SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lidocaine Hydrochloride 5% w/v and Phenylephrine Hydrochloride 0.5% w/v Topical Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Lidocaine Hydrochloride	5% w/v
Phenylephrine Hydrochloride	0.5% w/v

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cutaneous Solution for application to mucous membranes in nasal and pharyngeal areas.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

* Preparation of nasal mucosa for surgery or endoscopy

* Aid in removal of foreign bodies from the nose

* Analgesia of the pharynx prior to indirect or direct laryngoscopy

4.2 Posology and method of administration

Each bottle contains 2.5ml of solution to be used as a spray; equivalent to 125mg of Lidocaine Hydrochloride and 12.5mg of Phenylephrine Hydrochloride .

Prime the pump dispenser by activating the pump 3 times.

The pump dispenser will deliver a dose volume of 130µl in each spray. Each spray is equivalent to 6.5mg of Lidocaine Hydrochloride and 0.65mg of Phenylephrine Hydrochloride .

<u>Adults, and Children over 12 years:</u>
Up to a maximum of 8 sprays in total.

Children below 12 years of age
Not recommended

4.3 Contraindications

Hypersensitivity to Lidocaine Hydrochloride, local anaesthetics of the amide type, Phenylephrine Hydrochloride or to any of the excipients listed in section 6.1.

Lidocaine and phenylephrine topical solution should not be administered to those who are pregnant or breast-feeding.

Hypovolaemia, hypertension, acute ischaemic heart disease and complete heart block.

Thyrotoxicosis, glaucoma or urinary retention.

Patients receiving other sympathomimetic drugs.

Lidocaine and phenylephrine topical solution should not be given to patients taking monoamine oxidase inhibitors or within 2 weeks of their use. (see also 'Interactions' below).

4.4 Special warnings and precautions for use

Lidocaine and phenylephrine topical solution should be administered with caution to patients taking β-adrenergic blocking agents (see section below headed ‘Interactions with other Medicaments and other forms of Interaction’,) and those with cardiovascular disease, diabetes mellitus, hypertension or hyperthyroidism, hypoxia, hypercapnia and porphyria.

Lidocaine and phenylephrine topical solution should be used with caution in patients with traumatised mucosa and/or sepsis in the region of the proposed application.

Lidocaine and phenylephrine topical solution should also be used with caution in patients with epilepsy, impaired cardiac conduction, bradycardia, impaired hepatic function and in severe shock.

Oral topical anaesthesia may interfere with swallowing, and numbness of the tongue or buccal mucosa may increase the danger of biting trauma.

The physician or pharmacist should check that sympathomimetic containing preparations are not simultaneously administered by several routes i.e. orally and topically (nasal, aural and eye preparations)

Sympathomimetic-containing products should be used with great care in patients suffering from angina.

4.5 Interaction with other medicinal products and other forms of interaction

Monoamine Oxidase Inhibitors (MAOIs):

Phenylephrine is metabolised by MAOs in the gut. Irreversible MAOIs may therefore increase the effect of oral phenylephrine, resulting in a dangerous hypertensive crisis. This effect has not been reported with reversible MAOIs and phenylephrine given by nasal spray. In view of this risk however, this product should not be used on patients taking irreversible MAOIs, or within three weeks of their discontinuation.

Antihypertensive agents, Antiarrythmics and Cardiac glycosides:

Anti-hypertensive agents such as β-adrenergic blocking agents may have their effects reversed by the co-administration of phenylephrine, with possible fatal reactions.

Hypertensive reactions have been reported in a patient stabilised on *debrisoquine* when given phenylephrine by mouth, in patients receiving *reserpine* or *guanethidine* when given phenylephrine eye drops, and a fatal reaction occurred in a patient receiving *propranolol* and *hydrochlorothiazide* also after the instillation of phenylephrine eye drops.

Products that contain phenylephrine should be used with caution in patients receiving guanethedine, reserpine, digitalis and methyldopa.

Lidocaine may cause an increased risk of myocardial depression: increased risk of lidocaine toxicity with propranolol.

Lidocaine should be used with caution in patients receiving antiarrhythmic drugs, such as tocainide, since the toxic effects are additive.

Antimicrobials:
Increased risk of ventricular arrythmias with *quinuprisin/dalfoprisin*. Concomitant use should be avoided.

Diuretics:

Effects of lidocaine antagonised by hypokalaemia with acetazolamide, loop diuretics and thiazides.

Antidepressants:

Lidocaine should be used with caution if patients are being treated with the reboxitine.

Sympathomimetic-containing products should be used with great care in patients receiving phenothiazines or tricyclic antidepressants.

Muscle relaxants:

The action of Suxamethonium may be prolonged by lidocaine.

Phenylephrine may cause hypertension when used concomitantly with doxapram or oxytocin.

There is an increased risk of ergotism when phenylephrine and ergot alkaloids are taken concomitantly.

Halogenated anaesthetic agents

Concurrent use with halogenated anaesthetic agents such as chloroform, cyclopropane, halothane, enflurane or isoflurane may provoke or worsen ventricular arrhythmias.

4.6 Fertility, pregnancy and lactation

Lidocaine and phenylephrine topical solution should not be administered to those who are pregnant or breast-feeding.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

The lidocaine and phenylephrine topical solution may interfere with swallowing, and numbness of the tongue or buccal mucosa may increase the danger of biting trauma.

Local anaesthetics, (e.g. lidocaine) and sympathomimetics, (e.g. phenylephrine) may produce systemic adverse effects as a result of the raised plasma concentrations which ensue when the rate of absorption into the circulation exceeds the rate of breakdown, for example, by absorption of large amounts through mucous membranes or damaged skin or from highly vascular areas.

Possible Systemic Effects due to Lidocaine

The systemic toxicity of local anaesthetics mainly involves the central nervous system and the cardiovascular system. Excitation of the CNS may be manifested by restlessness, excitement, nervousness, dizziness, tinnitus, blurred vision, nausea and vomiting, muscle twitching and tremors, and convulsions. Numbness of the tongue and perioral region may appear as an early sign of systemic toxicity. Excitation may be transient and followed by depression with drowsiness, respiratory failure and coma. There may be simultaneous effects on the cardiovascular system with myocardial depression and peripheral vasodilatation resulting in hypotension and bradycardia; arrhythmias and cardiac arrest may occur.

Some local anaesthetics cause methaemoglobinaemia.

Possible Systemic Effects due to Phenylephrine.

Sympathomimetics may produce a wide range of adverse effects, most of which mimic the results of excessive stimulation of the sympathetic nervous system. These effects are mediated via the various types of adrenergic receptor, and the adverse effects of an individual drug depend to some extent upon its relative agonist activity on these different types of receptor at a given dose.

Central effects of sympathomimetic agents include fear, anxiety, nervousness, restlessness, tremors, insomnia, confusion, irritability, psychotic states and epileptiform convulsions. Appetite may be reduced and nausea and vomiting may occur.

Effects on the cardiovascular system are complex. Stimulation of alpha-adrenergic receptors produced vasoconstriction with resultant hypertension. This vasoconstriction is sometimes sufficiently severe to produce gangrene when sympathomimetics are infiltrated into the digits. The rise of blood pressure may produce cerebral haemorrhage and pulmonary oedema. There may also be a reflex bradycardia, but stimulation of β_1-adrenergic receptors of the heart may produce tachycardia and cardiac arrhythmias, anginal pain, palpitations, and cardiac arrest: hypotension with dizziness and fainting, and flushing, may occur. An increased incidence of sudden death, sometimes attributed to the induction of ventricular arrhythmias, has been associated with the excessive use of sympathomimetic agents in aerosol form; although the association has been questioned by some authorities, it is important to avoid excessive doses.

Other effects that may occur with sympathomimetic agents include difficulty in micturition, particularly in the case of prostatic hypertrophy, and urinary retention, dyspnoea, weakness, altered metabolism, sweating, hyperpyrexia and hypersalivation. Headache is also common.

Reporting of suspected adverse reactions
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 the Yellow Card Scheme: Website: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms
Because a severe toxic reaction to phenylephrine is of rapid onset and short duration, treatment is primarily supportive. Prompt injection of a rapidly acting alpha-adrenergic blocking agent such as phentolamine (dose 5 to 10mg i.v.) has been recommended.

Treatment
Treatment of a patient with toxic manifestations consists of ensuring adequate ventilation and arresting convulsions. Ventilation should be maintained with oxygen by assisted or controlled respiration as required. If convulsions occur they must be treated rapidly by intravenous administration of succinylcholine 50-100mg and/or 5-15mg diazepam. As succinylcholine will arrest respiration, it should only be used if the clinician has the ability to perform endotracheal

intubation and to manage a totally paralysed patient. Thiopentone may also be used to abort convulsions in dosage 100-200mg. Adrenaline in repeated doses and sodium bicarbonate should be given as rapidly as possible.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic groups:

Lidocaine: Anaesthetics for topical use, lidocaine, ATC Code: D04A B 01

Phenylephrine: Sympathomimetics excluding antiglaucoma preparations, ATC code: S01FB01

Lidocaine.

Lidocaine is primarily used for its local anaesthetic properties. Like other anaesthetics lidocaine impairs the generation and conduction of the nerve impulses by slowing depolarization. This results from blocking of the large transient increase in permeability of the cell membrane to sodium ions that follows initial depolarization of the membrane. Lidocaine also reduces the permeability of the resting axon to potassium and to sodium ions. The site of action of lidocaine is on a specific receptor site in the sodium channel.

Lidocaine is more effective as a local anaesthetic on small non-myelinated nerve fibres, while myelinated A fibres are blocked before C fibres. The actions of lidocaine are prolonged by the use of a vasoconstrictor such as adrenaline.

Lidocaine has effects on the central nervous system to produce restlessness and tremor, and frank convulsions may occur. Central stimulation may be followed by depression and death due to respiratory failure. Lidocaine has weak neuromuscular blocking activity.

In the heart lidocaine's main activity is to reduce automaticity by decreasing the rate of diastolic depolarization. Lidocaine has little or no effect on conduction in the His-Purkinje system. The duration of the action potential is decreased due to blockade of the sodium channel and the effective refractory period is shortened.

Phenylephrine

Phenylephrine is a relatively selective α_1-adrenoceptor agonist. It has weak α_2-adrenoceptor agonist activity and some activity as a β-adrenoceptor agonist. It is also termed a sympathomimetic vasoconstrictor. Most of the $_1$-stimulant activity is due to a direct action on the receptors and relatively little is due to an indirect effect via release of noradrenaline.

Phenylephrine causes a rise in blood pressure which is accompanied by a profound reflex bradycardia which can be antagonised by atropine. Cardiac output is slightly decreased but there is a marked fall in blood flow to the renal, cutaneous, splanchnic and skeletal muscle vascular beds. Coronary blood flow is however, increased by phenylephrine and pulmonary arterial pressure is increased.

5.2 Pharmacokinetic properties

Lidocaine

Absorption

Lidocaine is readily absorbed from the gastrointestinal tract, from mucous membranes and through damaged skin. Absorption through intact skin is poor. Local anaesthetics are weak bases and at tissue pH can diffuse through connective tissue and cellular membranes to reach the nerve fibre where ionisation can occur.

Biotransformation

Systemic bioavailability is only about 40% following administration, peak plasma concentrations are achieved in 1-2 hours. The mean plasma half-life is in the range 2-3 hours. Penetration into the brain appears to be minimal.

Distribution

The volume of distribution is between 200 and 500L.

Elimination

Both phenylephrine and its metabolites are excreted in urine with <20% as unchanged drug. There is no evidence that any of the metabolites are pharmacologically active.

5.3. Preclinical Safety Data

There are no pre-clinical safety data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric Acid
Sodium Hydroxide Solution
Water for Injections

6.2 Incompatibilities

Lidocaine

Lidocaine hydrochloride has been reported to be incompatible in solution with amphotericin, sulphadiazine sodium, methohexitone sodium, cephazolin sodium, or phenytoin sodium.

The lidocaine content of buffered cardioplegic solutions has been reported to decrease when stored in polyvinyl chloride containers at ambient temperatures but not when stored at 4°C. This loss appeared to result from pH-dependent sorption of lidocaine onto the plastic and did not occur when lidocaine solutions were stored in glass bottles.

Phenylephrine

No known incompatibilities.

6.3. Shelf Life

24 months.

6.4. Special Precautions for Storage

Do not store above 25°C. Keep in the original container.

6.5 Nature and contents of container

2.5 ml of Lidocaine Hydrochloride 5% w/v and Phenylephrine Hydrochloride 0.5% w/v topical solution in a Type 1 clear glass vial with halobutyl rubber stopper and natural plastic wad less screw cap as the closure.

6.6 Special precautions for disposal

Check tamper-evident seal is intact before use. Remove plastic screw cap and rubber stopper; screw on pump spray attachment and push on actuator for application of the topical solution to the area. The pump should then be primed 3 times prior to administration to the patient.

Keep out of the sight and reach of children.

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

Use once and discard any remaining topical solution at the end of the session. Each bottle of topical solution is to be used for one patient only.

7 MARKETING AUTHORISATION HOLDER

Aurum Pharmaceuticals Ltd,
Brampton Road,
Harold Hill,
Romford,
Essex,
RM3 8UG,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 12064/0027

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10 DATE OF REVISION OF THE TEXT

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