

NEW ZEALAND DATA SHEET

NAME OF MEDICINE

EMLA PATCH
lignocaine 2.5%, prilocaine 2.5%

PRESENTATION

EMLA PATCH is a unit-dose formulation of EMLA in the form of an occlusive dressing. An absorbent cellulose disc, saturated with 1 g of EMLA emulsion 5%, is affixed to a laminate backing equipped with an adhesive tape frame. The contact surface area of the EMLA saturated disc is approximately 10 cm².

EMLA emulsion is an oil-in-water emulsion system in which the oil phase consists of a eutectic mixture of the base forms of lignocaine and prilocaine in the ratio 1:1.

USES

ACTIONS

EMLA PATCH, applied to intact skin, provides dermal anaesthesia through the release of lignocaine and prilocaine into the epidermal and dermal layers of the skin and the accumulation of lignocaine and prilocaine in the vicinity of dermal pain receptors and nerve endings. Lignocaine and prilocaine are amide-type local anaesthetic agents. They both stabilise neuronal membranes by inhibiting the ionic fluxes required for the initiation and conduction of impulses, thereby producing local anaesthesia.

The quality of anaesthesia depends upon the application time. The time needed to achieve reliable anaesthesia of intact skin is at least 60 minutes.

In clinical studies of EMLA on intact skin, no differences in safety or efficacy (including anaesthetic onset time) were observed between geriatric patients (aged 65-96 years) and younger patients.

The depth of cutaneous anaesthesia increases with application time. In 90% of patients the anaesthesia is sufficient for the insertion of a biopsy punch (4 mm diameter) to a depth of 2 mm after 60 minutes and 3 mm after 120 minutes of EMLA treatment. EMLA is equally effective and has the same anaesthetic onset time across the range of light to dark pigmented skin (skin types I to VI).

The use of EMLA prior to measles-mumps-rubella or intramuscular diphtheria-pertussis-tetanus-inactivated poliovirus-*Haemophilus influenzae* b or Hepatitis B vaccines does not affect mean antibody titres, rate of seroconversion, or the proportion of patients achieving protective or positive antibody titres post immunisation, as compared to placebo treated patients.

The EMLA emulsion produces a biphasic vascular response involving initial vasoconstriction followed by vasodilatation at the application site (see ADVERSE EFFECTS). Irrespective of the vascular response, EMLA facilitates the needle puncture procedure compared to placebo.

In patients with atopic dermatitis, a similar but shorter reaction is seen, with erythema occurring after 30-60 minutes, indicating more rapid absorption through the skin (see WARNINGS AND PRECAUTIONS).

PHARMACOKINETICS

The systemic absorption of lignocaine and prilocaine from EMLA is dependent upon the dose, area of application, application time. Other factors are; following application to skin: thickness of the skin, which varies in different areas of the body, and the condition of the skin.

Intact skin. The available pharmacokinetic data refer to the application of EMLA cream 5% to intact skin. Following application to the thigh in adults (60 g cream / 400 cm² for 3 hours), the extent of absorption of lignocaine and prilocaine was approximately 5%. Maximum plasma concentrations (mean 0.12 and 0.07 µg/ml) were reached approximately 2-6 hours after application.

The extent of systemic absorption was approximately 10% following application to the face (10 g/100 cm² for 2 hours). Maximum plasma levels (mean 0.16 and 0.06 µg/ml) were reached after approximately 1.5-3 hours.

Plasma levels of lignocaine and prilocaine in both geriatric and non-geriatric patients following application of EMLA to intact skin are very low and well below potentially toxic levels.

Prilocaine and lignocaine are principally metabolised in the liver with only 1% and 10% respectively of the absorbed dose being excreted in the urine unchanged. Both prilocaine and lignocaine have short plasma half lives of 1.6 hours.

Children: Following the application of 1.0 g EMLA cream in neonates below 3 months of age, to approximately 10 cm² for one hour, the maximum plasma concentrations of lignocaine and prilocaine were 0.135 µg/ml and 0.107 µg/ml respectively. Following the application of 2.0 g EMLA cream in infants between 3 and 12 months of age, approximately 16 cm² for four hours, the maximum plasma concentrations of lignocaine and prilocaine were 0.155 µg/ml and 0.131 µg/ml respectively. Following the application of 10.0 g EMLA cream in children between 2 and 3 years of age, to approximately 100 cm² for two hours, the maximum plasma concentrations of lignocaine and prilocaine were 0.315 µg/mL and 0.215 µg/ml respectively. Following the application of 10.0-16.0 g EMLA cream in children between 6 and 8 years of age, to approximately 100-160 cm² for two hours, the maximum plasma concentrations of lignocaine and prilocaine were 0.299 µg/mL and 0.110 µg/mL respectively.

INDICATIONS

EMLA PATCH is indicated for

Topical anaesthesia of intact skin in connection with minor procedures, such as needle insertion and surgical treatment of localised lesions.

DOSAGE AND ADMINISTRATION

Adults and children over 1 year of age:

One or more PATCH(ES) are applied to the skin area(s) selected.

Minimum application time: 1 hour. After a longer application time than 5 hours the anaesthesia decreases.

Maximum dose for children between **1-5 years** is 10 patches.

Maximum dose for children between **6-12 years** is 20 patches.

Prior to curettage of mollusca in children with atopic dermatitis, an application time of 30 minutes is recommended.

Infants aged 3 -11 months:

The PATCH is applied to the skin area selected. Approximate application time: 1 hour.

Based on clinical data for EMLA cream, not more than two EMLA PATCHES should be applied at the same time. No clinically significant increase in methaemoglobin levels has been observed following the application of 2 g EMLA cream for 4 hours.

Neonates under 3 months of age:

The PATCH is applied to the skin area selected. Approximate application time: 1 hour, not more. A longer application time than 1 hour has not been documented. Not more than one EMLA PATCH should be applied at the same time.

The size of the PATCH makes it less suitable for use on certain parts of the body in neonates and infants.

Until further clinical data is available, EMLA should not be used in infants between 0 and 12 months of age receiving treatment with methaemoglobin inducing agents.

CONTRAINDICATIONS

Hypersensitivity to local anaesthetics of the amide type or any of the excipients.

WARNINGS AND PRECAUTIONS

Patients with glucose-6-phosphate dehydrogenase deficiency or congenital or idiopathic methaemoglobinaemia are more susceptible to drug-induced methaemoglobinaemia.

Due to insufficient data on absorption, EMLA should not be applied to open wounds.

Studies have been unable to demonstrate the efficacy of EMLA for heel lancing in neonates.

Care should be taken when applying EMLA to patients with atopic dermatitis. A shorter application time, 15-30 minutes, may be sufficient (refer ACTIONS). Prior to curettage of mollusca in children with atopic dermatitis an application time of 30 minutes is recommended.

Care should be taken not to allow EMLA to come in contact with the eyes as it may cause eye irritation (see FURTHER INFORMATION). Also the loss of protective reflexes may allow corneal irritation and potential abrasion. If eye contact occurs, immediately rinse the eye in water or sodium chloride solution and protect it until sensation returns.

In children / neonates younger than 3 months a transient, clinically insignificant, increase in methaemoglobin levels is commonly observed up to 12 hours after application of EMLA.

Lignocaine and prilocaine have bacteriocidal and antiviral properties in concentrations above 0.5 - 2%. For this reason, although one clinical study suggests that the immunisation response is not affected when EMLA is used prior to BCG vaccination, the results of intracutaneous injections of live vaccines should be monitored.

Until further clinical data are available, EMLA should not be used in the following cases:

- infants between 0 and 12 months of age receiving treatment with methaemoglobin reducing agents.
- in preterm infants with a gestational age less than 37 weeks.

EFFECT ON ABILITY TO DRIVE AND USE MACHINES

Not applicable at the recommended dosage.

USE IN PREGNANCY

Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

In both animals and humans, lignocaine and prilocaine cross the placental barrier and may be taken up by the foetal tissues. It is reasonable to assume that lignocaine and prilocaine have been used in a large number of pregnant women and women of child-bearing age. No specific disturbances to the reproductive process, such as an increased incidence of malformations or other direct or indirect harmful effects on the foetus have so far been reported. However, caution should be exercised when used in pregnant women.

USE IN LACTATION

Lignocaine and, in all probability, prilocaine are excreted in breast milk, but in such small quantities that there is generally no risk of the child being affected at therapeutic dose levels.

ADVERSE EFFECTS

Frequency of Adverse Events

Intact Skin	
Common Events (>1%)	Skin: Transient local reactions at the application site such as paleness, erythema (redness) and oedema.
Uncommon Events (>0.1% and <1%)	Skin: Skin sensations (an initial mild burning or itching sensation at the application site).
Rare Events (< 0.1%)	<p>General: Methaemoglobinaemia (see INTERACTIONS and OVERDOSAGE).</p> <p>Rare cases of discrete local lesions at the application site, described as purpuric or petechial, have been reported, especially after longer application times in children with atopic dermatitis or mollusca contagiosa.</p> <p>Corneal irritation after accidental eye exposure.</p> <p>In rare cases, local anaesthetic preparations have been associated with allergic reactions (in the most severe instances anaphylactic shock).</p>

INTERACTIONS

Prilocaine in high doses may cause an increase in the methaemoglobin level, particularly in conjunction with methaemoglobin-inducing agents (e.g. sulphonamides).

With large doses of EMLA, consideration should be given to the risk of additional systemic toxicity in patients receiving other local anaesthetics or agents structurally related to local anaesthetics, since the toxic effects are additive.

Medicines that reduce the clearance of lignocaine (eg, cimetidine or betablockers) may cause potentially toxic plasma concentrations when lignocaine is given in repeated high doses over a long time period. Such interactions should therefore be of no clinical importance following short term treatment with lignocaine (eg. EMLA PATCH) at recommended doses.

OVERDOSAGE

Rare cases of clinically significant methaemoglobinaemia in connection with treatment with EMLA Cream (see ADVERSE EFFECTS) have been reported. Prilocaine in high doses may cause an increase in the methaemoglobin level particularly in conjunction with methaemoglobin-inducing agents (e.g. sulphonamides). Clinically significant methaemoglobinaemia should be treated with slow intravenous injection of methylene blue.

Should other symptoms of systemic toxicity occur, the signs are anticipated to be similar in nature to those following the administration of local anaesthetics by other routes. Local anaesthetic toxicity is manifested by symptoms of nervous system excitation and, in severe cases, central nervous and cardiovascular depression.

Severe neurological symptoms (convulsions, CNS depression) must be treated symptomatically by respiratory support and the administration of anticonvulsive medicines.

PHARMACEUTICAL PRECAUTIONS

SHELF-LIFE AND STORAGE CONDITIONS

Shelf-life of 2 years at storage below 30°C.

MEDICINE CLASSIFICATION

Pharmacy Only Medicine.

PACKAGE QUANTITIES

EMLA PATCHES:

containing 1 g of EMLA emulsion in packs of 20.

containing 1 g of EMLA emulsion in packs of 2.

FURTHER INFORMATION

DESCRIPTION

EMLA (Eutectic Mixture of Local Anaesthetics) is a 1:1 oil/water emulsion of an eutectic mixture of lignocaine and prilocaine. If mixed in equal amounts, the solid pure bases of lignocaine and prilocaine form an oil at temperatures above 16°C (i.e. a eutectic mixture). By avoiding the need for a non-aqueous solvent, higher concentrations of local anaesthetic in the cream can be achieved and maintained during application.

LIST OF EXCIPIENTS

Carboxypolymethylene, polyoxyethylene hydrogenated castor oil, sodium hydroxide to pH 8.7-9.7, purified water.

NATURE AND CONTENTS OF CONTAINER

The PATCH consists of an occlusive dressing (user part) and a protective liner (closure part). The user part is composed of an aluminium/plastic backing laminate, an absorbent cellulose disc and a foam tape ring. The tape is a polyethylene foam coated with acrylate adhesive. The closure part is an aluminium/plastic laminate. A peel-off seal between the backing and closure laminates encloses the disc, which is impregnated with EMLA emulsion.

PRECLINICAL SAFETY INFORMATION

In animal studies the toxicity noted after high doses of either lignocaine or prilocaine, alone or in combination, consisted of effects on the central nervous and cardiovascular systems. When lignocaine and prilocaine were combined, only additive effects were seen, with no indication of synergism or unexpected toxicity. Both compounds were shown to have a low oral acute toxicity, providing a good safety margin in the event that EMLA is inadvertently

swallowed. No drug-related adverse effects were seen in the reproduction toxicity studies, using either compound separately or together.

Neither local anaesthetic showed a mutagenic potential in either *in vitro* or *in vivo* mutagenicity tests. Cancer studies have not been performed with either lignocaine or prilocaine alone or in combination, due to the indication and duration of therapeutic use of these drugs.

A metabolite of lignocaine, 2,6-dimethylaniline and a metabolite of prilocaine, o-toluidine, showed evidence of mutagenic activity. These metabolites have been shown to have carcinogenicity potential in preclinical toxicological studies evaluating chronic exposure. Risk assessments comparing the calculated maximum human exposure from intermittent use of lignocaine and prilocaine, with the exposure used in preclinical studies, indicate a wide margin of safety for clinical use.

Local tolerance studies using a 1:1 (w/w) mixture of lignocaine and prilocaine as an emulsion, cream or gel indicated that these formulations are well tolerated by intact and damaged skin and mucosal membranes.

A marked irritative reaction was seen after single ocular administration of a 50 mg/g lignocaine + prilocaine 1:1 (w/w) emulsion, in an animal study. This is the same concentration of local anaesthetics and a similar formulation as for EMLA cream. This ocular reaction may have been influenced by the high pH of the formulation of the emulsion (approximately 9), but is probably also partly a result of the irritative potential of the local anaesthetics themselves.

Preclinical studies on the adhesive used in the patch did not raise any concerns.

NAME AND ADDRESS

AstraZeneca Limited
Level 5, 15 Hopetoun Street, Freemans Bay.
P299 Private Bag 92175, Auckland 1142
Telephone: (09) 306 5650

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