Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:
Lidocaine Injection BP 20 mg/ml (GALAXY'S LIDO 2% INJECTION).

2. Qualitative and quantitative composition
Each ml contains: lidocaine Hydrochloride BP 20mg

Excipients with known effects
Benzyl alcohol
For a full list of excipients, see section 6.1

3. Pharmaceutical form
Solution for injection. A clear colorless solution free from foreign particles filled in 30 ml clear glass vial, plugged with grey butyl rubber stopper and sealed with green color flip off aluminum seal.

4. Clinical particulars
4.1 Therapeutic indications
Suppression of ventricular extra systoles and ventricular tachycardia, especially after an acute myocardial infarction. Local anaesthesia by surface infiltration, regional, epidural and caudal routes, dental anaesthesia, either alone or in combination with adrenaline. Lidocaine may also be administered by subcutaneous, intramuscular or intravenous injection. This particular medicinal product (i.e. hameln Lidocaine Hydrochloride Injection BP 2% w/v) is contraindicated for intraocular use because its formulation is neither isotonic nor pH neutral.

4.2 Posology and method of administration
Posology
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, to other anaesthetics of the amide type, or any of the excipients listed in section 6.1

In ventricular arrhythmia
- Sino-atrial disorders
- All grades of atrioventricular block
- Severe myocardial depression
- Porphyria (use with caution in local anaesthesia)

In local anaesthesia
- Complete heart block
- Hypovolaemia

Intraocular use
- This medicinal product (i.e. hameln Lidocaine Hydrochloride Injection BP 2% w/v) is neither isotonic nor pH neutral and is therefore contraindicated for intraocular should be considered.

4.4 Special warnings and precautions for use

As with other local anaesthetics, Lidocaine should be used with caution in patients with epilepsy, myasthenia gravis, cardiac conduction disturbances, congestive heart failure, bradycardia, severe shock, impaired respiratory function or impaired renal function with a creatinine clearance of less than 10mL/minute. Lidocaine is metabolised in the liver and it should be used with caution in patients with impaired hepatic function. Lower doses should be used in congestive cardiac failure and following cardiac surgery. Hypokalaemia, hypoxia and disorders of acid-base balance should be corrected before treatment with intravenous lidocaine begins.
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. Intra-articular

administration of lidocaine may cause chondrotoxicity.
Certain local anaesthetic procedures may be associated with serious adverse reactions, regardless of the 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.

• Blood pressure should be monitored during spinal anaesthesia. 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 the foetal heart rate is necessary • Injections in the head and neck regions 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 the local anaesthetic. For this reason, as with all local anaesthetics, the lowest effective concentration and dose of local anaesthetic should be used. 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.

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 aide-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 enhanced and prolonged neuromuscular blockade in patients treated concurrently with muscle relaxants (e.g. suxamethonium).

Effects of other medicinal products on Lidocaine
The clearance of Lidocaine may be reduced by beta-adrenoceptor blocking agents (e.g. propranolol) and by cimetidine, requiring a reduction in the dosage of lidocaine. Increase in serum levels of lidocaine may also occur with anti-viral agents (e.g. amprenavir, atazanavir, darunavir, lopinavir).
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).
While adrenaline (epinephrine) when used in conjunction with lidocaine might decrease vascular absorption, it greatly increases the danger of ventricular tachycardia and fibrillation if accidentally injected intravenously. Cardiovascular collapse has been reported following the use of bupivacaine in patients on treatment with verapamil and timolol; Lidocaine is closely related to bupivacaine.
Concomitant use of quinupristin/dalfopristin should be avoided.
Hypokalaemia produced by acetazolamide, loop diuretics and thiazides may antagonize the effect of lidocaine if administered concomitantly.
Inhibition of CYP1A2 by fluvoxamine considerably reduces elimination of lidocaine and increases the risk of lidocaine toxicity.
Concomitant use of both fluvoxamine and a CYP3A4 inhibitor such as erythromycin can further increase lidocaine concentrations. Because lidocaine possesses a narrow therapeutic window, doses of lidocaine may need to be adjusted accordingly. Conversely, reduced serum lidocaine concentrations may result from drugs that may stimulate the hepatic metabolism of lidocaine (e.g. phenytoin, oral HRT). Narcotics are probably pro convulsants 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.
Lidocaine is markedly bound to α -l-acid glycoprotein (AAG). AAG concentrations may be reduced by oestrogens leading to a higher free fraction of lidocaine in women than in men and the free fraction is further increased during pregnancy and in women taking oral contraceptives or HRT.

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 epidural or paracervical block, especially in large doses, or 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. Following regional blockade as when lidocaine is injected intrathecally or extradurally, hypotension, hypoventilation, Horners Syndrome and hypoglycaemia may be seen. The degree of these effects will depend on the dose and the height of the block. Urinary retention may occur following sacral or lumbar epidural block. It should not outlast the duration of the block. Apnoea and hemiparesis may occur following stellate ganglion block. The probable cause is a direct injection of lidocaine into the vertebral or carotid arteries.

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
This particular medicinal product (i.e. hameln Lidocaine Hydrochloride Injection BP 2% w/v) is contraindicated for intraocular use. Cases of corneal toxicity (e.g. corneal hazing/opacity) have been reported following off-label intraocular use of this hameln Lidocaine Hydrochloride Injection BP 2% w/v. 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. 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, oedema (including angioedema, face oedema)

Blood and the lymphatic system disorders
Methaemoglobinaemia.

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 pharmacy and poison board, Pharmacovigilance Electronic Reporting System(PvERS) https://pv.pharmacyboardkenya.org.

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 generalised convulsions. These signs must not be mistaken for neurotic behaviour. 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 jeopardise 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

The local anaesthetic effect of Lidocaine results from blockage of the sodium channels of neural fibres. Impulse generation and conduction are suppressed and the sensation of pain is discontinued without effects on consciousness. The anaesthesising effect is reversible and confined to the area of application.

The sensitivity of neural fibres to Lidocaine depends on their diameter; thin fibres are anaesthesized earlier than thicker ones. The order of loss of nerve function is as follows: pain, temperature, touch and pressure. The order of return of nerve function is inverse, i.e. return of pain sensation is latest.

In inflamed tissues, the efficacy of Lidocaine may be reduced due to the lower pH in such tissues.

Lidocaine is also a class Ib antiarrhythmic agent (acc. to VAUGHAN-WILLIAMS). In membranes of myocardial fibres Lidocaine inhibits the fast sodium influx and increases the potassium influx. In PURKINYE fibres the duration of action potentials and their effective refractory time are shortened while impulse conduction is slowed down. Impulse conduction in the sinus node and supraventricular regions remains virtually unaffected.

In the myocardium, the excitation and fibrillation thresholds are raised. Lidocaine suppresses heterotopic pacemakers and action potentials originating from delayed potentials, and tachyarrhythmias caused by circus rhythm. The antiarrhythmic effect is particularly marked in tachycardia. The effect of Lidocaine is enhanced if the resting potential is less negative, e.g. in hyperkalaemia and/or myocardial ischaemia. In situations of a more negative resting potential or hyperpolarisation e.g. due to hypokalaemia; the effect of Lidocaine is reduced.

The effects of Lidocaine on myocardial contractility, blood pressure, and cardiac output are very small. Patients with impaired function of the sinus node, however, may respond particularly markedly to the conduction suppressing effect of Lidocaine. Reduced coronary blood flow may be increased after correction of the arrhythmia

5.2 Pharmacokinetic properties

Onset of the local anaesthetic effect of Lidocaine is rapid, i.e. within less than 5 min. Its duration is between 1 and 2 hours. The elimination of Lidocaine from the region of application depends on tissue perfusion. Due to the concentration gradient in the area of application Lidocaine

diffuses into the surrounding tissue, into blood vessels and is eventually washed away by the bloodstream.
After intravenous administration, onset of the antiarrhythmic effect of Lidocaine is rapid. Maximum plasma concentrations are reached within 1 - 2 min. The effect of a bolus injection lasts for 10 - 20 min; in order to maintain the antiarrhythmic effect of Lidocaine, its administration must be continued in the form of an infusion. The therapeutic plasma concentration should be between 1.5 and 6 µg/l. Beyond 6 µg/l, toxic effects on the C.N.S. and the cardiovascular system are to be expected.
The plasma protein binding is 60 - 80 % in adults, 20 - 40 % in adolescents and about 25 % in newborns.
Intravenously administered Lidocaine is rapidly distributed in highly perfused organs (lungs, kidneys, liver, heart) and is re-distributed in muscles and adipose tissue. The distribution volume is 1.3 - 1.8 l/kg; it is greater in new-borns and in patients with hepatic or renal insufficiency; it is lower in patients with cardiac insufficiency.
Most of an administered Lidocaine dose (90 - 95 %) is hepatically metabolised by de-salkylation to monoethyl glycine xylidide (MEGX) and further to glycine xylidide (GX). MEGX has a weak antiarrhythmic potential. Both metabolites are potentially toxic. The degree of formation of 2,6-xylidine is not exactly known. Metabolism of Lidocaine strongly depends on liver perfusion. Vasoactive substances, e.g. glucagon or isoprenaline increase the hepatic perfusion and consecutively the elimination of Lidocaine.
The elimination of Lidocaine from the plasma is biphasic with an initial half life time of approx. 10 min. (distribution phase) and a terminal half life time of 1.5 - 3 h. (elimination phase). The half life time of Lidocaine is prolonged in new-borns (2.9 - 3 h), in patients with cardiac and particularly with hepatic insufficiency (3-19 h).
When Lidocaine is infused continuously, the half life time is extended to 3 - 5 h. The half life time of the metabolites are longer than that of Lidocaine (MEGX, 2 h, GX, 10 h). In situations of renal insufficiency, further extension of the half life time and accumulation of GX in the plasma must be considered.
5 - 10 % of Lidocaine are excreted unchanged in urine; the remaining proportion in the form of the metabolites. The predominant metabolite in urine is 4-hydroxy-2,6-xylidine (65 %).
Lidocaine passes the placental barrier and in foetal blood its concentration is about 60 % of that in maternal blood. Because of the low protein binding in fetal blood the concentration of free Lidocaine is about 1.4 times that of the maternal value.
Lidocaine is metabolised by the foetus; the half life time is about 3 hours.
Lidocaine appears in breast-milk. Its concentration is about 40 % of the concentration in maternal blood.

5.3 Preclinical safety data

The toxic effects of Lidocaine become manifest in the central nervous system and the cardiovascular system.
The toxic effects of Lidocaine depend on the level of the plasma concentration, the higher the plasma concentration and the more rapid its rise, the more frequent and more serious are the toxic reactions.
The basic causes of high plasma concentrations are actual overdose of Lidocaine, injection into a vein or artery and too rapid resorption from the injection site.
Depending on the individual sensitivity toxic reactions occur from a concentration of approx. 4-6 µg Lidocaine/ml venous blood.
The lethal concentration for humans is in the range 6 to 33 µg Lidocaine/ml.
Animal experiments have not provided any evidence of embryo-toxicity or teratogenicity.
There are findings indicating a mutagenic effect of Lidocaine. These indications come from *in vitro* tests with the metabolite 2,6 -xylidine at very high, almost toxic concentrations. There does not appear to be any relevance for the therapeutic administration.
In a carcinogenicity study of the metabolite 2-6 xylidine in rats, applying excessively high doses, benign and malignant tumours were detected particularly in the nasal cavity. The significance of this result for humans is unclear, but high dose administration over long periods should be avoided.

6. Pharmaceutical Particulars

6.1 List of Excipients

Benzyl alcohol
Water for injection

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.

6.3 Shelf-Life

24 months

6.4 Special Precautions for storage

Store below 30°C in a cool and dry place. Protect from light. Do not freeze.

6.5 Nature and Content of container

1 vial packed in a single carton along with pack insert.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder

GALAXY PHARMACEUTICAL LTD.
1 st Floor, Doctors Park, 3rd Parkland Avenue,
P.O.BOX 39107 - 00623, Nairobi (Kenya).

8. Marketing Authorization Number

CTD8468

9. Date of first authorization/renewal of the authorization

18/04/2024

10. Date of revision of the text

12/5/2025