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 given 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.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

When 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.

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

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.

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 disorders

Nausea, vomiting

Skin & subcutaneous tissue disorders

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 generalized convulsions. These signs must not be mistaken for neurotic behavior. 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 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, ATC code: N01BB02.

Lidocaine 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 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. 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

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

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 % 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.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Sodium Chloride BP

Methyl Paraben BP

Sodium Hydroxide BP
Water for Injections BP

6.2 INCOMPATIBILITIES

Lidocaine caused precipitation of Amphotericin, Methohexitone Sodium and Sulfadiazine Sodium in Glucose Injection. It is recommended that admixtures of Lidocaine & Glyceryl trinitrate should be avoided..

6.3 SHELF LIFE

36 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C in dry place. Protect from light. KEEP OUT OF REACH OF CHILDREN

6.5 NATURE AND CONTENTS OF CONTAINER

30 ml plain glass vial (USP Type-I) packed in a carton along with Insert.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

None