NEW ZEALAND DATA SHEET

1. PRODUCT NAME

EMLA CREAM 5%
EMLA PATCH

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

CREAM

Each gram of cream contains lidocaine 25 mg and prilocaine 25 mg.

PATCH

Each patch contains lidocaine 25 mg and prilocaine 25 mg.

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

CREAM

White, soft, hydrophilic cream.

PATCH

EMLA PATCH is a unit-dose formulation of EMLA in the form of an occlusive dressing. It is composed of a laminate backing, an absorbent cellulose disc and an adhesive tape frame.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

EMLA PATCH and CREAM
Topical anaesthesia of the skin prior to insertion of IV catheters, blood sampling, vaccination (see Section 4.4), superficial surgical procedures, including split skin grafting.

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

Topical anaesthesia of the female genital mucosa and male genital skin for example, prior to superficial surgical procedures or infiltration anaesthesia.

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

4.2 Dose and method of administration

EMLA CREAM

Surface / Age	Procedure	Application

Surface / Age	Procedure	Application
Skin		A thick layer of cream to the skin, under an occlusive dressing
Adults		Approximately 1.5g / 10 cm²
	Minor procedures, e.g. needle insertion, cosmetic procedures[8] and surgical treatment of localised lesions	2 g (approximately half a 5 g tube) for a minimum of 1 hour, maximum 5 hours[1])
	Dermal procedures on larger areas in a hospital setting, e.g. split-skin grafting	Approximately 1.5-2 g / 10 cm² for a minimum of 2 hours, maximum 5 hours[1]
	Newly shaven skin of large body areas (in an outpatient setting)	Maximum recommended dose: 60 g. Maximum recommended treated area; 600 cm² for a minimum of 1 hour, maximum 5 hours
Children Neonates 0-2 months[3)] Infants 3-11 months[3)] Children 1-5 years Children 6-11 years Children with atopic dermatitis	Minor procedures, e.g. needle insertion and surgical treatment of localised lesions Prior to curettage of mollusca	Approximately 1.0 g / 10 cm² application time: approximately 1 hour Up to 1.0 g and 10 cm²[2] Up to 2.0 g and 20 cm²[4] Up to 10.0 g and 100 cm² for a minimum of 1 hour, maximum 5 hours[1] Up to 20.0 g and 200 cm² for a minimum of 1 hour, maximum 5 hours[1] Application time: 30 minutes
Leg ulcer Adults	Mechanical cleansing / debridement of leg ulcer(s)	Apply a thick layer of the cream, approximately 1-2 g/10 cm² up to a total of 10 g to the leg ulcer(s).[5] Cover with an occlusive dressing[6]. 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
Female genital mucosa Adults **Female genital skin** Adults	Surgical treatment of localised lesions, e.g. removal of genital warts (condylomata acuminata) and prior to injection of local anaesthetics Cervical curettage Prior to injection of local anaesthetics[7]	Approximately 5-10 g EMLA for 5-10 minutes. No occlusive dressing is required. Commence procedure immediately thereafter 10 g in the lateral vaginal fornices for 10 minutes Apply a thick layer of EMLA Cream (1-2 g /10 cm²) under an occlusive dressing for 60 minutes
Male genital skin Adults	Surgical treatment of localised lesions, e.g. removal of genital warts (condylomata acuminata) and prior to injection of local anaesthetics	Apply a thick layer of EMLA Cream (1 g /10 cm²) under an occlusive dressing for 15-30 minutes

1) After a longer application time the anaesthesia decreases.
2) A longer application time 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 larger dose than 10 g to leg ulcers has not been studied with regard to plasma levels (See Section 5.2).
7) On female genital skin, EMLA alone applied for 60 or 90 minutes does not provide sufficient anaesthesia for thermocautery or diathermy of genital warts.
8) EMLA should be removed entirely before trichloroacetic acid (TCA) application when used for dermal peels.

1 g of EMLA CREAM administered from the 30 g aluminium tube corresponds to a length of extruded cream of approximately 3.5 cm.

EMLA PATCH

Topical anaesthesia of the skin

Adults and children over 1 year of age:

One or more EMLA 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:

EMLA 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:

EMLA 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 EMLA 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.

4.3 Contraindications

Known hypersensitivity to local anaesthetics of the amide type or to any of the excipients.

4.4 Special warnings and precautions for use

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 other than leg ulcers.

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

Care should be taken when applying EMLA CREAM to skin areas with atopic dermatitis. A shorter application time, 15-30 minutes, may be sufficient (seeSection 4.2). Prior to curettage of mollusca in children with atopic dermatitis, an application time of 30 minutes is recommended.

EMLA is not indicated for application to the genital mucosa of children, however when used in neonates for circumcision, a dose of 1.0 g EMLA on the prepuce has proved to be safe.

Care should be taken not to allow EMLA to come in contact with the eyes as it may cause eye irritation. Also the loss of protective reflexes may allow corneal irritation and potential abrasion from undetected foreign bodies. If eye contact occurs, immediately rinse the eye in water or sodium chloride solution and protect it until sensation returns. It is therefore important that the patch or occlusive dressing should be secured against accidental dislocation, especially in young children.

EMLA 5% CREAM is not recommended in any clinical situation in which its penetration into the middle ear is possible i.e. an impaired tympanic membrane. In studies in rodents 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. The relevance of these findings to the clinical situation is unknown.

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

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

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

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

VACCINATION

Lidocaine 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.

DERMAL PEELS

Clinical trial data on the safety and efficacy of EMLA use in dermal peels is limited and EMLA should be used with caution in these cases.

4.5 Interaction with other medicines and other forms of interaction

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.

Specific interaction studies with lidocaine/prilocaine and anti-arrhythmic drugs class III (e.g. amiodarone) have not been performed, but caution is advised (see Section 4.4).

Medicines that reduce the clearance of lidocaine (e.g. cimetidine or beta blockers) may cause potentially toxic plasma concentrations when lidocaine 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.

4.6 Fertility, pregnancy and lactation

Use in pregnancy

The safety of EMLA during pregnancy has not been established.

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, lidocaine and prilocaine cross the placental barrier and may be taken up by the foetal tissues. It is reasonable to assume that lidocaine 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

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 therapeutic amounts of EMLA, however, the amount of lidocaine and prilocaine that may be ingested by the breast-fed infant would be extremely small.

4.7 Effects on ability to drive and use machines

Not applicable at the recommended dosage.

4.8 Undesirable effects

FREQUENCY OF ADVERSE EVENTS

Intact skin

Common Events **Skin**: Transient local reactions at the application site such as

(>1%)	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%)	**General**: Increased methaemoglobin level. Methaemoglobinaemia and/or cyanosis. 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. Corneal irritation after accidental eye exposure. In rare cases, local anaesthetic preparations have been associated with allergic reactions (in the most severe instances anaphylactic shock).

Leg ulcer

Common Events (>1%)	**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 anaesthetic preparations have been associated with allergic reactions (in the most severe instances anaphylactic shock).

Genital mucosa

Common Events (>1%)	**Application site**: Transient local reactions such as, erythema (redness) oedema and paleness. Local sensations (an initial, usually mild burning sensation, itch or warmth at the application site).
Uncommon Events (>0.1% and <1%)	**Application site:** Local paraesthesia such as tingling.
Rare Events (< 0.1%)	**General**: In rare cases, local anaesthetic preparations have been associated with allergic reactions (in the most severe instances anaphylactic shock).

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Rare cases of clinically significant 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.

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 with slow onset of nervousness, dizziness, blurred vision and tremors followed by drowsiness and, in severe cases, central nervous and cardiovascular depression, convulsions, unconsciousness and possibly respiratory arrest.

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

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

EMLA is an oil-in-water emulsion, in which the oil phase consists of a eutectic mixture of lidocaine and prilocaine in the ratio 1:1. EMLA CREAM contains no preservative.

EMLA provides dermal anaesthesia through the release of lidocaine and prilocaine from the cream into the epidermal and dermal layers of the skin and the accumulation of lidocaine and prilocaine in the vicinity of dermal pain receptors and nerve endings. Lidocaine 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 and the dose.

EMLA is applied to **intact skin** under an occlusive dressing. The time needed to achieve reliable anaesthesia of intact skin is 1-2 hours, depending on the type of procedure.

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 duration of anaesthesia following the application of EMLA for 1-2 hours is at least 2 hours after removal of the dressing or patch.

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 min and 3 mm after 120 min 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 diptheria-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.

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 further. The cleansing procedure should start within 10 minutes of removal of the cream. Clinical data from a longer waiting period are not available. EMLA reduces the postoperative pain for up to 4 hours after debridement. EMLA reduces the number of cleansing sessions required to achieve a clean ulcer compared to debridement with placebo cream. No negative effects on ulcer healing or bacterial flora have been observed.

Absorption from the **genital mucosa** is more rapid and onset of time is shorter than after application to the skin. After a 5-10 minute application of EMLA to female genital mucosa the average duration of effective analgesia to an argon laser stimulus which produced a sharp, pricking pain was 15-20 minutes (individual variations in the range 5-45 minutes).

EMLA produces a biphasic vascular response involving initial vasoconstriction followed by vasodilatation at the application site (see Section 4.8). Irrespective of the vascular response, EMLA facilitates the needle procedure compared to placebo cream.

In patients with atopic dermatitis, a similar but shorter vascular reaction is seen, with erythema occurring after 30-60 minutes, indicating more rapid absorption through the skin (see SECTION 4.4).

5.2 Pharmacokinetic properties

The systemic absorption of lidocaine and prilocaine from EMLA is dependent upon the dose, area of application and application time. Additional factors include thickness of the skin, (which varies in different areas of the body), other conditions such as skin diseases, and shaving. Following application to leg ulcers, the characteristics of the ulcers may also affect the absorption.

Intact skin Following application to the thigh in adults (60 g cream / 400 cm² 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 application.

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 lidocaine and prilocaine respectively) were reached after approximately 1.5 - 3 hours.

Plasma levels of lidocaine 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.

In general after relatively short application of 2 hours or less, the time to maximum plasma concentration is less than 2 to 4 hours. With application of a large dose, over an extensive area for extended periods of up to 24 hours the time to maximum plasma concentration is increased 2 to 4 fold.

Maximum plasma concentrations observed in clinical studies were well below toxic levels of lidocaine and prilocaine (5 to 6 µg/mL).

Prilocaine and lidocaine 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 lidocaine 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 lidocaine and prilocaine were 0.135 µg/mL and 0.107 µg/mL respectively. Following the application of 2.0 g EMLA CREAM infants between 3 and 12 months of age, to approximately 16 cm² for four hours, the maximum plasma concentrations of lidocaine and prilocaine were 0.155 µg/mL and 0.131 µg/mL respectively. Following application of 10.0 g of EMLA CREAM in children between 2 and 3 years of age, to approximately 100 cm² 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 EMLA CREAM in children between 6 and 8 years of age, to approximately 100-160 cm² for two hours, the maximum plasma concentrations of lidocaine and prilocaine were 0.299 µg/mL and 0.110 µg/mL respectively.

Leg ulcer Following a single application of 5-10 g of EMLA CREAM to leg ulcers with an area of up to 64 cm² for 30 minutes, 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 to leg ulcers with an area of up to 50-100 cm², 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 application of 2-10 g EMLA CREAM to leg ulcers with an area of up to 62 cm² for 30-60 minutes 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.

Genital mucosa After the application of 10 g EMLA CREAM for 10 minutes to vaginal mucosa, maximum plasma concentrations of lidocaine and prilocaine (mean 0.18 µg/mL and 0.15 µg/mL respectively) were reached after 20-45 minutes.

5.3 Preclinical safety data

In animal studies the toxicity noted after high doses of either lidocaine or prilocaine, alone or in combination, consisted of effects on the central nervous and cardiovascular systems. When lidocaine 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 lidocaine or prilocaine alone or in combination, due to the indication and duration of therapeutic use of these drugs.

A metabolite of lidocaine, 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

lidocaine 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 lidocaine 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 lidocaine + 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

CREAM

- carboxypolymethylene
- polyoxyl hydrogenated castor oil
- sodium hydroxide
- purified water

PATCH

- carboxypolymethylene
- polyoxyl hydrogenated castor oil
- sodium hydroxide
- purified water
- acrylate (adhesive)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Cream: 3 years
Patch: 2 years

6.4 Special precautions for storage

Cream: Store below 30°C. Do not freeze.
Patch: Store below 30°C.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

EMLA CREAM:
1 x 5 g tube with 2 occlusive dressings
5 x 5 g tubes with 10 occlusive dressings

30 g tube

EMLA PATCHES: containing 1 g of EMLA emulsion in packs of 2 and 20.

EMLA 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.

6.6 Special precautions for disposal <and other handling>

The protective membrane of the tube is perforated by applying the cap. EMLA CREAM is intended for single use when used on leg ulcer: discard the tube with any remaining contents after each treatment.

7. MEDICINE SCHEDULE

Pharmacy Only Medicine.

8. SPONSOR

Pharmacy Retailing (NZ) Limited Trading as Healthcare Logistics
58 Richard Pearse Drive
Airport Oaks
Auckland
New Zealand
Telephone: (09) 918 5100
Email: aspen@aspenpharma.co.nz

9. DATE OF FIRST APPROVAL

18 September 1986

10. DATE OF REVISION OF THE TEXT

21 July 2017

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
	Update to the SPC-style format Additional pack size of 2 patches
All sections	Replacement of lignocaine with lidocaine