SUMMARY OF PRODUCT CHARACTERISTICS

1  NAME OF THE MEDICINAL PRODUCT
Lidocaine Hydrochloride Injection BP 2.0 w/v

2.  QUALITATIVE AND QUANTITATIVE COMPOSITION
Lidocaine Hydrochloride BP 2.0 % w/v

3.  PHARMACEUTICAL FORM
Solution for Injection

4.  CLINICAL PARTICULARS
4.1.  Therapeutic indications
(1) For treating ventricular arrhythmias after cardiac surgery, especially after myocardial infarction.

(2) For infiltration or nerve block anaesthesia

4.2.  Posology and method of administration
Lidocaine Hydrochloride Injection can be administered by subcutaneous, intramuscular or intravenous injection.

Adults

For treating ventricular arrhythmias: By slow intravenous injection or infusion. 50 - 100mg by slow intravenous injection followed by infusion at 2 - 4mg per minute. The usual maximum dose is 200-300mg in any one hour period.

Anaesthesia: The dosage is adjusted according to the response of the patient and the route of administration. The lowest concentration and the smallest dose that produces the desired effect should be given.
Infiltration anaesthesia

_Percutaneous anaesthesia:_ By injection of a 0.25 - 1% injection into the appropriate tissue. The dose is 5 - 300mg.

_Nerve block anaesthesia:_ By injection of a 1 - 2% injection into or around the appropriate nerve. The dose is 30 - 300mg.

The elderly and children

Reduced doses are necessary in the elderly and in children.

Lidocaine Hydrochloride Injection can be diluted to an appropriate strength for injection or infusion with 5% Glucose Injection BP or 0.9% Sodium Chloride Injection BP. Long term stability of the resulting solution cannot be guaranteed and it is recommended that administration is started immediately. Any excess or unused solution should be discarded.

### 4.3 Contraindications

Sino-atrial disorders, all grades of atrioventricular block, severe myocardial depression, porphyria, hypovolaemia, complete heart block or intraventricular block in the absence of an artificial pacemaker.

Hypersensitivity to amide local anaesthetics, Stokes-Adams syndrome or Wolff-Parkinson-White syndrome.

### 4.4 Special warnings and precautions for use

Constant ECG monitoring is essential for proper administration. Have emergency resuscitative equipment and drugs immediately available to manage adverse reactions involving the cardiovascular, respiratory or central nervous system.

Acceleration of ventricular rate may occur when administered to patients with atrial flutter or fibrillation.

**IV use:** Signs of excessive depression of cardiac conductivity, such as sinus node dysfunction, prolongation of PR interval, widening of the QRS interval and QRS complex and the appearance of aggravation of arrhythmias, should be followed by flow adjustment and, if necessary, prompt cessation of IV infusion.

**IM use:** May increase creatinine phosphokinase (CPK) levels. Use of this test without isoenzyme separation, as a diagnostic test for acute MI
Impaired renal or hepatic function: Lidocaine is metabolised mainly in the liver and excreted by the kidneys. Use caution with repeated or prolonged use in patients with liver or renal disease due to possible toxic accumulation of lidocaine or its metabolites.

Use with caution and in lower doses in patients with congestive heart failure (CHF), reduced cardiac, digitalis toxicity accompanied by AV block and in the elderly.

Electrolyte imbalance: Monitor changes in fluid balance, electrolyte concentrations and acid-base balance during prolonged parenteral therapy or when warranted. Administration of IV solutions can cause fluid or solute overload resulting in dilution of serum electrolytes, overhydration, congested states or pulmonary oedema. Excess administration of potassium-free solutions may cause significant hypokalaemia.

Labour and delivery: When used to manage cardiac arrhythmias during labour and delivery, the effects are not known. Lidocaine readily crosses the placental barrier.

Usage in children: Safety and efficacy for use in children has not been established; reduce dosage for children. The IM auto-injector device is not recommended.

Malignant hyperthermia: Amide local anaesthetic administration has been associated with acute onset of fulminant hypermetabolism of skeletal muscles known as malignant hyperthermic crisis. Recognition of early unexplained signs of tachycardia, tachyapnoea, labile blood pressure and metabolic acidosis may precede temperature elevation. Successful outcome depends on early diagnosis, prompt discontinuance of the triggering agent and institution of treatment, including oxygen supportive measures and IV Dandrolene Sodium.

The safety of amide local anaesthetics in patients with genetic predisposition of malignant hyperthermia has not been fully assessed; use lidocaine with caution in such patients. In hospitals where triggering agents for malignant hyperthermia are administered, a standard protocol for management should be available.

Cardiac effects: In sinus bradycardia or incomplete heart block, lidocaine administration for the elimination of ventricular ectopy without prior acceleration in heart rate (e.g. by atropine, isoproterenol or by electric pacing) may prompt more frequent and serious ventricular arrhythmias or complete heart block (see Contraindications). Use with caution in patients with hypovolaemia and shock, and all forms of heart block.
4.5. Interaction with other medicinal products and other forms of interaction

Hypokalaemia produced by Acetazolamide, loop diuretics and thiazide antagonises the effects of lidocaine.

Tubocurarine or polymyxin B: Lidocaine may enhance neuromuscular blockade by impairing the transmission of impulses at the motor nerve terminals.

Antibacterials (i.e. quinupristin/dalfopristin) and lidocaine concomitantly may increase the risk of ventricular arrhythmias.

Beta-adrenergic blockers (i.e. Propranolol and metoprolol) may increase the risk of myocardial depression. They also decrease the metabolic clearance of lidocaine, probably due to a reduction in hepatic blood flow and inhibition of metabolism of lidocaine second to the beta-adrenergic blocker. Propranolol may increase the risk of lidocaine toxicity. Pindolol did not affect lidocaine pharmokinetics.

Cimetidine may increase the serum levels and pharmacologic effects of lidocaine with concomitant administration. It also inhibits the metabolism of lidocaine, which may lead to an increased risk of toxicity.

Succinylcholine induced apnoea may be significantly prolonged when large doses of IV lidocaine are given concurrently, this may depend on the lidocaine dose.

Phenytoin and lidocaine may produce excessive cardiac depression with concomitant IV administration.

Antidepressants: the manufacturer of reboxetine advises caution.

Procainamide and lidocaine concomitantly may produce additive neurologic effects.

4.6. Pregnancy and lactation

Safety for use during pregnancy has not been established. Use only when clearly needed and when potential benefits outweigh unknown potential hazards to the foetus. No problems have been reported with breast feeding.

4.7. Effects on ability to drive and use machines

The ability to drive or use machinery may be impaired. If affected do not drive or operate machinery.
4.8. **Undesirable effects**

CNS: Light-headedness, drowsiness, dizziness, apprehension, confusion, euphoria, tinnitus, blurred or double vision, vomiting, sensation of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression and arrest.

Cardiovascular: Hypotension, cardiovascular collapse, bradycardia which may lead to cardiac arrest.

Hypersensitivity: Infrequent allergic reactions may occur, characterised by cutaneous lesions, urticaria, oedema, or anaphylactoid reactions. Skin testing has doubtful value.

Other: Occasional soreness at an IM injection site, febrile response, infection at the injection site, venous thrombosis, or phlebitis extending from the site of injection, extravasation and hypervolaemia.

4.9. **Overdose**

*Symptoms:* In the early stages the symptoms would be respiratory distress, hypertension, tachycardia and cyanosis.

*Treatment:* Standard procedures for cardiac arrest should be employed. Assisted respiration may be necessary and electrolytes or plasma infusions may be necessary to maintain circulation. If necessary convulsions can be controlled with diazepam.

5. **PHARMACOLOGICAL PROPERTIES**

5.1. **Pharmacodynamic properties**

Lidocaine is a class 1b anti-arrhythmic agent. It suppresses spontaneous automaticity in the ventricles and His-Purkinje system; both action potential duration and effective refractory period are decreased but the effect on action potential duration is much greater. It is the drug of choice for ventricular arrhythmias associated with acute myocardial infarction, digitalis toxicity or cardiac surgery.

Lidocaine is a local anaesthetic of the amide type and is widely used by injection and for local application to mucous membranes. It has a rapid onset of action when injected (about 1 minute followed by intravenous injection and 15 minutes following intramuscular injection) and spreads rapidly throughout surrounding tissues. The speed of onset and duration of action of lidocaine are
increased by the addition of a vasoconstrictor and absorption into the circulation from the site of injection is reduced. The effect lasts about 10 - 20 minutes and about 60 - 90 minutes following intravenous and intramuscular injections respectively.

5.2. Pharmacokinetic properties

After an intravenous dose lidocaine is rapidly and widely distributed into highly perfused tissue followed by redistribution into skeletal muscle and adipose tissue. Lidocaine is bound to plasma proteins including $\alpha$ - 1 - acid glycoprotein (AAG). The extent of binding is variable, depending in part on the concentrations of both lidocaine and AAG, but is approximately 70%. Plasma concentrations decline rapidly after an intravenous dose with an initial half life of less than 30 minutes; the elimination half life is 1 - 2 hours but may be prolonged if infusions are given for longer than 24 hours or if hepatic blood flow is reduced.

The therapeutic plasma concentration range is reported to be 1 - 6 mg per litre in the treatment of arrhythmias.

Lidocaine undergoes first pass metabolism in the liver and bioavailability is about 35% after oral administration. Metabolism in the liver is rapid and approximately 90% of a given dose is dealkylated to form monoethylglycinexylidide (MEGX) and glycinexylidide (GX).

Both of these metabolites may contribute to the therapeutic and toxic effects of lidocaine and since their half lives are longer than that of lidocaine, accumulation, particularly that of glycinexylidide may occur during prolonged infusions. Further metabolism occurs and metabolites are excreted in the urine with less than 10% of it unchanged lidocaine.

5.3. Preclinical safety data

No additional pre-clinical data of relevance to the prescriber.

6. Pharmaceutical particulars

6.1. List of excipients

Sodium Chloride BP and Water for Injection BP.
6.2. **Incompatibilities**

Methohexital Sodium and Phenytoin Sodium.

6.3. **Shelf life**

24 months.

6.4. **Special precautions for storage**

None stated

6.5. **Nature and contents of container**

Clear, colourless glass ampoules containing sufficient solution to permit the removal of 2, 5, 10 or 20ml. 10 ampoules are packed into a cardboard carton.

6.6. **Instructions for use/handling**

None stated.

7. **MARKETING AUTHORISATION HOLDER**

Macarthys Laboratories Limited T/A Martindale Pharmaceuticals
Bampton Road
Harold Hill
Romford
RM3 8UG

8. **MARKETING AUTHORISATION NUMBER(S)**

PL 01883/0038
9. **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

First authorised: 11 January 1985  
Last renewal: 20 January 1999

10. **DATE OF REVISION OF THE TEXT**

May 2004