SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lignospan Special
Utilycaine - Lignokent – Eurocaine 2% - Rexocaine

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Lidocaine hydrochloride 2% w/v
Adrenaline tartrate expressed in base 1/80,000 w/v

3 PHARMACEUTICAL FORM

Solution for injection

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Production of local anaesthesia for dental procedures by infiltration or nerve block injection.
LIGNOSPAN SPECIAL is indicated in adults, children and adolescents.

4.2 Posology and method of administration

Posology:
LIGNOSPAN SPECIAL is indicated in adults and children.

Adults:
A single cartridge is generally sufficient. Two are used in case of large interventions.
Do not exceed 3 cartridges.

Children
Special care has to be exercised when treating children below 4 years.
The quantity to be injected should be determined by the age and weight of the child and the magnitude of the operation.
The anaesthesia technique should be selected carefully. Painful anaesthesia techniques should be avoided.
The behaviour of the child during treatment has to be monitored carefully.
The average dose to be used is in the range of 20mg to 30mg lidocaine hydrochloride per session. The dose in mg of lidocaine hydrochloride which can be administered in children may alternatively be calculated from the expression: child’s weight (in kilograms) x 1.33.
Do not exceed the equivalent of 5 mg of lidocaine hydrochloride per kilogram of body weight.

Method of administration:
Infiltration or nerve block injection.

4.3 Contraindications
Lignospan Special is contra-indicated in patients with a known history of hypersensitivity to local anaesthetics of the amide type or to any components of the injectable formulation.
Lignospan Special, due to the presence of a vasoconstrictor (adrenaline) in the formula, is contra-indicated for patients suffering from:
- arterial hypertension,
- coronary disease,
- valvular cardiac disease (particularly sequelae to acute rheumatic fever).

4.4 Special warnings and precautions for use

Warnings:
Dental practitioners who employ local anaesthetic agents should be well versed in diagnosis and management of emergencies which may arise from their use. Resuscitative equipment, oxygen and other resuscitative drugs should be available for immediate use.
Do not inject into a blood vessel - Inject slowly:
To minimize the likelihood of intravascular injection, aspiration should be performed before the local anaesthetic solution is injected. If blood is aspirated, the needle must be repositioned until no return of blood can be elicited by aspiration. Note, however, that the absence of blood in the syringe does not assure that intravascular injection will be avoided and a double aspiration is always recommended.
Local anaesthetic procedures should be used with caution when there is inflammation and/or sepsis in the region of the proposed injection.
Use of the cartridge: Use on one patient during one session of treatment only, if only part is used, the remainder must be discarded.

Precautions:
General:
The safety and effectiveness of lidocaine depend on proper dosage, correct technique, adequate precautions and readiness for emergencies. Resuscitative equipment, oxygen and other resuscitative drugs should be available for immediate use.
The lowest dosage that results in effective anaesthesia should be used to avoid high plasma levels and serious adverse effects. Repeated doses of lidocaine may cause significant increases in blood levels with each repeated dose due to slow accumulation of the drug or its metabolites. Tolerance to elevated blood levels varies with the status of the patient, debilitated, elderly patients, acutely
ill patients, and children should be given reduced doses commensurate with their age and physical condition, (see 4.2. Posology and method of administration).

Patients with peripheral vascular disease may exhibit exaggerated vasoconstrictor response.

Cardiovascular and respiratory (adequacy of ventilation) vital signs and the patient’s state of consciousness should be monitored after each local anaesthetic injection. Restlessness, anxiety, tinnitus, dizziness, blurred vision, tremors, depression or drowsiness should alert the practitioner to the possibility of central nervous system toxicity. Signs and symptoms of depressed cardiovascular function may commonly result from a vasovagal reaction, particularly if the patient is in an upright position; placing the patient in the recumbent position is recommended when an adverse response is noted after injection of a local anaesthetic. (See Undesirable effect, Cardiovascular system).

Lidocaine should be used with caution in patients with hepatic disease, since amide-type local anaesthetics are metabolized by the liver. Patients with severe hepatic disease, because of their inability to metabolize local anaesthetics normally, are at greater risk of developing toxic plasma concentrations.

4.5 Interaction with other medicinal products and other forms of interaction

As in the case of all other local anaesthetic solutions containing adrenaline, the administration of LIGNOSPAN SPECIAL in patients receiving MAOI (monoamine oxidase inhibitors), tricyclic antidepressants, serotonine/noradrenaline reuptake inhibitors antidepressants or phenothiazines may produce severe prolonged hypotension or hypertension. 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 and ergot-type oxytocic drugs may cause severe, persistent hypertension or cerebrovascular accidents.

If sedatives are employed to reduce patient apprehension, reduced doses of anaesthetic solution should be used since local anaesthetic agents, like sedatives, are central nervous system depressants which in combination may have an additive effect.

Concurrent use of beta-adrenergic blocking agents with an anaesthetic solution containing a vasoconstrictor, may result in dose dependent hypertension and bradycardia.

4.6 Pregnancy and lactation

Pregnancy

Teratogenic effects: reproduction studies have been performed in rats at doses up to 6 times the human dose and have revealed no evidence of harm to the foetus caused by lidocaine, there are, however, no adequate and well-controlled studies in pregnant women. Animal reproduction studies are not always predictive of human response. General consideration should be given
to this fact before administering lidocaine to women of child-bearing potential, especially during early pregnancy when maximum organogenesis takes place.

*Nursing mothers*

Since lidocaine is distributed into milk, the drug should be used with caution in nursing women. Limited data suggests that the amount of drug that would be ingested by a breast fed infant is small.

4.7 Effects on ability to drive and use machines

None stated

4.8 Undesirable effects

Adverse experiences following the administration of lidocaine are similar in nature to those observed with other amide local anaesthetic agents, these adverse experiences are, in general, dose-related and may result from high plasma levels caused by excessive dosage, rapid absorption or unintended intra-vascular 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**

CNS manifestations are excitatory and/or depressant and may be characterized by lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, headaches, malaise, agitation, drowsiness, tinnitus, blurred or double vision, nausea, 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 blood level of the drug and may occur as a consequence of rapid absorption.

**Cardiovascular system**

Cardiovascular manifestations are usually depressant and are characterized by bradycardia or tachycardia, palpitations, hypotension, and cardiovascular collapse, which may lead to cardiac arrest, arrhythmias (ventricular premature beat and ventricular fibrillation) and conduction disorders (atrioventricular block).

Signs and symptoms of depressed cardiovascular function may commonly result from a vasovagal reaction, particularly if the patient is in an upright position less commonly, they may result from a direct effect of the drug. Failure to recognize the premonitory signs such as sweating, a feeling of faintness, changes in pulse or sensorium may result in progressive cerebral hypoxia and seizure or serious cardiovascular catastrophe. Management consists of placing the patient in the recumbent position and ventilation with
oxygen. Supportive treatment of circulatory depression may require the administration of intravenous fluids and, when appropriate, a vasopressor (e.g., ephedrine) as directed by the clinical situation.

**Allergic reactions**

Allergic reactions are characterized by cutaneous lesions, urticaria, edema or anaphylactoid reactions. Allergic reactions as a result of sensitivity to lidocaine are extremely rare and, if they occur, should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.

**4.9 Overdose**

Acute emergencies from local anaesthetics are generally related to high plasma levels encountered during therapeutic use of excessive dosage of local anaesthetics, or to unintended intravascular injection of local anaesthetic solution. (See 4.4. and 4.8).

**Management of local anaesthetic emergencies**

The first consideration is prevention, best accomplished by careful and constant monitoring of cardiovascular and respiratory vital signs and the patients state of consciousness after each local anaesthetic injection. 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 intravenously. Should convulsions persist despite adequate respiratory support, and if the status of the circulation permits, small increments of an ultra-short acting barbiturate (such as thiopental or thiamylal) or a benzodiazepine (such as diazepam) may be administered intravenously. The clinician should be familiar, prior to use of local anaesthetics, with these anticonvulsant drugs. Supportive treatment of circulation depression may require administration of intravenous fluids and, when appropriate vasopressor as directed by the clinical situation (e.g. ephedrine).

If not treated immediately, both convulsions and cardiovascular depression can result in hypoxia, acidosis, bradycardia, arrhythmia and cardiac arrest. If cardiac arrest should occur, standard cardio-pulmonary resuscitative measures should be instituted.

Endotracheal intubation, employing drugs and techniques familiar to the clinician, may be indicated, after initial administration of oxygen by mask, if difficulty is encountered in the maintenance of a patient airway or if prolonged ventilatory support (assisted or controlled) is indicated.

Dialysis is of negligible value in the treatment of acute overdosage with lidocaine.
5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Local anaesthetics/Lidocaine
ATC code: N01 BB 52

Mechanism of action:

Lidocaine stabilizes the neuronal membrane by inhibiting the ionic fluxes required for the initiation and conduction of nerve impulses, thereby effecting local anaesthetic action.

Since lidocaine, as most agents currently used for local anaesthesia, is not a vasoconstrictor, adrenaline is included in the solution with the anaesthetic:

- By localizing the solution at the site of the injection, this vasoconstrictor intensifies and prolongs the anaesthetic effect and decreases the rate at which the anaesthetic drug enters the systemic circulation.
- The presence of a vasoconstrictor also decreases surgical haemorrhage in the immediate area of injection.

Onset duration of anaesthesia:

- When used for infiltration anaesthesia in dental patients, the time of onset averages less than two minutes. LIGNOSPAN SPECIAL provides an average pulp anaesthesia of at least sixty minutes with an average duration of soft tissue anaesthesia of approximately two and a half hours.
- When used for nerve blocks in dental patients, the time of onset averages two to four minutes. LIGNOSPAN SPECIAL provides pulp anaesthesia averaging at least ninety minutes with an average duration of soft tissue anaesthesia of three to three and a quarter hours.
- Hemodynamics:

Excessive blood levels may cause changes in cardiac output, total peripheral resistance, and mean arterial pressure. These changes may be attributable to a direct depressant effect of the local anaesthetic agent on various components of the cardiovascular system and/or the beta-adrenergic receptor stimulating action of adrenaline when present.

5.2 Pharmacokinetic properties

Information derived from diverse formulations, concentrations and usages reveals that lidocaine is completely absorbed following parenteral administrations, its rate of absorption depending 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.

Lidocaine crosses the blood-brain and placental barriers, presumably by passive diffusion.

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.
Studies of lidocaine metabolism following intravenous bolus injections have shown that the elimination half-life of this agent 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 mcg free base per ml. In the rhesus monkey, arterial blood levels of 18-21 mcg/ml have been shown to be threshold for convulsive activity.

5.3 Preclinical safety data
Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Sodium chloride, potassium metabisulphite (E224), sodium edetate, sodium hydroxide solution and water for injections.

6.2 Incompatibilities
None stated.

6.3 Shelf life
2 years.

6.4 Special precautions for storage
Store in a dry place below 25°C
Do not freeze.
To protect from light and to aid stability, each time cartridges are taken, remember to replace the blister into the carton and to close this latter.

6.5 Nature and contents of container
Glass cartridges with rubber closures
50 dental cartridges of 1.8 ml or 2.2 ml in blister packs grouped in a cardboard box.
6.6 Special precautions for disposal
See Special Warnings and Precautions for Use.

7 MARKETING AUTHORISATION HOLDER
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