1.3.1 SUMMARY PRODUCT CHARACTERISTICS (SmPC)

1	**Name of the Finished Medicinal Product:**
1.1	**Product Name:** Lidocaine Hydrochloride 20 mg/ml & Adrenaline 0.005 mg/ml Injection BP
1.2	**Strength :** Lidocaine Hydrochloride 20 mg/ml & Adrenaline 0.005 mg/ml
1.3	**Pharmaceutical Form:** Injection
2	**Qualitative and Quantitative Compositions:**

Qualitative Declaration:
Active component

INN Name: 1) Lidocaine Hydrochloride 2) Adrenaline Acid Tartrate

Quantitative Declaration:

Each ml contains

Lidocaine Hydrochloride BP……21.3 mg

Equivalent to Anhydrous Lidocaine Hydrochloride…..20 mg

Adrenaline BP……0.005 mg

(as Adrenaline Acid Tartrate BP……0.009 mg)

Sr. No.	Content Name	Quality Standard	Quantity/ml
1	Lidocaine Hydrochloride	BP	21.3 mg
2	Adrenaline Bitartrate	BP	0.009 mg
3	Methyl Paraben	BP	1.0 mg
4	Sodium Chloride	BP	6.0 mg
5	Sodium Metabisulfite	BP	0.5 mg
6	Sodium Hydroxide	BP	q.s.
7	Hydrochloride Acid	BP	q.s.
8	Water for Injection	BP	q.s. to 1.0 ml

BP: British Pharmacopoeia

3	**Pharmaceutical Form:** Injection **Description:** A colourless solution.
4	**Clinical Particulars:**
4.1	**Therapeutic Indications:** Lidocaine Hydrochloride and Adrenaline Injection is indicated for production of local or regional anesthesia by infiltration techniques.
4.2	**Posology and Method of Administration** ***Adults*** For normal healthy adults, the individual maximum recommended dose of Lidocaine Hydrochloride with Adrenaline should not exceed 7 mg/kg (3.5 mg/lb) of body weight, and in general it is recommended that the maximum total dose not exceed 500 mg. ***Children*** It is difficult to recommend a maximum dose of any drug for children, since this varies as a function of age and weight. For children over 3 years of age who have a normal lean body mass and normal body development, the maximum dose is determined by the child's age and weight. For example, in a child of 5 years weighing 50 lbs the dose of Lidocaine Hydrochloride should not exceed 75-100 mg (1.5 to 2 mg/lb).
4.3	**Contra-indications:** • Hypersensitivity to the active substance, to any of the excipients or to local anaesthetics of the amide type. • Hypersensitivity to methylparaben or its metabolite para amino benzoic acid (PABA). Formulations of Lidocaine containing parabens should be avoided in patients allergic to ester local anaesthetics or their metabolite PABA. • Hypersensitivity to sodium metabisulphite. • Use intravenously or intrathecally. • Solutions containing adrenaline or other vasoconstrictor agents should not be used in the production of end-organ anaesthesia e.g. fingers, toes, ear lobe and penis, or in spinal anaesthesia.
4.4	**Special warning and precautions for use:** **Warnings:** To be given under the supervision of a well trained clinician who are well versed in diagnosis and management of dose-related toxicity and other acute emergencies and then only after ensuring the immediate availability of oxygen, other Resuscitative drugs, cardiopulmonary equipment, and the personnel needed for proper management of toxic reactions and related emergencies. To be administered after a test dose with adequate precaution to cope with any adverse reaction. To avoid intravascular injection, aspiration should be performed before the local anesthetic solution is injected. The needle must be repositioned until no return of blood can be elicited by aspiration. Local anesthetic solutions containing antimicrobial preservatives (e.g., methylparaben) should not be used for epidural or spinal anesthesia because the safety of these agents has not been established with regard to intrathecal injection, either intentional or accidental. Lidocaine Hydrochloride and Adrenaline Injection contains sodium metabisulfite, a sulfite

	that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people. **Precautions:** ***General:*** The safety and effectiveness of lidocaine depend on proper dosage, correct technique, adequate precautions, and readiness for emergencies. Standard textbooks should be consulted for specific techniques and precautions for various regional anesthetic procedures. The safety of amide local anesthetic agents in patients with genetic predisposition of malignant hyperthermia has not been fully assessed; therefore, lidocaine should be used with caution in such patients. In hospital environments where drugs known to be triggering agents for malignant hyperthermia (fulminant hypermetabolism) are administered, it is suggested that a standard protocol for management should be available. Lidocaine should be used with caution in persons with known drug sensitivities.
4.5	**Interaction with other drugs, other forms of interactions:** The administration of local anesthetic solutions containing adrenaline to patients receiving monoamine oxidase inhibitors or tricyclic antidepressants may produce severe prolonged hypertension. Phenothiazines and butyrophenones may reduce or reverse the pressor effect of adrenaline. Concurrent use of these agents should generally be avoided. In situations when concurrent therapy is necessary, careful patient monitoring is essential. Concurrent administration of vasopressor drugs (for the treatment of hypotension related to obstetric blocks) and ergot-type oxytocic drugs may cause severe persistent hypertension or cerebrovascular accidents.
4.6	**Usage in pregnancy& Lactation** ***Pregnancy -*** Pregnancy Category B. Reproduction studies have been performed in rats at doses up to 6.6 times the human dose and have revealed no evidence of harm to the fetus caused by lidocaine. There are, however, no adequate and well-controlled studies in pregnant women. General consideration should be given to this fact before administering lidocaine to women of childbearing potential, especially during early pregnancy when maximum organogenesis takes place. ***Labor and Delivery*** Local anesthetics rapidly cross the placenta and when used for epidural, paracervical, pudendal or caudal block anesthesia, can cause varying degrees of maternal, fetal and neonatal toxicity. The potential for toxicity depends upon the procedure performed, the type and amount of drug used, and the technique of drug administration. Adverse reactions in the parturient, fetus and neonate involve alterations of the central nervous system peripheral vascular tone and cardiac function. ***Lactation*** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when lidocaine is administered to a nursing woman.
4.7	**Effects on ability to drive and operate machine:** 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:** ***Systemic:*** Adverse experiences following the administration of Lidocaine are similar in nature to those observed with other amide local anesthetic agents. These adverse experiences are, in general, dose related and may result from high plasma levels caused by excessive dosage, rapid absorption or inadvertent intravascular injection, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. Serious adverse experiences are generally systemic in nature. The following types are those most commonly reported: ***Central Nervous System*** Lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred or double vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest. ***Cardiovascular System*** Bradycardia, hypotension, and cardiovascular collapse, which may lead to cardiac arrest. ***Allergic*** Cutaneous lesions, urticaria, edema or anaphylactoid reactions. ***Neurologic*** The incidences of adverse reactions associated with the use of local anesthetics may be related to the total dose of local anesthetic administered and are also dependent upon the particular drug used, the route of administration and the physical status of the patient. In a In a prospective review of 10,440 patients who received Lidocaine for spinal anesthesia, the incidences of adverse reactions were reported to be about 3 percent each for positional headaches, hypotension and backache; 2 percent for shivering; and less than 1 percent each for peripheral nerve symptoms, nausea, respiratory inadequacy and double vision. Many of these observations may be related to local anesthetic techniques, with or without a contribution from the local anesthetic. There have been reported cases of permanent injury to extraocular muscles requiring surgical repair following retrobulbar administration.
4.9	**Overdose :** Overdosage of Lidocaine Hydrochloride usually results in signs of central nervous system or cardiovascular toxicity. Should convulsions or signs of respiratory depression and arrest develop the patency of the airway and adequacy of ventilation must be assured immediately. Should convulsions persist despite ventilator therapy with oxygen, small increments of anticonvulsive agents may be given intravenously. Examples of such agents include a benzodiazepine (e.g., diazepam), an ultrashort-acting barbiturate (e.g., thiopental or thiamylal) or a short-acting barbiturate (e.g., pentobarbital or secobarbital). If the patient is under general anesthesia, a short-acting muscle relaxant (e.g., succinylcholine) may be administered. Should circulatory depression occur, vasopressors may be used. Should cardiac arrest occur, standard CPR procedures should be instituted. Dialysis is of negligible value in the treatment of acute overdosage with Lidocaine.

5	**Pharmacological Properties:**
5.1	**Pharmacodynamics Properties:** ***Mechanism of action:*** Lidocaine stabilizes the neuronal membrane by inhibiting the Ionic fluxes required for the initiation and conduction of impulses, thereby effecting local anesthetic action. ***Hemodynamics:*** Excessive blood levels may cause changes in cardiac output, total peripheral resistance, and mean arterial pressure. With central neural blockade these changes may be attributable to block of autonomic fibers, a direct depressant effect of the local anesthetic agent on various components of the cardiovascular system and/or the beta-adrenergic receptor stimulating action of epinephrine when present. The net effect is normally a modest hypotension when the recommended dosages are not exceeded.
5.2	**Pharmacokinetic Properties:** Information derived from diverse formulations, concentrations and usages reveals that Lidocaine is completely absorbed following parenteral administration, its rate of absorption depending, for example, upon various factors such as the site of administration and the presence or absence of a vasoconstrictor agent. Except for intravascular administration, the highest blood levels are obtained following intercostal nerve block and the lowest after subcutaneous administration. The plasma binding of Lidocaine is dependent on drug concentration, and the fraction bound decreases with increasing concentration. At concentrations of 1 to 4 µg of free base per mL, 60 to 80 percent of Lidocaine is protein bound. Binding is also dependent on the plasma concentration of the alpha-1-acid glycoprotein. Lidocaine crosses the blood-brain and placental barriers, presumably by passive diffusion. Lidocaine is metabolized rapidly by the liver, and metabolites and unchanged drug are excreted by the kidneys. Biotransformation includes oxidative N-dealkylation, ring hydroxylation, cleavage of the amide linkage, and conjugation. N-dealkylation, a major pathway of biotransformation, yields the metabolites monoethylglycinexylidide and glycinexylidide. The pharmacological/toxicological actions of these metabolites are similar to, but less potent than, those of Lidocaine. Approximately 90% of Lidocaine administered is excreted in the form of various metabolites, and less than 10% is excreted unchanged. The primary metabolite in urine is a conjugate of 4-hydroxy-2, 6-dimethylaniline. The elimination half-life of Lidocaine following an intravenous bolus injection is typically 1.5 to 2.0 hours. Because of the rapid rate at which Lidocaine is metabolized, any condition that affects liver function may alter Lidocaine kinetics. The half-life may be prolonged two-fold or more in patients with liver dysfunction. Renal dysfunction does not affect Lidocaine kinetics but may increase the accumulation of metabolites. Factors such as acidosis and the use of CNS stimulants and depressants affect the CNS levels of Lidocaine required to produce overt systemic effects. Objective adverse manifestations become increasingly apparent with increasing venous plasma levels above 6.0 µg free base per mL. In the rhesus monkey arterial blood levels of 18-21 µg/mL have been shown to be threshold for convulsive activity.
5.3	**Pre-clinical Safety Data:** Oral and subcutaneous LD50 values in mice ranged between 200 and 400 mg/kg bw while intramuscular LD50 values of Lidocaine in rats were 260 mg/kg bw. No studies concerning repeated dose toxicity were conducted. Genotoxicity studies were carried out with Lidocaine and its metabolites conducted in Salmonella microsomal assay (Salmonella typhimurium strains TA100, TA98, and TA1538 with 1, 10, 100 and 500 mg/plate), did not reveal any mutagenic activity.

	Long term studies in animals to evaluate the carcinogenic potential of Lidocaine Hydrochloride have not been conducted. Reproduction studies have been performed in rats at doses up to 6.6 times the human dose and have revealed no evidence of harm to the fetus caused by Lidocaine.
6	**Pharmaceuticals Particulars:**
6.1	**List of Excipients:** Methyl Paraben BP Sodium Chloride BP Sodium Metabisulfite BP Sodium Hydroxide BP Hydrochloric Acid BP Water for Injection BP
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:** 24 Months
6.4	**Special Precaution for Storage:** Store below 30°C.
6.5	**Nature and Contents of Container:** Lidocaine Hydrochloride Injection 20 mg/ml & Adrenaline 0.005 mg/ml Injection BP is packed in 30 ml amber colour glass vial USP Type - I with bromo butyl rubber plug and red colour aluminium flip off seal. 1 such vial packed in a carton along with pack insert.
6.6	**Special Precautions for Disposal:** Not applicable
7	**Registrant:** **Marketing Authorization Holder:** **M/s PHILLIPS PHARMACEUTICALS (NIGERIA) LTD** Address : Afprint Industrial Estate, Plot 122-132, Apapa Oshodi Expressway Lagos. Country : Nigeria. Telephone : +234 806761764 Fax : --- E-mail : --- **Manufacturing Site Address:** **M/s THEMIS MEDICARE LIMITED** Sector 6A, Plot No. 16, 17 & 18, IIE, SIDCUL, Haridwar – 249 403, Uttarakhand, INDIA. Telephone: 91-1334-239321/22 Fax: 91-334-239217 E-mail: hwdgmtech@themismedicare.com
8	**Date of Revision of the Text:** Not Applicable
9	**Dosimetry (if applicable):** Not Applicable
10	**Instruction for preparations of Radiopharmaceutical (if applicable):** Not Applicable