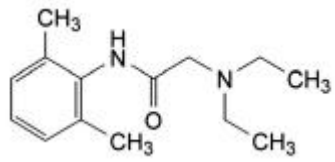
EMLA® PRODUCT INFORMATION

(lidocaine (lignocaine)/prilocaine eutectic mixture for dermal anaesthesia)

NAME OF THE MEDICINE

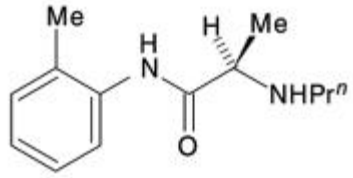
EMLA (Eutectic Mixture of Local Anaesthetics) is a 1:1 oil/water emulsion of an eutectic mixture of lidocaine (lignocaine) and prilocaine.
Lidocaine is the new medicine ingredient name for lignocaine and is mostly used in this product information.

Lidocaine



$C_{14}H_{22}N_2O$ molecular weight 234.3 *CAS no. 137-58-6*

Prilocaine



$C_{13}H_{20}N_2O$ molecular weight 220.3 *CAS no. 721-50-6*

DESCRIPTION

When lidocaine and prilocaine are mixed in equal amounts, the solid pure bases of lidocaine 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.

EMLA CREAM 5% contains in 1 g lidocaine 25 mg, prilocaine 25 mg as the active ingredients; and carbomer 934P, polyoxyethylene hydrogenated castor oil, sodium hydroxide to a pH of approximately 9.2 and purified water to 1 g.

EMLA PATCH 5% is a single dose unit in the form of an occlusive dressing. It is composed of a laminate backing, an absorbent cellulose disc and an adhesive tape ring. The disc provides a contact area of approximately 10 cm^2 and contains 1 g of EMLA emulsion. Each 1 g of EMLA emulsion contains lidocaine 25 mg and

prilocaine 25 mg as active ingredients, and excipients as for EMLA cream 5%. The emulsion contains a lower concentration of the thickening agent, carbomer 934P.

EMLA is non-sterile and does not contain preservatives.

PHARMACOLOGY

Lidocaine and prilocaine are both amide-type local anaesthetic agents. Both agents stabilise the neuronal membrane preventing the initiation and conduction of nerve impulses thereby effecting local anaesthetic action.

EMLA provides dermal anaesthesia. The depth and quality of anaesthesia depends upon the application time and the applied dose.

Local anaesthesia with EMLA is achieved after 60 minutes application. EMLA should be applied as EMLA patch; or EMLA cream should be applied under an occlusive, impermeable dressing. Following the application of EMLA cream for 1 - 2 hours, the duration of anaesthesia is at least 2 hours after removal of the occlusive dressing.
Reliable anaesthesia for the cleansing of leg ulcers is achieved after an application time of 30 minutes in most patients. An application time of 60 minutes may improve the anaesthesia. The cleansing procedure should start within 10 minutes of removal of the cream. There is no clinical data regarding cleaning started after 10 minutes of cream removal.

A reduced number of cleansing sessions are required to achieve a clean ulcer when EMLA is used compared to a placebo.

No negative effects on ulcer healing or bacterial flora have been observed when EMLA has been used.

EMLA may cause transient local peripheral vasoconstriction or vasodilation, observed as transient paleness or redness, at the treated area.

Pharmacokinetics

Systemic absorption and anaesthetic efficacy of lidocaine and prilocaine from EMLA is dependent upon the characteristics of the leg ulcer, the applied dose, total application area, application time, thickness of the skin (which varies between different areas of the body), other conditions such as skin diseases, and shaving.

Intact skin

The extent of systemic absorption was approximately 10% following application to the face (10 g/100 cm^2 for 2 hours). Maximum plasma levels (mean 0.16 and 0.06 µg/mL of lidocaine and prilocaine respectively) were reached after approximately 2.5 hours.

After application to the thigh in adults (60 g cream/400 cm^2 for 3 hours) the extent of absorption was approximately 5% of lidocaine and prilocaine. Maximum plasma

concentrations (mean 0.12 and 0.07 µg/mL) were reached approximately 2 - 6 hours after the application.

In adults, a thick layer of EMLA Cream 5% (corresponding to approximately 150 g) has been applied to intact skin areas of up to 1,300 cm^2 for application times of up to 7 hours. The highest individual plasma levels observed to date were 1.1 µg/mL lidocaine and 0.2 µg/mL prilocaine. These levels were below those at which symptoms of toxicity would be expected to occur (5 - 10 µg/mL either agent; see also ADVERSE REACTIONS).

Leg ulcers
Following a single application for 30 minutes of 5 to 10 g of EMLA cream to leg ulcers, the maximum plasma levels of lidocaine (range 0.05 - 0.25 µg/mL, one individual value of 0.84 µg/mL) and of prilocaine (0.02 - 0.08 µg/mL) were reached within 1 - 2.5 hours.

After an application time of 24 hours the maximum plasma levels of lidocaine (0.19 - 0.71 µg/ml) and of prilocaine (0.06 - 0.28 µg/ml) were usually reached within 2 - 4 hours.

Following repeated applications for 30 - 60 minutes of 2 - 10 g EMLA cream 3 - 7 times a week, for up to 15 doses, during a period of one month, there was no apparent accumulation in plasma of lidocaine and its metabolites monoglycinexylidide and 2,6-xylidine or of prilocaine and its metabolite ortho-toluidine. The maximum observed plasma levels for lidocaine, monoglycinexylidide and 2,6-xylidine were 0.41, 0.03 and 0.01 µg/mL respectively. The maximum observed plasma levels for prilocaine and ortho-toluidine were 0.08 µg/mL and 0.01 µg/mL respectively.

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

CLINICAL TRIALS

In clinical trials, venepuncture or venous catheterisation was pain-free in 50 - 59% patients, slightly painful in 35 - 40% and painful in 3 - 6%. Anaesthesia may be less for skin structures below the deep fascia.

In clinical trials in adults assessing pain associated with intramuscular influenza vaccination and intramuscular and subcutaneous injections of saline solution, EMLA significantly reduced injection pain relative to placebo.

In clinical trials in infants and children assessing pain associated with subcutaneous and intramuscular vaccination, EMLA significantly reduced injection pain behaviours and pain scores relative to placebo.

In clinical trials assessing the effects of EMLA on intramuscular and subcutaneous, live and non-live vaccines, it was demonstrated that EMLA does not adversely affect antibody response. A clinical trial assessing the effect of EMLA application prior to intracutaneous BCG injection demonstrated that EMLA did not affect the immunisation response.

INDICATIONS

EMLA Cream and EMLA Patch
Topical anaesthesia of the skin prior to insertion of i.v. catheters, blood sampling, vaccination; superficial surgical procedures, including split skin grafting.

EMLA Cream
Topical anaesthesia of leg ulcers to facilitate mechanical cleansing or debridement.

Topical anaesthesia of genital skin prior to superficial surgical procedures or infiltration anaesthesia.

Topical anaesthesia of the skin prior to minor superficial cosmetic procedures.

CONTRAINDICATIONS

Hypersensitivity to prilocaine, lidocaine or any local anaesthetics of the amide type.

Hypersensitivity to any of the excipients of EMLA cream or emulsion, or to the adhesive used in the patch.

Glucose-6-phosphate dehydrogenase deficiency or congenital or idiopathic methaemoglobinaemia.

PRECAUTIONS

1. **Open wounds**
   EMLA should not be applied to open wounds other than leg ulcers, due to insufficient data on absorption from these sites.

2. **Atopic dermatitis**
   Care should be taken when applying EMLA to skin areas with atopic dermatitis. A shorter application time (15 - 30 minutes) may be sufficient.

3. Eyes

EMLA should not be applied to or near to the eyes since it causes corneal irritation. Damage to the eye may also occur from undetected foreign bodies. Special care should be employed to reduce the risk of rubbing the eyes with EMLA. It is therefore important that the patch or occlusive dressing should be secured against accidental dislocation, especially in young children.

4. Middle ear

EMLA is not recommended in any clinical situation in which its penetration into the middle ear is possible. In studies in rodents (guinea pigs) EMLA was found to have an ototoxic effect when instilled directly into the middle ear, however no abnormalities were observed when EMLA was applied to the animals' external auditory canal. EMLA cream 5% caused minor structural damage to the tympanic membrane in rats when applied directly to the membrane. The relevance of these findings to the clinical situation is unknown.

5. Genital mucosa

EMLA is presently not recommended for use on genital mucosa. Available data suggest that the anaesthetic efficacy of EMLA on genital mucosa may be variable.

6. Application of EMLA patch 5%

Care should be taken that the patch does not become detached (especially in young children) during the 60 minute wait. The possibility that this may occur can be reduced if the patch is applied to the non-dominant hand; or lightly bandaged if applied to the antecubital fossa to protect it from lifting if rubbed by clothing.

7. Paediatric use

Until further clinical data are available, EMLA should not be used in infants between 0 and 12 months of age receiving treatment with methaemoglobin-inducing agents such as sulphonamides (see also OVERDOSAGE) or in preterm infants with a gestational age less than 37 weeks.

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

EMLA should not be applied to the genital mucosa of children owing to insufficient data on absorption. However, when used in neonates for circumcision (genital skin), a dose of 1.0 g EMLA on the prepuce has proven to be safe.

In children/neonates younger than 3 months of age, a transient increase in methaemoglobin is commonly observed up to 12 hours after an application of EMLA. Caution is required in those at risk of tissue hypoxia, e.g. those with anaemia, respiratory and/or cardiac conditions. Prolonged exposure, e.g. greater than 60 minutes application, significantly increases the risk of methaemoglobinaemia. Repeated applications of EMLA in neonates and infants have not been studied and should be avoided.

8. Vaccination

Lidocaine and prilocaine have bactericidal and antiviral properties in concentrations above 0.5 – 2%. A clinical trial with MMR vaccine administered subcutaneously demonstrated that EMLA does not adversely affect antibody response. There are no data on effects of EMLA on other live viral vaccines administered subcutaneously. When EMLA is used prior to intradermal BCG vaccination, the results of vaccination should be monitored.

9. Anti-arrhythmic drugs class III

Patients treated with anti-arrhythmic drugs class III (eg, amiodarone) should be kept under close surveillance and ECG monitoring considered, since cardiac effects may be additive.

10. Drugs reducing clearance of lidocaine

Drugs that reduce the clearance of lidocaine (for example, cimetidine or betablockers) may cause potentially toxic plasma concentrations when lidocaine (e.g. EMLA) 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 lignociane (e.g. EMLA) at recommended doses.

Carcinogenic and Mutagenic Potential

Genotoxicity tests with lidocaine are inconclusive. In genotoxicity studies, a metabolite of lidocaine, 2,6-xylidine, showed evidence of activity in some tests but not in other tests. This metabolite has been shown to have carcinogenic potential (nasal and subcutaneous tumours) in preclinical toxicological studies evaluating chronic exposure. A metabolite of prilocaine, o-toluidine, has also shown evidence of mutagenic activity in some genotoxicity tests but not others. o-toluidine has also been shown to have carcinogenic potential (e.g. renal, bladder, spleen, subcutaneous tumours) in preclinical toxicological studies.

Use in pregnancy Category A

Although the safety of EMLA during pregnancy has not been established in animal reproductive toxicology studies, lidocaine and prilocaine have been used by a large number of pregnant women and women of child-bearing age, without an increased incidence of malformations or other direct or indirect harmful effects on the foetus having been observed.

Use in lactation

No information is available on the excretion of lidocaine, prilocaine or their metabolites into breast milk following the administration of EMLA.

Following parenteral administration, lidocaine is excreted into breast milk. Because of low maternal systemic absorption following application of recommended doses of EMLA, the amount of lidocaine and prilocaine that may be ingested by the breast-fed infant would be extremely small.

INTERACTIONS WITH OTHER DRUGS

1. Methaemaglobinaemia-inducing agents.

EMLA may accentuate the formation of methaemoglobin in patients treated with other drugs known to induce methaemaglobinaemia (e.g. sulphonamides).

2. Other local anaesthetic agents.
With large doses of EMLA, the risk of additional systemic toxicity should be considered in patients receiving other local anaesthetics or agents structurally related to local anaesthetics eg. mexiletine.

3. Anti-arrhythmic drugs class III.
Specific interaction studies with lidocaine and anti-arrhythmic drugs class III (e.g. amiodarone) have not been performed, but caution is advised.

4. Drugs reducing clearance of lidocaine
Drugs that reduce the clearance of lidocaine (for example, cimetidine or betablockers) may cause potentially toxic plasma concentrations when lidocaine (e.g. EMLA) 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 lidocaine (e.g. EMLA) at recommended doses.

ADVERSE EFFECTS

FREQUENCY OF ADVERSE EVENTS

Intact skin

Common Events (≥1% and < 10%)	*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, usually mild burning sensation, itch or warmth at the application site).
Rare Events (< 0.1%)	*General*: In rare cases, local anesthetic preparations have been associated with allergic reactions (in the most severe instances anaphylactic shock). 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. Increased methaemoglobin level. Methaemoglobinaemia and/or cyanosis. Corneal irritation after accidental eye exposure.

Leg ulcer

Common Events (≥1% and < 10%)	*Skin*: Transient local reactions at the application site such as, paleness, erythema (redness) and oedema. Skin sensations (an initial, usually mild burning sensation, itch or

	warmth at the application site).
Uncommon Events (≥0.1% and < 1%)	*Skin:* Skin irritation (at the application site)
Rare Events (< 0.1%)	*General*: In rare cases, local anesthetic preparations have been associated with allergic reactions (in the most severe instances anaphylactic shock).

DOSAGE AND ADMINISTRATION

In order to avoid cross-contamination, infection control procedures and principles should be strictly adhered to during application of EMLA.

Pharmacokinetic data for application longer than 4 hours is not available in children. In adults, there is no benefit in application times longer than 5 hours, as the analgesic effectiveness of the cream dissipates over time.

Use in the elderly

No dosage adjustment is required when EMLA is applied to intact skin in the elderly.

Use in premature infants with a gestational age of less than 37 weeks is not recommended (see PRECAUTIONS).

EMLA CREAM 5%

The protective membrane of the tube is perforated by reversing the cap and piercing the membrane. When used on leg ulcers discard the tube with any remaining EMLA after each occasion that a patient is treated.

Surface/Age	Procedure	Application
Skin		A thick layer of cream to the skin, under an occlusive dressing. Following application for 1 – 2 hours, the minimum duration of anaesthesia is 2 hours after removal of the dressing.
Adults		Approx 1.5 g/10 cm^2
	Minor procedures:needle insertion, cosmetic procedures (on small areas) and surgical treatment of localised lesions.	Up to 2 g (Approx half a 5g tube) for a minimum of 1 hour, maximum 5 hours[1)]
	Procedures on larger areas of skin e.g. cosmetic procedures	Maximum dose: 60g. Maximum treatment area: 600 cm^2 for a minimum of 1 hour, maximum 5 hours[1)]

Surface/Age	Procedure	Application
	such as hair removal or other superficial surgical procedures (in an outpatient setting).	[9]
	Dermal procedures on larger areas in a hospital setting (e.g. split-skin grafting).	Approx 1.5 - 2 g/10 cm^2 for a minimum of 2 hours, maximum 5 hours [1]
Children		Approx 1.0 g/10 cm^2 Application time: approx 1 hour
Neonates and infants 0 up to 3 months[3]	Minor procedures, eg, needle insertion and surgical treatment of localised lesions.	Up to 1.0 g and 10 cm^2 [2]
	Circumcision	1 g applied to the prepuce
Infants 3 up to 12 months[3]	Minor procedures, eg, needle insertion and surgical treatment of localised lesions.	Up to 2.0 g and 20 cm^2 [4]
Children 1 up to 6 years	Minor procedures, eg, needle insertion and surgical treatment of localised lesions.	Up to 10.0 g and 100 cm^2 [8] for a minimum of 1 hour, maximum 4 hours
Children 6 up to 12 years	Minor procedures, eg, needle insertion and surgical treatment of localised lesions.	Up to 20.0 g and 200 cm^2 [8] for a minimum of 1 hour, maximum 4 hours
Male genital skin Adults	Prior to injection of local anaesthetics.	Apply a thick layer of EMLA Cream (1 g/10 cm^2) under an occlusive dressing for 15 minutes.
Female genital skin Adults	Prior to injection of local anaesthetics.[7]	Apply a thick layer of EMLA Cream (1 - 2 g/10 cm^2) under an occlusive dressing for 60 minutes.
Leg ulcer Adults	Mechanical cleansing /debridement of leg ulcer(s).	Apply a thick layer of the cream, approx 1 - 2 g/10 cm^2 up to a total of 10 g to the leg ulcer(s).[5] [6]Cover with an occlusive dressing. Application time: at least 30 minutes. Up to 60 minutes may improve the anaesthesia further. Cleansing should start without delay after removal of the cream.

1) After a longer application time the anaesthesia decreases.
2) An application time longer than 1 hour has not been documented.
3) Until further clinical data is available, EMLA should not be used in infants between 0 - 12 months of age receiving treatment with methaemoglobin-inducing agents
4) No clinically significant increase in methaemoglobin levels has been observed after an application time of up to 4 hours on 16 cm^2
5) EMLA has been used for the treatment of leg ulcers up to 15 times over a period of 1 - 2 months with no loss of efficacy or increase in local reactions
6) The application of a larger dose than 10 g has not been studied with regard to plasma levels
7) On female genital skin, EMLA alone applied for 60 or 90 min does not provide sufficient anaesthesia for thermocautery or diathermy of genital warts
8) Doses significantly larger than 2 g are applicable to procedures on larger dermal areas.
9) Rates of absorption may be higher for shaved skin compared to unshaved skin due to possible removal of parts of the protective skin barrier during shaving.

A 1 g dose of EMLA cream is achieved by squeezing EMLA from the tube into a circular area with diameter of approximately 20 mm (the size of a 2 dollar coin) to a depth of approximately 4 mm. Keep the tube in close contact with the skin until the correct amount has been applied.

A 1 g dose of EMLA cream can also be achieved by squeezing a length of EMLA of approximately 3.5 cm from the tube.

EMLA PATCH 5%

Maximum doses
Neonates and infants up to 3 months old should not have more than 1 patch applied at the same time.

Infants aged 3 months up to 12 months old should not have more than 2 patches applied at the same time.

Children aged 1 year up to 12 years old should not have more than 5 patches applied at the same time.

Minor procedures
(e.g. needle insertion)
The patch is applied to the skin area selected. Care should be taken that the patch does not become detached during the minimum application time of 60 minutes (see PRECAUTIONS).

The EMLA patch should be applied **at least** 1 hour prior to the start of the procedure.

OVERDOSAGE

In the event of an overdose, contact the Poisons Information Centre on 13 11 26.

Rare cases of methaemoglobinaemia 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 a slow intravenous injection of methylene blue.

In the unlikely event of systemic toxicity following epidermal application of EMLA, the signs and symptoms anticipated would be similar in nature to those observed following other routes of administration of local anaesthetics. Owing to slow absorption into the circulation from intact skin, a patient with signs of toxicity should be observed for several hours after treatment.

Systemic toxicity to amide type local anaesthetics is initially manifested as CNS excitation and may result in a slow onset of nervousness, dizziness, blurred vision and tremors followed by drowsiness, convulsions, unconsciousness and possibly respiratory arrest.

Toxic cardiovascular reactions to local anaesthetics are usually depressant in nature, may occur rapidly and with little warning and can lead to peripheral vasodilation, hypotension, myocardial depression, bradycardia and possible cardiac arrest. Severe neurological symptoms (convulsions, CNS depression) must be treated symptomatically by respiratory support and the administration of anticonvulsive drugs.

PRESENTATION AND STORAGE CONDITIONS

EMLA cream 5%: containing lidocaine 25 mg and prilocaine 25 mg per gram.
- 5 g tubes in packs of 5 with 10 occlusive dressings or packs of 1 with 2 occlusive dressings.
- 5g and 30 g tube.

EMLA patch 5%: patches containing 1 g of EMLA emulsion in packs of 2 or 20.

STORAGE
EMLA cream 5%: Store below 30°C.
EMLA patch 5%: Store below 25°C.

NAME AND ADDRESS OF THE SPONSOR

Aspen Pharmacare Australia Pty Ltd
34-36 Chandos Street
St Leonards NSW 2065
Australia

POISONS SCHEDULE OF THE MEDICINE

S2 (Pharmacy medicine)

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTICS GOODS (THE ARTG)

13 August 1991

DATE OF MOST RECENT AMENDMENT

8 Dec 2017