This product is an unapproved therapeutic good in Australia. It is manufactured in a TGA approved pharmaceutical manufacturing facility in Australia and is provided under Schedule 5A – subregulation 12(1A) of the Therapeutic Goods Act and Regulations. The product is supplied under contract between a public or private hospital or public institution and the licensed manufacturer in Australia in accordance with a specified formulation.

Approval for use is required from the hospital pharmacist and / or drug committee as appropriate. Informed consent should be obtained in accordance with good medical practice where applicable and practicable. Records of the use of the product should be fully detailed and include dose, route of administration, duration of treatment, clinical, biochemical, haematological and immunological monitoring as appropriate. Adverse events and reactions must be reported to Phebra Pty Ltd and the TGA.

The responsibility for the use of this product remains with the prescriber and the institution. The following product information has not been evaluated or approved by the Therapeutic Goods Administration. Physicians should consult the medical literature for the most recent advice concerning the appropriate dose, route of administration, warnings and adverse effects.

NAME OF THE MEDICINE

(1) Lignocaine Hydrochloride

Chemical Name: 2-diethylamino-aceto-2',6'-xylidide hydrochloride monohydrate.

The molecular weight is 288.8 and the CAS registry number is 6108-05-0. The molecular formula is C14H22N2O.HCl.H2O.

Lignocaine hydrochloride is a white, crystalline powder, which is practically odourless. It is very soluble in water, freely soluble in chloroform and in ethanol (96%) and practically insoluble in ether. It is also known by the name of lignocaine hydrochloride.

Structural Formula:

(2) Amethocaine Hydrochloride

Chemical Name: 2-(dimethylamino) ethyl 4-(butylamino) benzoate hydrochloride.

The molecular weight is 300.83 and the CAS registry number is 94-24-6 (Base) 136-47-0 (Hydrochloride). The molecular formula is C15H24N2O2·HCl.

Structural Formula:
(3) Adrenaline Acid Tartrate

Chemical Name: 1-(3, 4-Dihydroxyphenyl)-2-(methylamino) ethanol.

The molecular weight is 333.3 and the CAS registry number is 51-42-3. The molecular formula is C_{9}H_{13}NO_{3} \cdot C_{4}H_{6}O_{6}.

Structural formula:

![Structural formula]

DESCRIPTION

Laceraine Topical Wound Anaesthetic is a clear to slightly yellow solution in an amber glass vial with a bright yellow flip off-tear off top. It is a mixture of two local anaesthetics with a vasoconstrictor to increase the duration of the effect of the two local anaesthetics.

If the yellow plastic top is lifted or removed the product should not be used.

Ingredients

Laceraine Topical Wound Anaesthetic is a mixture of 4% w/v lignocaine hydrochloride (lidocaine hydrochloride) 40mg/mL (amide type anaesthetic), 0.5% w/v amethocaine hydrochloride (tetracaine hydrochloride) 5mg/mL (ester type anaesthetic) and 0.1% w/v adrenaline (epinephrine) 1.8mg/mL as adrenaline acid tartrate (vasoconstrictor). Excipients include sodium metabisulphite.

PHARMACOLOGY

Pharmacodynamics

Local anaesthetics function by preventing or diminishing the conduction of sensory nerve impulses near the site of application. They may also have an analgesic effect by reducing the feeling of pain without the loss of nervous control. They also have a membrane stabilising effect through reduction in the permeability of nerve cell membrane to sodium ions. These effects are reversible.

Application to damaged skin brings the anaesthetic into intimate and prolonged contact with the tissue, giving effective anaesthesia of long duration (approx. 30-60 minutes).

Adrenaline acts as a vasoconstrictor increasing the duration of action of the two anaesthetics and reducing local bleeding at the site of application. Adrenaline also reduces the rate of absorption of the two anaesthetics into the general circulation from the site of application.

Most local anaesthetics are readily absorbed through mucous membranes and through damaged skin. They are weak bases and at tissue pH they can diffuse through connective tissue and cellular membranes to reach the nerve fibres.

Lignocaine hydrochloride and amethocaine hydrochloride are absorbed following topical administration to mucous membranes and damaged skin, their rate and extent of absorption being dependent upon concentration and the total dose administered, the specific site of application, and the duration of exposure. This product should not be used in the trachea or bronchi.

Pharmacokinetics

Lignocaine Hydrochloride

Lignocaine hydrochloride is a relatively fast acting anaesthetic of the amide type. Normally about 65% of the lignocaine hydrochloride is bound to plasma proteins. Amide local anaesthetics are mainly bound to alpha-1-acid glycoprotein but also to albumin. Lignocaine hydrochloride crosses the blood-brain and placental barriers, presumably by passive diffusion.
PRODUCT INFORMATION
Laceraine Topical Wound Anaesthetic

The main elimination pathway of lignocaine hydrochloride is by liver metabolism. The primary route of elimination of lignocaine hydrochloride in human is N-dealkylation to monoethylglycine xylidine (MEGX), followed by hydrolysis to 2,6-xylidine and hydroxylation to 4-hydroxy-2,6-xylidine. MEGX can also be further de-alkylated to glycine xylidine (GX). The pharmacological/toxicological actions of MEGX and GX are similar to, but less potent than, those of lignocaine hydrochloride. GX has a longer half-life (about 10h) than lignocaine hydrochloride and may accumulate during long-term administration.

About 70-80% of the dose is excreted in the urine. Because of the rapid rate at which lignocaine hydrochloride is metabolised, any condition that affects liver function may alter lignocaine hydrochloride kinetics. The half-life may be prolonged two-fold or more in patients with liver dysfunction. Renal dysfunction does not affect lignocaine hydrochloride kinetics but may increase the accumulation of metabolites.

**Amethocaine Hydrochloride**
Amethocaine hydrochloride is a potent long acting local anaesthetic of the ester type. It has a relatively slow onset of action and prolonged activity compared to lignocaine hydrochloride. It may exhibit systemic toxicity. It is metabolised by plasma esterases to para-aminobenzoic acid and other metabolites and is excreted mainly by the kidneys. A small amount may be metabolised in the liver. There is generally little protein binding.

**Adrenaline**
Adrenaline is an active principle of the adrenal medulla and is a fast and direct acting sympathomimetic agent causing stimulation of adrenergic nerves leading to potent effects such as vasoconstriction when used topically. When used topically its absorption is slowed by the vasoconstriction it may cause. It is very readily inactivated by processes, which include uptake into adrenergic neurones, diffusion and enzymatic degradation in the liver and other body tissues.

**INDICATIONS**
Laceraine Topical Wound Anaesthetic is indicated for topical application to superficial local wounds and lacerations to provide local surface anaesthesia. It may be used to provide topical anaesthetic relief for wound closure.

The solution should only be used topically and locally on broken skin.

It should not be used for wounds greater than 7 cm or where the wound is contaminated or complex.

**CONTRAINDICATIONS**
Do not use Laceraine Topical Wound Anaesthetic on appendages such as digits, pinnae, tip of the nose or penis etc. or allow patients to rub it with their fingers since the profound adrenaline mediated ischaemia that may follow may lead to gangrene.

It is not indicated for other topical uses such as on mucous membranes, the eyes, nose, throat or larynx.

It is not indicated for any dental use, nor on any sites where there is a possible entry to major veins or arteries.

It should not be used for wounds greater than 7 cm across or where the wound is contaminated or complex. It is not meant to be used on intact skin.

It should not be used on patients with burns since adrenaline has been reported to increase capillary oozing from the burned area.

It should not be used on patients with any known history of hypersensitivity to local anaesthetics of the amide or ester type, or with patients with sensitivity to para-aminobenzoic acid and its derivatives.

Do not use on bites - animal or human.

Do not use on patients who are undergoing anaesthesia with Cyclopropane, Halothane or any other halogenated anaesthetics due to a risk of induction of ventricular fibrillation.

An increased risk of arrhythmias may occur in patients under therapy with cardiac glycosides, quinidine or tricyclic antidepressants. When a patient has been treated with monoamine oxidase inhibitors they should not be given Laceraine Topical Wound Anaesthetic until at least 14 days after treatment has ceased.
Prolonged use of Laceraine Topical Wound Anaesthetic is not recommended in any patient.

PRECAUTIONS

Adrenaline may cause oedema, hyperaemia, and inflammation of mucous membranes if applied frequently.

Excessive doses of local anaesthetics or short intervals between doses, can result in high plasma levels and serious adverse effects. It is recommended that dosage be strictly adhered too. The management of serious adverse reactions may require the use of resuscitative equipment, oxygen and other resuscitative drugs (see Treatment of Adverse Effects or Overdosage).

Patients with any known history of sensitivity to local anaesthetics should not be treated with Laceraine Topical Wound Anaesthetic. When using Laceraine Topical Wound Anaesthetic, facilities for resuscitation should be immediately available.

Absorption from wound surfaces is low. Local anaesthetic drugs may have effects on excitable membranes in the brain and myocardium. If excessive amounts of drug reach the systemic circulation rapidly, symptoms and signs of toxicity will appear, emanating from the central nervous and cardiovascular systems (see Adverse Effects or Overdosage).

Laceraine Topical Wound Anaesthetic should be given cautiously to patients with:

- Epilepsy
- Hyperthyroidism
- Hypovolaemia
- Diabetes Mellitus, especially if accompanied with any peripheral vascular disorders
- Close angle Glaucoma
- Asthma
- Cardiac diseases such as partial or complete heart block, bradycardia or congestive heart failure, impaired cardiac conduction or heart block, ischaemic heart disease, arrhythmia or tachycardia, and occlusive vascular disorders including arteriosclerosis, hypertension, or aneurysms. Anginal pain may be precipitated in patients with Angina Pectoris
- Shock
- Respiratory depression
- Circulatory failure
- Liver damage
- Myasthenia gravis
- The elderly and patients in poor general health
- Patients with severe injuries where systemic arteries or veins are exposed
- Patients with advanced liver disease or severe renal dysfunction
- Ester type anaesthetics such as Amethocaine Hydrochloride (Amethocaine Hydrochloride) are contra-indicated in patients with low plasma or in those receiving anti-cholinesterases.

These precautions especially apply where the dose or administration is likely to result in high blood levels.

Central nervous system toxicity (see Adverse Effects or Overdosage) usually precedes the cardiovascular effects as it occurs at lower plasma concentrations. Direct effects of local anaesthetics on the heart include slow conduction, negative inotropism and possibly cardiac arrest.

Ensure that patients do not rub the site of application and then transfer any Laceraine Topical Wound Anaesthetic to their eyes or mucous membranes.

Do not use Laceraine Topical Wound Anaesthetic on appendages such as digits, pinnae, tip of the nose or penis etc or allow patients to rub it with their fingers since the profound adrenaline mediated ischaemia that may follow may lead to gangrene.

Use in Pregnancy

Use of Laceraine Topical Wound Anaesthetic in pregnancy not indicated.

Use in Lactation
Use of Laceraine Topical Wound Anaesthetic on nursing mothers is not indicated.

See Adverse Reactions and Overdosage.

Paediatric Use

Laceraine Topical Wound Anaesthetic may be used for local anaesthesia in children older than 1 year. However, special care should be taken with the dose using the special applicator supplied with the vial. Care should be taken to ensure that any site is not given more than four applications in a 24-hour period. See Dosage and Administration.

Care should be taken to ensure that any children do not transfer any Laceraine Topical Wound Anaesthetic from the site of application to the eyes, mouth or any other mucous membranes.

INTERACTIONS WITH OTHER MEDICINES

Amethocaine hydrochloride is metabolised by plasma esterases to para-aminobenzoic acid and other metabolites and may antagonise the action of sulphonamides. Amethocaine hydrochloride is a potent local anaesthetic of the ester type. It has a relatively slow onset of action and systemic toxicity.

Patients on non-selective beta-blockers such as propanolol should not be treated with Laceraine Topical Wound Anaesthetic since there are reports of potential fatal interactions between these non-selective beta-blockers and adrenaline. This is characterised by marked hypotension followed by reflex bradycardia. This sequence may lead to cardiac arrest or hypertensive stroke.

ADVERSE EFFECTS

Adverse reactions to local anaesthetics in this formulation are uncommon. There appears to be no cross reactivity between ester and amide types.

The side effects apparent after Laceraine Topical Wound Anaesthetic may be due to the adrenaline, to the anaesthetics, errors in technique, dosage or may be the result of blockade of the sympathetic nervous system.

Local anaesthetics may have systemic adverse effects due to raised plasma concentrations, which ensue when the rate of absorption into the circulation exceeds the rate of breakdown. Mostly this may occur with Laceraine Topical Wound Anaesthetic following either excessive dosage or via accidental transfer to mucous membranes and/or to the circulation via the lungs. The vasoconstrictive effect of adrenaline should reduce the entry of the local anaesthetics to the circulation, provided that the application is kept away from contact with mucous membranes or where it is used in areas where there is the possibility of significant entry via a major blood vessel such as a femoral artery or areas of major vascularisation.

Care must be taken to avoid exposure via the lungs or mucous membranes or on severely damaged sites, which allow access to major blood vessels.

Allergic reactions (in most severe instances anaphylactic shock) to local anaesthetics of the amide type are rare. Idiosyncratic reactions to local anaesthetics have been reported. Vasovagal attacks may be associated with local anaesthesia. Local anaesthetics are potent sensitisers and allergic reactions may occur as a result of repeated handling or repeated topical use.

Any systemic toxicity of local anaesthetics mainly involves the central nervous system and the cardiovascular system. Excitation of the CNS may manifest as 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 also be simultaneous effects on the cardiovascular system with myocardial depression and peripheral vasodilation resulting in hypotension and bradycardia; arrhythmias and cardiac arrest may occur. Direct effects of local anaesthetics on the heart also include slow conduction, negative inotropism and possibly cardiac arrest.

Central nervous system toxicity usually precedes the cardiovascular effects as it occurs at lower plasma concentrations. In some instances some local anaesthetics may cause methaemoglobinemia.
Other side effects may include burning, itching, or redness in the treated area, skin rashes, hives, or shortness of breath. Contact dermatitis may occur with amethocaine hydrochloride. Sensitised patients may subsequently develop a widespread eruption when similar drugs are given systemically.

Adrenaline mediated side effects may be complex and will depend on the level of exposure. It is possible for adrenaline to infiltrate the skin especially via wounds in the appendages, in some cases it may generate a vasoconstriction sufficiently enough to cause gangrene and resultant hypertension.

Do not use Laceraine Topical Wound Anaesthetic on appendages such as digits, pinnae, tip of the nose or penis etc or allow patients to rub it with their fingers since the profound adrenaline mediated ischaemia that may follow may lead to gangrene.

Other adverse effects related to adrenaline may include hypokalaemia, and severe skin necrosis, and cellulitis, hypotension, dizziness and fainting, flushing, difficulty in micturition and urinary retention, dyspnoea, altered metabolism including disturbances in glucose metabolism, sweating and hypersalivation. Headache may occur.

**DOSAGE AND ADMINISTRATION**

As with any local anaesthetic, their safety and effectiveness depend on the proper dosage, the correct technique, adequate precautions and readiness for emergencies. The smallest effective dose should be used.

The clinician's experience and knowledge of the patient's physical status and age are of importance in calculating the required dose. Debilitated or elderly patients or acutely ill patients should be given doses commensurate with their age, weight and physical condition.

No more than four applications should be given in a 24-hour period.

The suggested method of use is as follows:

1. Gloves must be worn while using Laceraine.
2. Flip open the plastic top of the Laceraine vial.
3. Grasp the plastic top and pull open slowly, pulling the plastic top backwards so that the metal seal starts to tear open.
4. Remove the metal seal to reveal the rubber vial stopper.
5. Remove the rubber stopper carefully.
6. Remove the plastic cover from the sterile dropper and carefully attach the dropper to the top of the glass vial, making sure it is securely in place.
7. Gently clean the wound of any clotted blood and debris with saline solution and gauze. More thorough cleaning can be done once the wound is anaesthetised and just before suturing.
8. Pour Laceraine into two (2) medicine cups.
9. Wet a cotton wool applicator with Laceraine and dab the wound with it a number of times and discard. This may cause some bleeding but it is nothing to be alarmed about unless the bleeding is excessive. There may be an initial stinging sensation when Laceraine is applied.
10. Soak a piece of cotton ball the size of the wound in the other medicine cup containing Laceraine solution, one mL per cm of laceration. The cotton ball should not be dripping.
11. Apply the cotton ball soaked in Laceraine to the wound so that it covers the entire wound and all edges.
12. Apply a dressing to hold the soaked cotton ball firmly to the wound.
13. The dressing and the cotton ball are removed after 20-30 minutes but can be left for up to 60 minutes. The skin around the wound should look white (blanched).
14. The wound can then be irrigated and thoroughly cleaned. The doctor will check that the wound is numb before suturing.

Follow all precautions for use. See Precautions and Adverse Effects and Overdosage sections.
Laceraine Topical Wound Anaesthetic contains no preservative. Use immediately after dropper has been attached to vial. Discard after use. Discard if solution is discoloured.

OVERDOSAGE

Absorption of local anaesthetics from the site of application may be reduced if necessary by use of a tourniquet. When systemic reactions occur steps should be taken to maintain the circulation and respiration and to control convulsions. A patent airway must be established and oxygen given, together with assisted ventilation if necessary. The circulation should be maintained with infusions of IV plasma or fluids.

Convulsions may be controlled with the IV administration of diazepam or sodium thiopentone. Care should be taken that anti-convulsive treatment does not depress respiration and circulation. A short acting neuromuscular blocking agent, together with endotracheal intubation and artificial respiration has been used when convulsions persist.

Methaemoglobinemia may be treated with IV Methylene Blue solution (1%).

Because of the short duration of action of adrenaline (adrenaline) it is unlikely to cause adverse reactions other than the possibility of ischaemia in appendages. Treatment should be supportive, however, prompt injection of a rapidly acting alpha-adrenergic blocking agent such as Phentolamine, followed by a beta-blocker may be used to counteract the pressor and arrhythmogenic effect of adrenaline. Rapidly acting vasodilators such as glyceryl trinitrate may be used.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

PRESENTATION AND STORAGE CONDITIONS

Laceraine Topical Wound Anaesthetic contains adrenaline acid tartrate, amethocaine hydrochloride and lignocaine hydrochloride. It is presented in a 5mL vial with a dropper in a carton of 5 vials.

Store at 2°C to 8°C. Refrigerate. Do not freeze. Protect from light.

Phebra product code: SOL037

NAME AND ADDRESS OF THE SPONSOR

Phebra Pty Ltd, 19 Orion Road, Lane Cove West, NSW 2066, Australia.
Telephone: 1800 720 020

POISON SCHEDULE OF THE MEDICINE

Schedule 3- Pharmacist Only Medicine

Date of most recent amendment: 29th October 2015

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