LIDOCAINE AND PRILOCAINE (Topical)

Revision Date

Revised: 08/05/1998

Introduction

INN: none; BAN: **Lidocaine**—Lignocaine

VA CLASSIFICATION (Primary): DE700

Commonly used brand name(s): *EMLA*.

Another commonly used name for **lidocaine** is lignocaine.

Note: For a listing of dosage forms and brand names by country availability, see *Dosage Forms* section(s).

Category

Anesthetic, local.

Indications

Note: Bracketed information in the *Indications* section refers to uses that are not included in U.S. product labeling.

Accepted

Anesthesia, local — Indicated for application to normal, intact skin, to provide topical anesthesia [1,2] prior to procedures such as insertion of an intravascular cannula [1,4,30], venipuncture [1,5,6] or other needle insertion [1,5,7,13]; skin graft harvesting [1]; the cleansing and debridement of leg ulcers; minor dermal procedures [12], such as laser treatment of port-wine stains [1,8] and removal of mollusca [9], warts [2], or tattoos [2]; lumbar puncture [5]; and diathermy [10].
This topical anesthetic is also applied to the genital mucosa of men or [women], to provide anesthesia for infiltration of additional anesthetic prior to the surgical removal of localized lesions [11] (e.g., removal of condolymata via carbon dioxide laser [14] or thermocautery [32]), or [to provide anesthesia for surgical removal of localized lesions][3,14,32]. It is used for this purpose only in adults; application to the mucosa of children is *not* recommended [3,33].

Unaccepted

Application of this medication to mucous membranes other than the genital mucosa of adults, especially application to the gums or other oral mucosa, is not recommended [43].

Application of this medication to the ear is not recommended because ototoxicity occurred in animal studies in which **lidocaine** and **prilocaine** topical cream was applied to the tympanic membrane or to the middle ear. Application of this medication to any area from which migration to or beyond the tympanic membrane is possible is not recommended [1].

Application of this medication to or near the eye is not recommended because corneal irritation can result.

Pharmacology/Pharmacokinetics

Note: Information reported below on various pharmacokinetic parameters and on the onset of action, time to peak effect, and duration of action after application to the skin was obtained in studies in Caucasians. Preliminary evidence from a study in a limited number of subjects indicates that the rate and extent of absorption are decreased, the onset of action and time to peak effect are increased, and the overall efficacy of the medication is reduced, after application to black skin [39].

Physicochemical characteristics:

Chemical group — Both **lidocaine** and **prilocaine** are amide-type local anesthetics [1,2].

Molecular weight —
Lidocaine: 234.34 [16]
Prilocaine: 220.32 [17]

Octanol-to-aqueous buffer solution (pH 7.4) partition ratio —

Lidocaine: 43 [44].
Prilocaine: 25 [44].

Mechanism of action/Effect:

Local anesthetics block both the initiation and conduction of nerve impulses by decreasing the neuronal membrane's permeability to sodium ions. This reversibly stabilizes the membrane and inhibits depolarization, resulting in the failure of a propagated action potential and subsequent conduction blockade [18].

The base (nonionized) form of a local anesthetic is able to diffuse across neuronal membranes to produce local anesthesia much more readily than a salt (ionized) form of the agent [15,42]. However, penetration through intact skin of effective concentrations of the highly lipophilic base form of an anesthetic is generally not achieved after application of topical formulations that contain single anesthetics [5,15]. This **lidocaine** and **prilocaine** - containing formulation is an oil-in-water emulsion in which the oil phase is a eutectic mixture formed by combining equal parts by weight of **lidocaine** and **prilocaine** bases [1,2,3]. Because the eutectic mixture is a liquid, the anesthetics need not be dissolved in oil before being incorporated into the water phase of the formulation; this increases the concentration of active substance in droplets of the emulsion and permits larger quantities of anesthetic to penetrate to the nerve endings in deeper skin layers [5,15].

The depth at which anesthesia is present after application to intact, healthy skin, as determined by needle insertion, increases with the length of time that the medication remains on the skin, about 3 mm after a 60-minute application, 4 mm after a 90-minute application, and 5 mm after a 120-minute application [2,19]. However, when the medication remains on the skin for less than 120 minutes, the depth at which anesthesia is present may continue to increase for an additional 30 to 60 minutes after the anesthetic is removed [19], depending on the location at which the medication is applied [41].

Other actions/effects:

This medication may produce vascular responses, i.e., vasoconstriction (manifested by blanching of the skin) and/or vasodilatation (manifested by erythema) [1,2,20,21]. In a study in which the medication was applied to normal skin, maximal blanching occurred after a 90-minute application, and erythema occurred only after a much longer application time (more than 3 hours) [20]. In another study in a limited number of patients, a product twice as strong as the formulation now commercially available in the U.S. and Canada produced vascular responses much more rapidly in skin affected by atopic dermatitis or eczema than in normal skin [21]. In patients with atopic dermatitis or eczema, blanching and erythema occurred after application times of only 5 to 15 minutes and 30 to 60 minutes, respectively, whereas in individuals with normal skin, blanching and erythema occurred after application times of 30 to 60 minutes and 2 to 4 hours, respectively [21].

Absorption:

Application to the skin—The rate and extent of systemic absorption are dependent on the thickness of the skin [2] and the size of the area [1,2] to which the medication is applied as well as the duration of application [1,2]. In general, mean absorption rates in children and adults are 45 ± 16 mcg per square centimeter of skin area (mcg/cm ^{2}) per hour and 77 ± 36 mcg/cm ^{2} per hour for **lidocaine** and **prilocaine**, respectively [1]. Absorption may be increased when the formulation is applied to broken or inflamed skin or to areas 2000 cm ^{2} or larger in size [1]. Also, absorption is more rapid when the cream is applied to the skin of patients with atopic dermatitis and generalized eczema [21] or other patients with damaged or thin skin [47].

Application to genital mucosa—The rate and extent of absorption are significantly greater than after application to normal, intact skin [1].

Distribution:

Both **lidocaine** and **prilocaine** cross the blood-brain barrier and the placenta [1].

Note: The mean volumes of distribution at steady state, determined after intravenous administration, are 1.5 ± 0.3 liters per kg of body weight (L/kg) for **lidocaine** and 2.6 ± 1.3 L/kg for **prilocaine** [1].

Protein binding:

Lidocaine—High (70%), primarily to alpha-1-acid glycoprotein, at plasma concentrations produced by application of this topical formulation. At much higher concentrations (> 1 mcg per mL [mcg/mL] [4.3 micromoles/L]), binding is dependent on the concentration [1].

Prilocaine—Moderate (40%) [42].

Biotransformation:

Lidocaine—Hepatic; rapid. One metabolite is active, but a less potent local anesthetic [45] than the parent compound;

another metabolite has no local anesthetic activity, but may be more toxic than **lidocaine** itself [45]. Whether metabolism occurs in the skin after topical application has not been determined [1].

Prilocaine—Hepatic, by amidases; metabolism in renal tissues has also been demonstrated *in vitro* [42]. One or more of the metabolic products is toxic (causing methemoglobinemia) [42]. Whether metabolism occurs in the skin after topical application has not been determined [1].

Half-life:

Elimination (mean values)—
Lidocaine: 110 ± 24 minutes (determined after intravenous administration [1] of **lidocaine** hydrochloride [42]); may be increased in patients with cardiac or hepatic function impairment [1].
Prilocaine: 70 ± 48 minutes; may be increased in patients with hepatic or renal function impairment [1].

Onset of action:

Application to the skin—Dependent on the epidermal and dermal thickness at the location to which the medication is applied [22]; about 1 hour after application to intact skin [1,2], but much more rapid (less than 15 minutes) after application to skin areas affected by atopic dermatitis or eczema [21].

Time to peak serum concentration

Application to normal, intact skin—Dependent on the area to which the medication is applied and subject to interpatient variability [34]; about 4 hours [1] (range, 2 to 6 hours) [2] when 60 grams is applied to a 400-cm ^{2} area of the thigh and allowed to remain, under an occlusive dressing, for 3 hours [1,2] and 1.5 to 3 hours when 10 grams is applied to a 100-cm ^{2} area of the face and allowed to remain for 2 hours [2].

Peak serum concentration:

Application to intact skin—
Lidocaine: The highest concentration measured after application of about 150 grams of the **lidocaine** and **prilocaine** formulation to up to 1300 cm ^{2} of intact skin for up to 3 hours is 1.1 mcg/mL (4.73 micromoles/L) [2].
Prilocaine: The highest concentration measured after application of about 150 grams of the **lidocaine** and **prilocaine** formulation to up to 1300 cm ^{2} of intact skin for up to 3 hours is 0.2 mcg/mL (0.87 micromoles/L) [2].

Note: The total quantity of **prilocaine** absorbed over a given time is greater than that of **lidocaine**, even though equal quantities of each are present in the formulation [1]. However, **prilocaine**'s larger volume of distribution [1] and more rapid clearance [42] result in lower plasma concentrations [1].

Time to peak effect:

Application to intact skin—About 2 to 3 hours [1]. In general, 1 hour of application under occlusion produces sufficient anesthesia for procedures such as intravascular catheter placement or venipuncture; 2 hours of application under occlusion produces sufficient anesthesia for procedures such as split skin graft harvesting [1]. However, one study showed that 2 hours of application under occlusion may be required to provide sufficient anesthesia for venipuncture in children with black skin [40].

Application to genital mucosa—Sufficient anesthesia for removal of localized lesions occurs about 5 to 7 minutes after application [14,32]; efficacy begins to decrease as soon as 10 to 15 minutes after application [14,32].

Duration of action:

Application to intact skin—Effective anesthesia following a 1- or 2-hour application generally persists for an additional 1 or 2 hours after the medication is removed [1,2]. However, the duration of anesthesia is dependent on the blood flow in the underlying tissue [10,22]; efficacy may decline more rapidly in highly perfused areas, such as the face [10]. One study demonstrated that a relatively short duration follows a rapid onset and a more prolonged duration follows a delayed onset [22].

Elimination:

Lidocaine—More than 98% of the quantity absorbed is eliminated in the urine [1]; less than 3% [42] as unchanged **lidocaine** and the remainder as metabolites. Mean systemic clearance is 13 ± 3 mL per minute per kg of body weight (mL/min/kg) [1].

Prilocaine—Renal; less than 3% as unchanged **prilocaine** [42]. Mean systemic clearance is 38 ± 15 mL/min/kg [1].

Precautions to Consider

Note: In the animal studies reported in the *Carcinogenicity*, *Mutagenicity*, and *Pregnancy/Reproduction* sections below, the doses administered to, or blood concentrations achieved in, the animals are compared to the equivalent in humans of a Single Dermal Administration (SDA), defined as a single application of 60 grams of the local anesthetic formulation over 400 square centimeters (cm^2) of the skin area of a 50-kg person for 3 hours.

Cross-sensitivity and/or related problems

Patients sensitive to other amide-type local anesthetics may rarely [18] be sensitive to **lidocaine** and/or **prilocaine** also [1,2].

Carcinogenicity

Lidocaine—
A 2-year study showed the metabolite 2,6-xylidine to be carcinogenic, causing carcinomas, adenomas, and rhabdomyosarcomas in the nasal cavities of both male and female rats; subcutaneous fibromas and/or fibrosarcomas in both male and female rats; and neoplastic nodules of the liver in female rats when given in daily oral doses of 150 mg per kg of body weight (mg/kg) per day (900 mg per square meter of body surface area [mg/m^2] [60 times the SDA] per day). Statistically significant increases in nasal carcinomas and/or adenomas in male and female rats did not occur with oral doses of 50 mg/kg per day (300 mg/m^2 [30 times the SDA] per day), and no nasal tumors occurred with oral doses of 15 mg/kg per day (90 mg/m^2 [6 times the SDA] per day) [1].

Prilocaine—
The metabolite ortho-toluidine, given chronically to mice in oral doses of 150 to 2400 mg/kg per day (900 to 14,400 mg/m^2 [60 to 90 times the SDA] per day) or to rats in oral doses of 150 to 800 mg/kg per day (900 to 4800 mg/m^2 [60 to 320 times the SDA] per day), was carcinogenic in both species at all dosage levels tested. Tumors included hepatocarcinomas and adenomas in female mice; hemangiosarcomas and hemangiomas in male and female mice; sarcomas of multiple organs and transitional-cell carcinomas and papillomas of the urinary bladder in both sexes of rats; subcutaneous fibromas, fibrosarcomas, and mesotheliomas in male rats; and mammary gland fibroadenomas and adenomas in female rats [1].

Mutagenicity

Lidocaine—
No evidence of mutagenicity was shown with **lidocaine** hydrochloride in the Ames *Salmonella*/mammalian microsome test or analysis of structural chromosome aberrations in human lymphocytes *in vitro*, or in the mouse micronucleus test *in vivo*. The metabolite 2,6-xylidine was weakly mutagenic in the Ames test only under metabolic activation conditions. The metabolite was also mutagenic at the thymidine kinase locus, with or without activation, and induced chromosome aberrations and sister chromatid exchanges at concentrations at which the substance precipitated out of solution (1.2 mg/mL). No evidence of genotoxicity was found in the *in vivo* assays measuring unscheduled DNA synthesis in rat hepatocytes, chromosome damage in polychromatic erythrocytes, or preferential killing of DNA repair-deficient bacteria in liver, lung, kidney, testes, and blood extracts from mice. However, covalent binding studies of DNA from liver and ethmoid turbinates in rats indicate that the metabolite may be genotoxic under certain conditions *in vivo* [1].

Prilocaine—
The metabolite ortho-toluidine produced positive results in *Escherichia coli* DNA repair and phage-induction assays in a concentration of 0.5 mcg/mL. Urine concentrates from rats given the metabolite (300 mg/kg orally [300 times the SDA]) were mutagenic for *Salmonella typhimurium* with metabolic activation. Several other tests on the metabolite, including reverse mutations in five different *Salmonella typhimurium* strains with or without activation and with single strand breaks in DNA of V79 Chinese hamster cells, were negative [1].

Pregnancy/Reproduction

Fertility—

Prilocaine—
Studies in rats given 300 mg/kg intramuscularly as the hydrochloride salt [42] (188 times the SDA) have not shown evidence of impaired fertility [1].

Pregnancy—

Lidocaine and prilocaine mixture—
Adequate and well-controlled studies have not been done in humans [1].
Studies in rats given subcutaneous injections of an aqueous mixture of the hydrochloride salts of **lidocaine** and **prilocaine** (40 mg/kg of each [equivalent to 29 times the SDA for **lidocaine** and 25 times the SDA for **prilocaine**] per day) have not shown evidence of teratogenicity, embryotoxicity, or fetotoxicity. Also, studies in rats with the individual anesthetics (30 mg/kg subcutaneously [22 times the SDA] of **lidocaine** hydrochloride or 300 mg/kg intramuscularly [188 times the SDA] of

prilocaine hydrochloride) have not shown evidence of harm to the fetus [1].

FDA Pregnancy Category B [1].

Breast-feeding

Lidocaine is, and **prilocaine** probably is, distributed into breast milk [1,2,3] in small quantities [3]. The risk of adverse effects in nursing infants is considered to be minimal [2].

Pediatrics

Neonates (up to 1 month of age)—
Use in neonates is not recommended [53] because of the risk of methemoglobinemia [35].

Infants and children—
Application to the mucosa of pediatric patients is not recommended [3].
Methemoglobin concentrations are increased in infants and children after application of this medication [2,23]. Although the concentrations generally do not reach clinically significant levels [2,23], overt methemoglobinemia developed after use of the anesthetic mixture in a 3-month-old infant who was also receiving other medication known to cause methemoglobinemia [1,2]. It is recommended that the anesthetic formulation not be used for infants up to 12 months of age who are receiving such medications [1,2]. Also, a study in children 1 to 6 years of age found that methemoglobin concentrations remain elevated for 24 hours after a 2-hour application of 5 grams of the medication [23]. The possibility of cumulative effects on methemoglobin concentrations should be considered if the medication is needed on a daily basis [23].
Studies have shown that, because of fearfulness [48], in children younger than 7 years of age, this medication provides less overall benefit (as determined by reaction to needle insertion) to these patients than it does to older children and adults [1]. Use of this product does not eliminate the need for emotional and psychological support for young children who are undergoing medical or surgical procedures [1].

Geriatrics

No information is available on the relationship of age to the effects of this **lidocaine** and **prilocaine** topical formulation in geriatric patients. However, experience with other local anesthetic formulations has shown that geriatric patients are more likely than younger adults to develop local anesthetic - induced systemic toxicity after the medications are administered by injection [18], or applied to mucous membranes [24].

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (>> = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

Anesthetics, general[36,54] — (symptoms of local anesthetic - induced CNS toxicity, which may occur if excessive quantities of the medication are absorbed, may be masked if the local anesthetic is used in conjunction with a general anesthetic)

Anesthetics, local, other[1,2,3] or
Structurally related medications, such as mexiletine[1] or tocainide[1,2] — (the risk of systemic toxicity may be increased, especially if large quantities of the **lidocaine** and **prilocaine** topical formulation are used concurrently with any of these medications)

Methemoglobinemia-inducing medications, other, especially:

Acetaminophen, chronic use of
Chloroquine
Dapsone
Nitrates or nitrites, including nitrofurantoin, nitroglycerin, and nitroprusside
Para-aminosalicylic acid
Phenacetin—not commercially available in the U.S. or Canada
Phenobarbital
Phenytoin
Primaquine

>> Sulfonamides, including mafenide — (concurrent use with the **lidocaine** and **prilocaine** topical formulation may increase the risk of overt methemoglobinemia [1,2,3], especially in infants [2]; concurrent use in infants younger than 12 months

of age is not recommended [1,2])

Laboratory value alterations

The following have been selected on the basis of their potential clinical significance (possible effect in parentheses where appropriate)—not necessarily inclusive (>> = major clinical significance):

With diagnostic test results

Skin tests, intradermal or epicutaneous — (application of the **lidocaine**- and **prilocaine**-containing topical anesthetic prior to skin testing may reduce flare induced by injection of histamine [often used as a positive control for these tests]; false-negative interpretation of weakly positive tests may result [25])

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate) — not necessarily inclusive (>> = major clinical significance).

Risk-benefit should be considered when the following medical problems exist:

Note: Caution is recommended in geriatric, acutely ill, or debilitated patients, who may be predisposed to local anesthetic-induced systemic toxicity [1].

>> Any situation in which absorption may be increased, such as:
Application to open wounds[30], burns[30,34], or broken or inflamed skin[30] or
Atopic dermatitis[2,3,21] or
Eczema[21] — (the rate and extent of anesthetic absorption may be increased, leading to a higher risk of systemic toxicity; application to open wounds is not recommended [2,3])
(in burn patients, the presence of a pre-existing hemoglobin abnormality [carboxyhemoglobin] may also increase the risk of systemic toxicity [30])
(a study in a limited number of patients has shown that, after the medication is applied to skin affected by atopic dermatitis or eczema, the onset of action is more rapid than after application to healthy skin; a shorter application time may be appropriate for patients with these conditions [21], but additional clinical experience is needed before guidelines for use in these patients can be established [3])

Connective tissue disease, Ehlers Danlos Type III — (a study in a limited number of patients has shown that the topical lidocaine and **prilocaine** formulation does not provide adequate anesthesia in individuals with this condition [26])

>> Glucose-6-phosphate dehydrogenase (G6PD) deficiency or other predisposition to methemoglobinemia or
>> Methemoglobinemia, congenital or idiopathic — (medication may induce, or exacerbate pre-existing, methemoglobinemia [1])

patic function impairment, severe — (capacity for metabolizing the anesthetics is reduced, which increases the risk of systemic effects [1])

>> Sensitivity to lidocaine, **prilocaine**, or other amide-type local anesthetics, history of — (increased risk of allergic reaction [1,2,3])

Side/Adverse Effects

Note: Like other local anesthetics, lidocaine and **prilocaine** (individually) have rarely caused allergic and anaphylactoid reactions, including angioedema, bronchospasm, urticaria, and shock [1,3].

Systemic effects are unlikely when recommended guidelines for use of this medication are followed [2], but central nervous system (CNS) toxicity and/or cardiovascular depression may occur if sufficiently high plasma concentrations of the anesthetics are produced [1]. Early signs of cardiovascular depression include bradycardia and hypotension [1]. If treatment is not initiated promptly, decreases in cardiac output, total peripheral resistance, and mean arterial pressure may occur and may progress to hypoxia, acidosis, heart block, and cardiac arrest [18].

CNS toxicity induced by local anesthetics consists of CNS stimulation and/or CNS depression. CNS stimulation (signs and symptoms may include apprehension, nervousness, or euphoria; confusion; dizziness, light-headedness, or drowsiness; blurred or double vision; nausea and vomiting; ringing or buzzing in the ears; sensations of heat, cold, or numbness; and twitching, tremors, or convulsions) often occurs first, followed by CNS depression, characterized by drowsiness, unconsciousness, and respiratory depression and arrest. However, CNS excitation may be transient or absent, so that

drowsiness may be the first sign of CNS toxicity in some patients, especially children [1,18].

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)—not necessarily inclusive:

Those indicating need for medical attention

Incidence rare

Methemoglobinemia[1,2,3] (blue or blue-purple color of lips, fingernails, or skin; fatigue; weakness; breathing problems; rapid heartbeat; headache; dizziness; collapse; altered mental status; dark urine)

Note: If *methemoglobinemia* is relatively mild, cyanosis may be the only sign. The other signs and symptoms occur when *methemoglobinemia* is severe and/or the patient cannot tolerate the reduced oxygen-carrying capacity of the blood [18].

Those indicating need for medical attention only if they continue or are bothersome

Incidence more frequent

Localized skin reactions[1,2] (burning feeling, swelling, itching, or skin rash at place of application); ***vasoconstriction*** (very white skin at place of application); ***vasodilatation*** (red skin at place of application)

te: *Localized skin reactions* generally resolve spontaneously within 1 or 2 hours [1]. The adhesive in the occlusive dressing may also cause localized *sensitivity reactions* manifested by skin rash, itching, and/or redness [41].

Vasoconstriction-induced blanching generally occurs first and may be followed, depending on the application time, by *vasodilatation-induced erythema*[1,20,21].

Overdose

For specific information on the agents used in the management of lidocaine and prilocaine overdose, see:
- *Ascorbic Acid (Systemic)* monograph;
- *Benzodiazepines (Systemic)* monograph;
- *Methylene Blue (Systemic)* monograph; and/or
- *Sympathomimetic Agents—Cardiovascular Use (Parenteral-Systemic)* monograph.

For more information on the management of overdose or unintentional ingestion, **contact a Poison Control Center** (see *Poison Control Center Listing*).

Clinical effects of overdose

The following effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate)—not necessarily inclusive:

Acute and chronic

Circulatory depression; ***convulsions***; ***methemoglobinemia***

Treatment of overdose

To decrease absorption—
For systemic reactions caused by excessive absorption: Removing any remaining medication from the skin surface [46].

Specific treatment—
For circulatory depression: Administering a vasopressor and intravenous fluids [24].
For seizures: Administering an anticonvulsant. Benzodiazepines are most commonly used. Because intravenously administered benzodiazepines may cause respiratory [50] and circulatory [28] depression, especially when administered rapidly [49,51], medications and equipment needed for support of respiration and for resuscitation must be immediately available [52].
For methemoglobinemia: Administering methylene blue and/or ascorbic acid [27].

Supportive care—
Securing and maintaining a patent airway, administering 100% oxygen, and instituting assisted or controlled respiration as needed. In some patients, endotracheal intubation may be required [24].

Patient Consultation

As an aid to patient consultation, refer to *Advice for the Patient, Lidocaine and Prilocaine (Topical).*

In providing consultation, consider emphasizing the following selected information (>> = major clinical significance):

Before using this medication

>> Conditions affecting use, especially:

Sensitivity to lidocaine, **prilocaine**, or other amide-type local anesthetics

Use in children — Increased risk of adverse effect (methemoglobinemia) in infants younger than 1 year of age; use of medication does not eliminate need for comforting frightened children

Use in the elderly — Possibility of increased risk of systemic effects, based on experience with local anesthetics administered by other routes

Other medications, especially sulfonamides

Other medical problems, especially conditions that may increase absorption and methemoglobinemia or predisposition to [illegible] g., glucose-6-phosphate dehydrogenase deficiency)

Proper use of this medication

>> Using only for appropriate indications, as directed by physician or nurse

>> Not applying to open wounds, burns, or broken or inflamed skin, unless otherwise directed by physician or nurse

>> Avoiding contact with eyes; if inadvertent contact does occur, not touching eyes and contacting physician immediately

>> Avoiding contact with lips or mouth

>> Following instructions provided by physician or nurse and/or patient information provided by manufacturer

>> Contacting health care provider if any questions about method, site, or time of application

>> Proper application technique for cream:
Applying a thick layer of medication to specified area or areas; not spreading the medication
Unless applying to genital area, covering the medication with an occlusive dressing; sealing tightly, making sure a thick layer remains under the dressing; not disturbing the dressing; not covering the medication with an occlusive dressing if the medication is applied to the genital area
If directed to do so, removing the dressing after 1 or 2 hours, wiping off the medication, then cleaning the area with antiseptic solution; if not directed to do so, keeping medication and dressing in place until removed by physician or nurse

>> Proper application technique for disc:
Applying anesthetic disc to specified area, and leaving in place for 1 hour; making sure the disc stays in place and attached to skin during this time

>> Proper dosing

>> Proper storage

Precautions while using this medication

>> Monitoring small children after administration, to make sure they do not disturb the dressing and/or ingest any medication

>> Caution that injury may occur undetected while numbness persists in the affected area; using care to prevent injury (e.g., not scratching, rubbing, or exposing the affected area to extreme hot or cold temperatures) until sensation has returned

Side/adverse effects

Possibility of allergic reactions (anaphylactoid reactions, angioedema, bronchospasm, urticaria) and systemic effects (cardiovascular and/or CNS toxicity); obtaining medical assistance immediately if signs and/or symptoms occur

Signs and symptoms of other potential adverse effects, especially methemoglobinemia

General Dosing Information

Contact with the eyes should be avoided, because the medication may cause severe corneal irritation [1,3]. Also, the anesthetic effect results in loss of protective reflexes, which may allow damage to the eye [1,2]. If contact with an eye occurs, the eye should be washed with water or 0.9% sodium chloride solution and protected against injury until sensation returns [1].

The medication should not be applied to open wounds [2,3].

Although application of the medication to small sites (approximately 20 to 25 square centimeters [2 inches square]) may take place at home, before the patient travels to a medical appointment, it is recommended that the medication be applied to larger sites only under the supervision of medical personnel (e.g., in the office, clinic, or hospital) [37].

The optimal application time may depend on the thickness and structure of the surface to which the medication is applied [10], as well as the procedure being performed [1,2,3].

Prior to the procedure, the dressing should be removed, the medication wiped off, and the entire skin area cleaned with an antiseptic solution [1].

Application of this medication to the ear is not recommended because ototoxicity was noted in animal studies in which lidocaine and **prilocaine** topical cream was applied to the tympanic membrane or to the middle ear. Application of this medication to any area from which migration beyond the tympanic membrane is possible is not recommended [1].

This medication may not provide sufficient anesthesia when used as the sole anesthetic agent for cryotherapy for the removal of genital warts on men. In this case, application of lidocaine and **prilocaine** topical cream should be followed by infiltration of lidocaine to provide sufficient anesthesia for this procedure [1].

Topical Dosage Forms

Note: Bracketed uses in the *Dosage Forms* section refer to categories of use and/or indications that are not included in U.S. product labeling.

LIDOCAINE AND PRILOCAINE CREAM

Usual adult dose

Anesthesia, topical —

Dermal procedures—
Topical, to intact skin, a thick layer to be applied and covered with an occlusive dressing.
For minor procedures involving a small area (e.g., intravascular cannulation, venipuncture)—2.5 grams, applied over twenty to twenty-five square centimeters of skin surface area and allowed to remain in contact with the skin surface for at least one hour [1,2]. A second site may be prepared, to be used if a technical problem with cannulation or needle insertion should arise at the first site [1].
For major dermal procedures involving larger areas (e.g., split thickness skin graft harvesting)—2 grams per ten square centimeters of skin surface area. The medication should be allowed to remain in contact with the skin surface for at least two hours [1].
For laser treatment (removal of warts, tattoos, etc.)—1 to 2 grams per ten square centimeters of skin surface area [2].

Note: A study performed in children has shown that application of smaller quantities of medication in a thin layer over a given surface area is not as effective as the recommended thick layer [29].

Longer application times may be needed after application to black skin [39,40].

Genital mucosal procedures (e.g., removal of condylomata or other localized lesions)—
Topical, to the mucosa, 2.5 grams. Covering the medication with an occlusive dressing is not necessary. The medication should be allowed to remain in contact with the mucosa for 5 to 10 minutes, after which the procedure should be started immediately [3] or infiltration with additional local anesthetic should be performed immediately.

Usual adult prescribing limits

Dermal procedures —

The maximum recommended duration of exposure is four [1] to five [2,3] hours. Leaving the medication on the skin for longer than five hours is not likely to provide additional benefit [2], and may actually result in decreased anesthetic efficacy [3] as well as an increased risk of systemic toxicity [30].

Usual pediatric dose

Anesthesia, topical —

Neonates up to 1 month of age—
Use is not recommended [1].

Infants and children—
Dermal procedures: See *Usual adult dose* [1,2].

Usual pediatric prescribing limits

Dermal procedures —

The maximum recommended area of application in pediatric patients of various weights is—
Up to 10 kg—100 square centimeters [1].
10 to 20 kg—600 square centimeters [1].
More than 20 kg—2000 square centimeters [1].

Usual geriatric dose

See *Usual adult dose*.

Strength(s) usually available

U.S. —

5% (2.5% [25 mg per gram] of each anesthetic) (Rx) [*EMLA*].

Canada —

5% (2.5% [25 mg per gram] of each anesthetic) (OTC) [*EMLA*].

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

- For topical use only.
- Keep away from eyes.
- Keep away from mouth.

LIDOCAINE AND PRILOCAINE TOPICAL DISC

Usual adult dose

Anesthesia, topical —

Dermal procedures—
Topical, to intact skin, one anesthetic disc should be applied and allowed to remain in contact with the skin surface for at least one hour [1].
A second site may be prepared, to be used if a technical problem with cannulation or needle insertion should arise at the first site [1].

Usual pediatric dose

Anesthesia, topical —

Neonates up to 1 month of age—

Use is not recommended [1].

Infants and children—
Dermal procedures: See *Usual adult dose*[1,2].

Usual pediatric prescribing limits

A maximum of two discs may be applied.

Usual geriatric dose

See *Usual adult dose*.

Strength(s) usually available

U.S. —

1 gram of the anesthetic emulsion (Rx) [*EMLA*].

Canada —

1 gram of anesthetic emulsion (OTC) [*EMLA*].

Packaging and storage:

Store between 15 and 30 °C (59 and 86 °F), unless otherwise specified by manufacturer. Protect from freezing.

Auxiliary labeling:

- For topical use only.
- Keep away from eyes.
- Keep away from mouth.

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