1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

EMLA PATCH 25 mg/ 25 mg transdermal therapeutic system

2. QUALITATIVE AND QUATITATIVE COMPOSITION

Each EMLA PATCH contains 25 mg of lidocaine and 25 mg of prilocaine.

For full list of excipients, see section 6.1

3. PHARMACETICAL FORM

Patches

EMLA PATCH is a unit-dose formulation of lidocaine and prilocaine 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 cm^2.

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

EMLA PATCH consists of an occlusive dressing (user part) and a protective liner (closure part).

The user part is composed of an absorbent white or off-white circular cellulose disc with a diameter of 3,5 cm, affixed to a thin, flexible backing (aluminium/plastic laminate) equipped with an adhesive tape around the cellulose disc. The cellulose disc is impregnated with 1 g of EMLA 5 % emulsion.

The closure part is composed of a closure laminate (aluminium/plastic laminate) comprising a recessed portion for the cellulose disc and a release liner for the adhesive. There is a hermetic peel-off seal between the backing and the closure laminate around the cellulose disc.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

EMLA PATCH is indicated for:

Topical anaesthesia of intact skin for minor procedures, such as needle insertion and superficial surgical treatment of localised lesions, where application of EMLA PATCH 1 hour before the procedure is feasible.

4.2. Posology and method of administration

Posology

Adults

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.

Minor procedures, for example, needle insertion:

EMLA PATCH should be applied to the skin area selected with a minimum application time of 1 hour. After a longer application time (more than 5 hours), the anaesthesia decreases. In the event of any allergic reaction developing, EMLA PATCH should be removed immediately.

Paediatric population

Paediatric population 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 aged 1 to 5 years is 10 patches.

Maximum dose for children aged 6 to 11 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 to 11 months

The patch is applied to the skin area selected. Approximate application time: 1 hour. Not more than 2 patches should be applied at the same time. No clinically significant increase in methaemoglobin fractions has been observed following the application of 2 g EMLA cream for up to 4 hours.

Term newborn infants and infants under 3 months of age

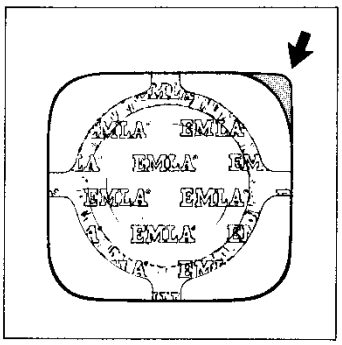
The EMLA PATCH is applied to the selected skin area. Approximate application time: 1 hour, not more. A longer application time than 1 hour has not been documented.

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.

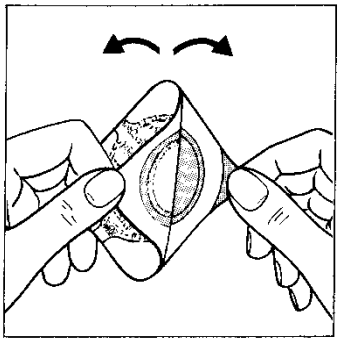
Until further clinical data is available, EMLA PATCH should not be used in infants between 0 and 12 months of age receiving treatment with methaemoglobin inducing medicines.

Method of administration

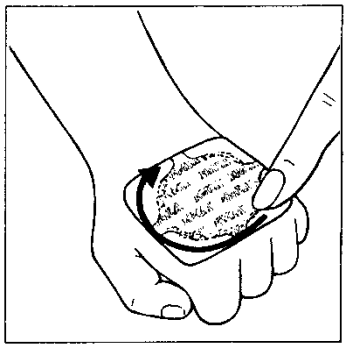
EMLA PATCH must be applied at least *1 hour* before the start of the procedure (if necessary, shave the area prior to application).



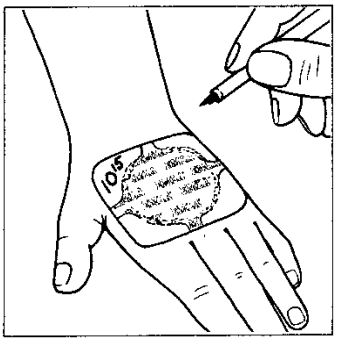
1. Make sure that the area of skin to be anaesthetised is clean and dry.
Take hold of the aluminium flap at the corner of the patch and bend it backwards.
Next, take hold of the corner of the skin-coloured patch layer.



2. Pull the two layers apart, separating the adhesive surface from the protective liner, as shown. Make sure that you do not touch the white round pad, which contains EMLA.



3. Do not press on the centre of the patch. This may cause EMLA to spread under the adhesive. **Press firmly around the edges to ensure good adhesion to the skin.**



4. The time of application may be easily marked directly on the patch (a ballpoint pen may be used for this purpose).

4.3. Contraindications

EMLA PATCH is contraindicated in:

- Patients with hypersensitivity to local anaesthetics of the amide type or to any other component of EMLA PATCH.
- Infants between 0 and 12 months receiving treatment with methaemoglobin-inducing medicines e.g. dapsone, local anaesthetics such as prilocaine and benzocaine, nitrates and sulphonamides.

4.4. Special warnings and precautions for use

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

In glucose-6-phosphate dehydrogenase deficient patients the antidote methylene blue is ineffective at methaemoglobin reduction, and is capable of oxidising haemoglobin itself, and therefore methylene blue therapy cannot be given.

EMLA PATCH should not be applied to open wounds owing to insufficient data on absorption.

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

Care should be taken when applying EMLA PATCH to patients with atopic dermatitis. A shorter application time of 15 to 30 minutes, may be sufficient (see section 5.1). Prior to curettage of mollusca in children with atopic dermatitis, an application time of 30 minutes is recommended (see section 4.2).

Care should be taken not to allow EMLA PATCH 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. If eye contact occurs, immediately rinse the eye in water or saline and protect it until sensation returns.

Lidocaine and prilocaine have bactericidal and antiviral properties in concentrations above 0,5 % to 2 %. For this reason, the results of intracutaneous injections of live vaccines should be monitored.

EMLA PATCH should not be used in any clinical situation where it can penetrate or migrate into the middle ear as ototoxic effects have been shown in laboratory animals.

Clinical trial data on the safety and efficacy of EMLA PATCH use in dermal peels is limited and EMLA PATCH should be used with caution in these cases.
Patients treated with anti-dysrhythmic medicines class III (e.g. amiodarone) should be under close surveillance and ECG monitoring considered, since cardiac effects may be additive.

Paediatric population

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

Lidocaine and prilocaine have bacteriocidal and antiviral properties in concentrations above 0,5 to 2 %. For this reason, although one clinical study suggests that the immunization response is not affected when EMLA PATCH is used prior to BCG vaccination, the results of intracutaneous injections of live vaccines should be monitored.

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

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

4.5. Interaction with other medicines and other forms of interaction

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

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

Specific interaction studies with lidocaine/prilocaine and anti- dysthymic 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 betablockers) may cause potentially toxic plasma concentrations of lidocaine when EMLA PATCH is applied concomitantly in repeated high doses.

4.6. Fertility, pregnancy and lactation

Pregnancy

Safety in pregnancy and lactation has not been established. Although topical application is associated with only a low level of systemic absorption, the use of EMLA PATCH in pregnant women should be undertaken with care because

insufficient data are available concerning the use of EMLA PATCH in pregnant women. Animal studies do not indicate any direct or indirect negative effects on pregnancy, parturition or postnatal development. Embryofoetal toxicity has been shown with subcutaneous/intramuscular administration of high doses of lidocaine or prilocaine much exceeding the exposure from topical application, as in EMLA PATCH.

In both animal and humans, lidocaine and prilocaine as in EMLA PATCH, cross the placental barrier and may be absorbed by the foetal tissues.

Breastfeeding

Lidocaine and prilocaine, as in EMLA PATCH cross the placental barrier and may be absorbed by the foetal tissues, but in such small quantities that there is generally no risk of the child being affected at therapeutic dose levels.
Lidocaine and prilocaine are excreted in human breast milk.

EMLA PATCH can be used during breastfeeding if clinically needed, provided that EMLA PATCH is not applied directly to the breast where ingestion by the infant may occur.

Fertility

Animal studies have shown no impairment of the fertility of male or female rats.

4.7. Effect on ability to drive and use machines

EMLA PATCH has no or negligible influence on the ability to drive and use

machines.

Patients should not drive, use machinery or perform any tasks that require concentration until they are certain that EMLA PATCH does not adversely affect their ability to do so safely (see section 4.4 and 4.8).

4.8. Undesirable effects

a) Summary of the safety profile

The most frequently reported adverse experiences in association with the use of EMLA PATCH were local reactions such as paleness, erythema (redness) and oedema. Other serious adverse experiences reported rarely include anaphylactic shock.

b) Tabulated list of adverse reactions

System organ class	Frequent	Less frequent
Blood and the lymphatic system disorders		Methaemoglobinaemia[1].
Immune system disorders		Allergic reactions (in the most severe instances anaphylactic shock)[1,2,3].
Eye disorders		Corneal irritation[1]
General disorders and administrative site conditions	Transient local reactions at the application site such as paleness, erythema (redness) and oedema[1,2,3], iocal sensations (an initial, usually mild, burning sensation, itch or warmth at the application site)[1,2,3], skin sensations (an initial mild burning or itching sensation at the application site)[3].	Skin sensations (an initial mild burning or itching sensation at the application site)[1]. local lesions at the application site, described as purpuric or petechial[1], local paraesthesia such as tingling[2].

[1] Skin

[2] Genital mucosa

[3] Leg ulcer

c) Description of selected adverse reactions

Skin sensations – an initial mild burning or itching sensation at the application site.

Methaemoglobinaemia – 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.

Allergic reactions – in rare cases, local anaesthetic preparations have been associated with allergic reactions (in the most severe instances anaphylactic shock).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to:

SAHPRA: https://www.sahpra.org.za/Publications/Index/8.

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

4.8. Overdose

Symptoms

EMLA PATCH in high doses may cause an increase in the methaemoglobin level particularly in conjunction with methaemoglobin- inducing medicines (e.g. sulphonamides) (see section 4.8). Clinically significant methaemoglobinaemia should be treated with a slow intravenous injection of methylene blue.

Consideration should be given to the fact that pulse oximeter values may overestimate the actual oxygen saturation in case of increased methaemoglobin fraction; therefore, in cases of suspected methaemoglobinaemia, it may be more helpful to monitor oxygen saturation by CO-oximetry.

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.

Treatment

Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacological classification : A4 Local anaesthetics

Pharmacotherapeutic group: Anaesthetics, local. ATC code: N01BB20

Mechanism of action

Lidocaine and prilocaine, applied to intact skin, provides dermal anaesthesia through the release of lidocaine and prilocaine into the epidermal and dermal layers of the skin. Lidocaine and prilocaine are amide-type local anaesthetic medicines. 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 the anaesthesia depends on the application time.

The depth of cutaneous anaesthesia increases with application time to a depth of 2 mm after 60 minutes and 3 mm after 120 minutes of lidocaine and prilocaine treatment. Lidocaine and prilocaine has the same anaesthetic onset time across the range of light to dark pigmented skin (skin types I to VI).

The lidocaine and prilocaine emulsion produces a biphasic vascular response involving initial vasoconstriction followed by vasodilatation at the application site (see section 4.8).
In patients with atopic dermatitis, a similar but shorter vascular reaction is seen, with erythema occurring after 30 to 60 minutes, indicating more rapid absorption through the skin (see section 4.4 and 4.8).

5.2. Pharmacokinetic properties

Absorption

The systemic absorption of lidocaine and prilocaine from EMLA PATCH is dependent upon the dose, area of application, application time, thickness of the skin, which varies in different areas of the body, and other conditions of the skin.

Distribution

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

5.3 Pre-clinical 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 at clinically relevant doses.

In studies on reproduction toxicity, embryotoxic or foetotoxic effects of lidocaine were detected at doses of 25 mg/kg s.c. in the rabbit and foetal hydronephrosis for prilocaine starting at doses of 100 mg/kg i.m. in the rat. At doses below the maternal toxic range in the rat, lidocaine or prilocaine has no effect on the postnatal development of the offspring. An impairment of the fertility of male or female rats by lidocaine or prilocaine was not observed. Lidocaine crosses the placental barrier by means of simple diffusion. The ratio of the embryofoetal dose to the maternal serum concentration is 0,4 to 1,3.

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 medicines.

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.

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 and patch. 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

Carbomer, macrogolglycerol hydroxystearate, sodium hydroxide (for pH adjustment), purified water

Adhesive: Acrylate

6.2. Incompatibilities

Not applicable

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store at or below 25 °C.

Do not refrigerate or freeze.

Keep in original packaging until required for use.

6.5. Nature and contents of container

EMLA PATCH is available in cardboard boxes containing 2 patches per box.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

8. REGISTRATION NUMBER

30/4/0478

9. DATE OF FIRST AUTHORISATION

25 February 1998

10. DATE OF REVISION OR TEXT

02 February 2023

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