1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

1. NAME OF THE MEDICINAL PRODUCT:

1.1 (INVENTED) NAME OF THE MEDICINAL PRODUCT

International Non-Proprietary Name: Lidocaine Injection BP 2%, 30 ml

1.2 STRENGTH

20mg/ml

1.3 PHARMACEUTICAL FORM

Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 QUALITATIVE DECLARATION

Lidocaine Hydrochloride BP

2.2 QUANTITATIVE DECLARATION

Each ml contains:

Lidocaine Hydrochloride BP ----20 mg

Sodium Chloride BP….....6 mg

Water for Injections BP...……q.s.

3. PHARMACEUTICAL FORM

Solution for Injection

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.

The treatment of ventricular tachycardia occurring during cardiac manipulation, such as surgery or catheterization, or which may occur during acute myocardial infarction, digitalis toxicity, or other cardiac diseases.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Single I.V. injection: The usual dose is 50 to 100 mg administered under ECG and blood pressure monitoring. This dose may be administered at the rate of approximately 25 to 50 mg/min. Sufficient time should be allowed to enable a slow circulation to carry the drug to the site of action. If the initial injection of 50 to 100 mg does not produce a desired response, a second dose may be repeated after 10 minutes. No more than 200 to 300 mg of lidocaine should be administered during a 1 hour period.

Continuous I.V. infusion: Following i.v. injection, lidocaine may be administered by i.v. infusion at a rate of 1 to 2 mg/min. (approximately 15 to 30 µg/kg/min in the average 70 kg patient) in those patients in whom the arrhythmia tends to recur, and who are incapable of receiving oral antiarrhythmic therapy.

I.V. lidocaine infusions must be administered under constant ECG and blood pressure monitoring, and with meticulous regulation of infusion rate, in order to avoid potential overdosage and toxicity.

I.V. infusions should be terminated as soon as the patient's basic cardiac rhythm appears to be stable or at the earliest signs of toxicity. It should rarely be necessary to continue i.v. infusion beyond 24 hours. As soon as possible, and when indicated, patients should be changed to an oral antiarrhythmic agent for maintenance therapy.

Solutions for i.v. infusion may be prepared by the addition of 1 g of lidocaine (i.e., contents of 50 mL single use vial, or contents of 5 mL disposable additive unit) to 1 L of an appropriate

infusion solution. Approximately a 0.1% solution will result from this procedure; that is, each mL will contain approximately 1 mg of lidocaine.

In those cases in which fluid restriction is medically desirable a more concentrated solution may be prepared. A solution of approximately 0.2% can be prepared by adding 1 g of lidocaine (i.e., contents of 50 mL single use vial, or contents of 5 mL disposable additive unit) to 500 mL of diluent. The resulting 0.2% solution will contain 2 mg/mL of lidocaine.

Solutions should be prepared using aseptic technique. As with all i.v. admixtures, dilution should be made just prior to administration. Prepared solutions should be used within 24 hours.

4.3 CONTRAINDICATIONS

Known hypersensitivity to local anesthetics of the amide type or to other components of the solution; Adams-Stokes syndrome, or severe degrees of sinoatrial, atrioventricular or intraventricular block.

The safety of lidocaine in the treatment of arrhythmias in children has not been established.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Warnings:

Constant ECG monitoring is essential for the proper administration of lidocaine i.v.. Signs of excessive depression of cardiac conductivity, such as prolongation of PR interval and QRS complex, and the appearance of aggravation of arrhythmias, should be followed by prompt cessation of the i.v. infusion.

It is mandatory to have emergency resuscitative equipment and drugs immediately available to manage possible adverse reactions involving the cardiovascular, respiratory, or central nervous systems.

In emergency situations, when a ventricular rhythm disorder is suspected, and ECG equipment is not available, a single dose may be administered when the physician in attendance has determined that the potential benefits outweigh the possible risks. If possible, emergency resuscitative equipment and drugs should be available.

Precautions

Lidocaine should be used with caution in patients with bradycardia, severe digitalis intoxication, or first or second degree heart block in the absence of a pacemaker .

Caution should be employed in the repeated use of lidocaine in patients with severe liver or renal disease, since possible accumulation of lidocaine or its metabolites may lead to toxic phenomena.

In unconscious patients, circulatory collapse should be watched for, since CNS effects may not be apparent as an initial manifestation of toxicity.

I.V. administration of lidocaine is sometimes accompanied by a hypotensive response, and, in overdosage, this may be precipitous. For this reason the i.v. dose should not exceed 100 mg in a single injection, and no more than 200 to 300 mg in a 1 hour period .

When high doses are used and the patient's myocardial function is impaired, combination with other drugs which reduce the excitability of cardiac muscle requires caution.

Repeated doses of lidocaine may cause significant increases in blood levels with each repeated dose because of slow accumulation of the drug or its metabolites. Tolerance to elevated blood levels varies with the status of the patient. Debilitated, elderly patients and acutely ill patients should be given reduced doses commensurate with their age and physical condition. Lidocaine should also be used with caution in patients with epilepsy, impaired cardiac conduction, bradycardia, impaired hepatic function or renal function and in severe shock.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Cimetidine: Cimetidine reduces liver blood flow and thus systemic clearance of drugs that are highly extracted by the liver. Clinical experiments showed that the concomitant administration of cimetidine reduces the systemic clearance of lidocaine and increases lidocaine serum concentration by as much as 50%. Thus therapeutic serum levels of lidocaine may rise to toxic levels when cimetidine is used concomitantly. Ranitidine has not displayed this effect.

Propranolol: Administration of propranolol during infusion of lidocaine may increase the plasma concentration of lidocaine by about 30%. Patients already receiving propranolol tend to have higher lidocaine levels than controls. The combination should be avoided.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Studies of lidocaine in animals to evaluate the carcinogenic and mutagenic potential or the effect on fertility have not been conducted.

4.6 PREGNANCY AND LACTATION

Pregnancy: It is reasonable to assume that lidocaine has been used, mainly as a local anesthetic, by a large number of pregnant women and women of childbearing age. No specific disturbances to the reproductive process have so far been reported, e.g., no increased incidence of malformations. However, care should be taken during early pregnancy when maximum organogenesis takes place.

There are no adequate and well-controlled studies with i.v. administration of lidocaine in pregnant women.

Lactation: Lidocaine is excreted in the breast milk, but in such small quantities that there is generally no risk of affecting the infant at therapeutic dose levels.

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

Adverse experiences following the administration of lidocaine are similar in nature to those observed with other amide type agents. These adverse experiences are, in general, dose-related and may result from high plasma levels caused by excessive dosage or rapid absorption, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient.

Most frequent adverse reactions are those from the central and peripheral nervous system. They occur in 5 to 10% of the patients and are mostly dose-related.

Systemic reactions of the following types have been reported:

CNS: CNS manifestations are excitatory and/or depressant and may be characterized by circumoral paresthesia, lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, hyperacusis, tinnitus, blurred vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest. The excitatory manifestations may be very brief or may not occur at all, in which case the first manifestation of toxicity may be drowsiness merging into unconsciousness and respiratory arrest. Drowsiness following the administration of lidocaine is usually an early sign of a high lidocaine plasma level and may occur as a consequence of rapid absorption.

Cardiovascular: Cardiovascular manifestations are usually depressant and are characterized by bradycardia, hypotension and cardiovascular collapse which may lead to cardiac arrest.

Allergic: Allergic reactions are characterized by cutaneous lesions, urticaria, edema, or in the most severe instances, anaphylactic shock. Allergic reactions of the amide type are rare and may occur as a result of sensitivity either to the drug itself, or to other components of the formulation.

Idiosyncratic reactions have been reported at low doses in some patients. Cross-sensitivity between lidocaine and procainamide or lidocaine and quinidine has not been reported.

4.9 OVERDOSAGE AND TREATMENT

Symptoms of overdose or idiosyncratic reactions are described under Adverse Effects.Symptoms: CNS toxicity is a graded response, with symptoms and signs of escalating severity. The first symptoms are circumoral paresthesia, numbness of the tongue, lightheadedness, hyperacusis and tinnitus. Visual disturbance and muscular tremors are more serious and precede the onset of generalized convulsions. Unconsciousness and grand mal convulsions may follow, which may last from a few seconds to several minutes. Hypoxia and hypercarbia occur rapidly following convulsions due to the increased muscular activity, together with the interference with normal respiration. In severe cases apnea may occur. Acidosis increases the toxic effects.

Recovery is due to redistribution and metabolism of the drug. Recovery may be rapid unless large amounts of the drug have been administered.

Cardiovascular effects may be seen in cases with high systemic concentrations. Severe hypotension, bradycardia, arrhythmia and cardiovascular collapse may be the result in such cases.

Cardiovascular toxic effects are generally preceded by signs of toxicity in the CNS, unless the patient is receiving a general anesthetic or is heavily sedated with drugs such as a benzodiazepine or barbiturate.

Treatment:

The first consideration is prevention, best accomplished by careful and constant monitoring of cardiovascular and respiratory vital signs and the patient's state of consciousness. At the first sign of change, oxygen should be administered.

The first step in the management of convulsions consists of immediate attention to the maintenance of a patent airway and assisted or controlled ventilation with oxygen and a delivery system capable of permitting immediate positive airway pressure by mask. Immediately after the institution of these ventilatory measures, the adequacy of the circulation should be evaluated, keeping in mind that drugs used to treat convulsions sometimes depress the circulation when administered i.v.

An anticonvulsant should be given i.v. if the convulsions do not stop spontaneously in 15 to 20 seconds. Thiopental 100 to 150 mg i.v. will abort the convulsions rapidly. Alternatively, diazepam 5 to 10 mg i.v. may be used, although its action is slower. Succinylcholine will stop the muscle convulsions rapidly, but will require tracheal intubation and controlled ventilation, and should only be used by those familiar with these procedures.

Hypotension may be counteracted by giving sympathicomimetic drugs (e.g., epinephrine). Adrenergic agents of both a-adrenoceptor stimulating (e.g., metaraminol) and b-adrenoceptor stimulating type (e.g., isoprenaline) are generally effective. The bradycardia may be treated with parasympatholytic agents (e.g., atropine).

Should circulatory arrest occur, immediate cardiopulmonary resuscitation should be instituted. Optimal oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance, since hypoxia and acidosis will increase the systemic toxicity of local

anesthetics. Epinephrine (0.1 to 0.2 mg as i.v. or intracardial injections) should be given as soon as possible and repeated, if necessary.

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-acid-glycoprotein. 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

Methyl Paraben

Sodium Hydroxide

Water for Injections

6.2 INCOMPATIBILITIES

Lidocaine causes precipitation of amphotericin, methohexitone sodium and sulfadiazine sodium in glucose injection. It is recommended that admixtures of lidocaine and glyceryl trinitrate should be avoided.

6.3 SHELF LIFE

36 Months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30ºC. Protect from light.

KEEP OUT OF THE REACH OF CHILDREN

6.5 NATURE AND CONTENTS OF CONTAINER

30 ml Plain Glass vial packed in a carton along with insert.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Not Applicable