Summary of Product Characteristics

1. Name of the medicinal product

Compound Lidocaine Cream

2. Qualitative and quantitative composition

Lidocaine :Prilocaine (1: 1, w/w)

For full list of Excipients, see section 6.1

3. Pharmaceutical form

White soft cream.

4. Clinical particulars

4.1 Therapeutic indications

Compound Lidocaine Cream is indicated for the topical anaesthesia of , (1) needle insertion, e.g. intravenous catheters or blood sampling; (2)on superficial surgical procedures

4.2 Posology and method of administration

Administration of Compound Lidocaine Cream on genital mucosa and genital skin should only be performed by or under the supervision of a healthcare professional.

Posology

Skin usage : A thick layer of cream would be applied on the skin surface, covered with occlusive dressing, for minor procedures in adults and paediatrics above 1year old, 2 g or approx. 1.5 g/10 cm2 for 1 to 5 hour; for dermal surgical procedures on larger areas, , approximately 1.5-2 g/10 cm2 for 2 to 5 hours; for infants at 3-12months, up to 2g and 16 cm2 for one hour.

Genital mucosa usage : Approximately 5-10 g of cream for 5-10 minutes before procedure started, no occlusive dressing needed.

Method of administration Cutaneous use

The protective membrane of the tube is perforated by applying the cap.

A thick layer of Compound Lidocaine Cream should be applied to the skin, including genital skin, under an occlusive dressing. For application to larger areas, such as split-skin grafting, an elastic bandage should be applied on top of the occlusive dressing to give an even distribution of cream and protect the area. In the presence of atopic dermatitis, the application time should be reduced.

For procedures related to genital mucosa, no occlusive dressing is required. The procedure should be commenced immediately after removal of the cream.

4.3 Contraindications

(1) Patient who is highly allergic to amides-type local anesthetics or any other component of the product;

(2) Patients with congenital or idiopathic methemoglobinemia.

4.4 Special warnings and precautions for use

Patients with defective glucose-6-phosphate dehydrogenase, hereditary or idiopathic methaemoglobinaemia are more susceptible to active-substance-induced signs of 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.

Due to insufficient data on absorption, Compound Lidocaine Cream is not supposed to apply to open wounds (excluding leg ulcers).

Care should be taken when applying Compound Lidocaine Cream to patients with atopic dermatitis. A shorter application time, 15-30 minutes, may be sufficient . Application times of longer than 30 minutes in patients with atopic dermatitis may result in an increased incidence of local vascular reactions, particularly application site redness and in some cases petechia and purpura. Prior to removal of mollusca in children with atopic dermatitis it is recommended to apply cream for 30 minutes.

When applied in the vicinity of the eyes, Compound Lidocaine cream should be used with particular care since it may cause eye irritation. Also the loss of protective reflexes may allow corneal irritation and potential abrasion. If eye contact occurs, the eye should immediately be rinsed with water or sodium chloride solution and protected until sensation returns.

Compound Lidocaine Cream should not be applied to an impaired tympanic membrane. Tests on laboratory animals have shown that Compound Lidocaine cream has an ototoxic effect when instilled into the middle ear. Animals with an intact tympanic membrane, however, show no abnormality when exposed to Compound Lidocaine Cream in the external auditory canal.

Patients treated with anti-arrhythmics of class III (e.g., amiodarone) should be carefully monitored and ECG monitoring considered, as cardiac effects may be additive.

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, as assessed by local wheal formation, is not affected when Compound Lidocaine Cream is used prior to BCG vaccination, the results of intracutaneous injections of live vaccines should be monitored.

Paediatric population

Compound Lidocaine Cream should not be used

- in newborn infants/infants up to 12 months of age receiving concomitant treatment with methaemoglobin-inducing agents.
- in preterm newborn infants with a gestational age less than 37 weeks as they are at risk of developing increased methaemoglobin levels.

Safety and efficacy for the use of Compound Lidocaine Cream on genital skin and genital mucosa have not been established in children younger than 12 years.

Available paediatric data do not demonstrate adequate efficacy for circumcision.

4.5 Interaction with other medicinal products and other forms of interaction

Prilocaine in high doses may cause an increase in methaemoglobin levels particularly in conjunction with methaemoglobin-inducing medicinal products (e.g. sulphonamides, nitrofurantoin, phenytoin, phenobarbital).

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

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

Medicinal products that reduce the clearance of lidocaine (e.g., cimetidine or betablockers) may cause potentially toxic plasma concentrations when lidocaine is given in repeated high doses over a long time period.

Paediatric population

Specific interaction studies in children have not been performed. Interactions are likely to be similar to the adult population.

4.6 Fertility, pregnancy and lactation

Pregnancy

Although topical application is associated with only a low level of systemic absorption, the use of Compound Lidocaine Cream in pregnant women should be undertaken with care because insufficient data are available concerning the use of Compound Lidocaine Cream in pregnant women. However, animal studies do not indicate any direct or indirect negative effects on pregnancy, embryo-foetal development, parturition or postnatal development. Reproduction toxicity has been shown with subcutaneous/intramuscular administration of high doses of lidocaine or prilocaine much exceeding the exposure from topical application.

Lidocaine and prilocaine cross the placental barrier and may be absorbed 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 childbearing age. No specific disturbances to the reproductive process have so far been reported, e.g. an increased incidence of malformations or other directly or indirectly harmful effects on the foetus.

Breast-feeding

Lidocaine and, in all probability, prilocaine are excreted into breast milk, but in such small quantities that there is generally no risk of the child being affected at therapeutic dose levels. Compound Lidocaine Cream can be used during breast-feeding if clinically needed, under professional advice.

Fertility

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

4.7 Effects on ability to drive and use machines

Compound Lidocaine Cream has no or negligible influence on the ability to drive and use machines when used at the recommended doses.

4.8 Undesirable effects

Compound Lidocaine Cream has been widely used in China, and similar products have been marketed in various countries. Safety profile has been well established and Summary of the safety profile from studies with Compound Lidocaine Cream and similar products in market is list as below,

The most frequently observed adverse drug reactions (ADRs) are related to administration site conditions (transient local reactions at the application site), reported as common.

Tabulated list of adverse reactions

The incidences of the Adverse Drug Reactions (ADRs) associated with Compound Lidocaine Cream therapy is tabulated below. The table is based on adverse events reported during clinical trials, and/or post-marketing use.

Their frequency of Adverse Reactions is listed by MedDRA System Organ Class (SOC) and at the preferred term level.

Within each System Organ Class, adverse reactions are listed under frequency categories of: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥ 1/10,000 to <1/1,000), very rare (<1/10,000). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 3 Adverse reactions

System Organ Class	Common	Uncommon	Rare
Blood and lymphatic system disorders			Methaemoglobinaemia[1]
Immune system disorders			Hypersensitivity[1, 2, 3]
Eye disorders			Corneal irritation[1]
Skin and subcutaneous tissue disorders			Purpura[1], Petechiae[1] (especially after longer application times in children with atopic dermatitis or mollusca contagiosa)
General disorders and administration site conditions	Burning sensation[2, 3] Application site pruritus [2, 3] Application site erythema[1, 2, 3] Application site oedema [1, 2, 3] Application site warmth [2, 3] Application site pallor [1, 2, 3]	Burning sensation[1] Application site irritation[3] Application site pruritus[1] Application site paraesthesia[2] such as tingling Application site warmth[1]	

[1] Skin

[2] Genital mucosa

[3] Leg ulcer

Paediatric population

Frequency, type and severity of adverse reactions are similar in the paediatric and adult age groups, except for methaemoglobinaemia, which is more frequently observed, often in connection with overdose (see section 4.9), in newborn infants and infants aged 0 to 12 months.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after Authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org/

4.9 Overdose

Rare cases of clinically significant methaemoglobinaemia have been reported. Prilocaine in high doses may cause an increase in methaemoglobin levels particularly in susceptible individuals (section 4.4), with too frequent dosing in newborn infants and infants below 12 months of age (section 4.2)

and in conjunction with methaemoglobin-inducing medicinal products (e.g. sulphonamides, nitrofurantoin, phenytoin and phenobarbital). 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.

Clinically significant methaemoglobinaemia should be treated with a slow intravenous injection of methylene blue (see also section 4.4).

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 of administration. 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 medicinal products; circulatory signs are treated in line with recommendations for resuscitation.
Since the rate of absorption from intact skin is slow, a patient showing signs of toxicity should be kept under observation for several hours following emergency treatment.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anaesthetics, local; ATC code: N01B B20 Mechanism of action

Compound Lidocaine Cream provides dermal anaesthesia through the release of lidocaine and prilocaine from the cream into the epidermal and dermal layers of the skin and the vicinity of dermal pain receptors and nerve endings.

Lidocaine and prilocaine are amide-type local anaesthetics. 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.

Skin

Compound Lidocaine Cream is applied to intact skin under an occlusive dressing. The time needed to achieve reliable anaesthesia of intact skin is 1 to 2 hours, depending on the type of procedure. The local anaesthetic effect improves with longer application times from 1 to 2 hours in most parts of the body, with the exception of the skin of the face and the male genitals.
Because of thin facial skin and high tissue blood flow, maximal local anaesthetic effect is obtained after 30-60 minutes on the forehead and on the cheeks. Similarly, local anaesthesia of the male genitals is achieved after 15 minutes. The duration of anaesthesia following the application of Compound Lidocaine Cream for 1 to 2 hours is at least 2 hours after removal of the dressing, except in the face where the duration is shorter.

Compound Lidocaine Cream is equally effective and has the same anaesthetic onset time across the range of light to dark pigmented skin (skin types I to VI).

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

Compound Lidocaine Cream produces a biphasic vascular response involving initial vasoconstriction followed by vasodilatation at the application site (see section 4.8). Irrespective of the vascular response, Compound Lidocaine Cream 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). Compound Lidocaine Cream may cause a transient increase in skin thickness, partly caused by hydration of the skin under the occlusive dressing. The skin thickness decreases over the course of 15 minutes air exposure.

The depth of cutaneous anaesthesia increases with application time. In 90% of patients the anaesthesia is sufficient for the insertion of a biopsy punch (4 mm diameter) to a depth of 2 mm after 60 minutes and 3 mm after 120 minutes Compound Lidocaine Cream treatment.

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

Genital mucosa

Absorption from the genital mucosa is more rapid and onset time is shorter than after application to the skin.

After a 5-10 minute application of Compound Lidocaine Cream 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).

Paediatric population

Clinical studies involved more than 2,300 paediatric patients of all age groups and demonstrated efficacy for needle pain (venipuncture, cannulation, s.c. and i.m. vaccinations, lumbar puncture), laser treatment of vascular lesions, and curettage of molluscum contagiosum. Compound Lidocaine Cream diminished the pain of both needle insertion and injection of vaccines.

Analgesic efficacy increased from 15 to 90 minutes application on normal skin but on vascular lesions 90 minutes provided no benefit over 60 min.

There was no benefit of Compound Lidocaine Cream versus placebo for liquid nitrogen cryotherapy of common warts. No adequate efficacy for circumcision could be demonstrated.

Eleven clinical studies in newborn infants and infants showed that peak methaemoglobin concentrations occur about 8 hours after epicutaneous Compound Lidocaine Cream administration, are clinically insignificant with recommended dosage, and return to normal values after about 12-13 hours. Methaemoglobin formation is related to the cumulative amount of prilocaine percutaneously absorbed, and may therefore increase with prolonged application times of Compound Lidocaine Cream.

The use of Compound Lidocaine Cream prior to measles-mumps-rubella or intramuscular diphtheria-pertussis-tetanus- inactivated poliovirus-Haemophilus influenzae b or Hepatitis B vaccines did 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.

5.2 Pharmacokinetic properties

Absorption, distribution, biotransformation and elimination

The systemic absorption of lidocaine and prilocaine from Compound Lidocaine Cream 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. Plasma concentrations after treatment with Compound Lidocaine Cream are 20-60% lower for prilocaine than for lidocaine, because of a larger volume of distribution and more rapid clearance.

The major elimination pathway of lidocaine and prilocaine is via hepatic metabolism and metabolites are renally excreted. However, the rate of metabolism and elimination of the local anaesthetics after topical application of Compound Lidocaine Cream are governed by the rate of absorption. Therefore, a decrease in clearance, such as in patients with severely impaired liver function, has limited effects on the systemic plasma concentrations after a single dose of Compound Lidocaine Cream, and after single doses repeated once daily short term (up to 10 days).

Symptoms of local anaesthetic toxicity become increasingly apparent at increasing plasma concentration from 5 to 10

µg/ml of either active substance. It should be assumed that the toxicity of lidocaine and prilocaine are additive.

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 cm2 for 2 hours).

Maximum plasma concentrations (mean 0.16 and 0.06 µg/ml) were reached after approximately 1.5-3 hours.

In studies of split-skin grafting in adults application for up to 7 hours 40 minutes to the thigh or upper arm to an area of up to 1,500 cm2 resulted in maximum plasma concentrations not exceeding 1.1 µg/ml lidocaine and 0.2 µg/ml prilocaine.

Genital mucosa

After the application of 10 g Compound Lidocaine 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.

Special populations Elderly patients

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

Paediatric population
The maximum plasma concentrations of lidocaine and prilocaine after application of COMPOUND LIDOCAINE Cream in paediatric patients of different ages were also below potentially toxic levels. See table 4.

Table 4 Plasma concentrations of lidocaine and prilocaine in paediatric age groups from 0 months to 8 years of age

Age	**Applied amount of cream**	**Application time of the cream on the skin**	**Plasma concentration [ng/ml]**	
			Lidocaine	**Prilocaine**
0 - 3 months	1 g/10 cm^2	1 hour	135	107
3 - 12 months	2 g/16 cm^2	4 hours	155	131
2 - 3 years	10 g/100 cm^2	2 hours	315	215
6 - 8 years	10 - 16 g/100-160 cm^2 (1 g/ 10 cm^2)	2 hours	299	110

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 active substances were shown to have a low oral acute toxicity, providing a good safety margin in the event that Compound

Lidocaine Cream is inadvertently swallowed. In studies on reproduction toxicity, embryotoxic or fetotoxic effects of lidocaine were detected at doses of 25 mg/kg s.c. in the rabbit and 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 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 embryofetal dose to the maternal serum concentration is 0.4 to 1.3.

Neither local anaesthetic showed a genotoxic potential in either in vitro or in vivo genotoxicity 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 active substances.

A metabolite of lidocaine, 2,6-dimethylaniline, and a metabolite of prilocaine, σ-toluidine, showed evidence of genotoxic 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 Compound Lidocaine 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.

6. Pharmaceutical particulars

6.1 List of excipients

Ethoxylated hydrogenated(54) castor oil , Carbomer 934F, sodium hydroxide and water purified.

6.2 Shelf life

36 months

6.3 Special precautions for storage

Do not store above 30°C, do not freeze.

6.5 Nature and contents of container

“Pre-medication pack” containing 10 g tube/box Compound Lidocaine Cream. Pack containing 1 x 10 g tube of Compound Lidocaine Cream

6.6 Special precautions for disposal and other handling

Precautions to be taken before handling or administering the medicinal product

Persons frequently applying or removing cream should ensure that contact is avoided in order to prevent the development of hypersensitivity.

The most updated IFU approved by CMDE is as below,

Manuscript of Package Insert of Compound Lidocaine Approval and Revision Date Externally
Package Insert of Compound Lidocaine Cream

Please read the package insert carefully and use it under the guidance of a physician [Drug Name]
Generic Name: Compound Lidocaine Cream English Name: Compound Lidocaine Cream Chinese Pinyin: Fufang Liduokayin Rugao [Ingredients]

This product is a compound preparation containing prilocaine and lidocaine, 25 mg of prilocaine and lidocaine respectively per gram.

[Description] White cream [Indications]

This product is indicated for local anesthesia of skin in the following situations:

(1) Needle puncture, e.g., catheter placement or blood sample collection;

(2) Superficial surgical procedure.
[Strength] 25 mg of prilocaine and lidocaine respectively per gram
[Dosage and Administration]

Skin: Apply a thick layer of cream on the skin surface, cover with sealed coating, about 1.5 g/10 cm2 for adults and children over 1 year old, approximately 2 g for minor surgery, with an application duration of 1 h in minimum and 5 h in maximum; about 1.5 - 2 g/10 cm2 for the skin surgery with a large area, with an application duration of 2 h in minimum and 5 h in maximum. Infants aged 3 - 12 months are applied with 2 g of cream in maximum on a skin area of 16 cm2 for approximately 1 h.

Genital mucosa: Apply 5 - 10 g of the product on the mucosa for about 5 - 10 min, and the surgery can be initiated without covering sealed coating.

[Adverse Reactions]

The product may induce local reactions in the application site, frequently manifested as pallor, erythema (redness) and edema, which are transient and mild.

It may also cause burning sensation or pruritus at the beginning of use in rare cases. Anaphylaxis to amide local anesthetics (anaphylactic shock in the most severe case) is rare. High-dose of prilocaine may increase the level of methemoglobin in the blood. [Contraindications]

(1) Patients with hypersensitivity to amide local anesthetics or any other ingredients in the product;

(2) Patients with congenital or idiopathic methemoglobinemia. [Warnings and Precautions]

(1) Lacking sufficient absorption information, this product cannot be used on open wounds or mucosa of reproductive organs of children;

(2) Laboratory findings showed that the product caused ototoxicity in the middle ear, but no abnormal findings in the external auditory canal of animals with intact tympanic membrane. Therefore, this product cannot be used on damaged tympanic membrane;

(3) Particular care should be taken when this product is used near eyes as it may cause corneal irritation;

(4) Patients with atopic dermatitis should use this product with special caution, applying for a shorter duration (15- 30 min);

(5) For leg ulcers, it should be disinfected before application;

(6) Prolonged application duration will reduce the anesthetic effect;

(7) This product cannot be used in the following cases until further clinical data are available: Infants under 3 months;

Infants aged 3 - 12 months on treatment with methemoglobin inducer. [Use in Pregnancy and Lactation]

Lidocaine and prilocaine can be absorbed by fetuses through placental barrier. So far many pregnant women and women of childbearing age have received lidocaine and prilocaine, but no special disorders during reproductive process are reported, e.g., increased incidence of malformation or other direct or indirect fetal injury.

Lidocaine and prilocaine are also secreted in the breast milk; however, infants will not be affected at a therapeutic dose due to the little secretion amount.

[Pediatric Use]

This product cannot be used in the following cases until further clinical data are available: Infants under 3 months;

Infants aged 3 - 12 months on treatment with methemoglobin inducer. [Geriatric Use]

This product has not been tested in this population and no reliable references are available. [Drug Interactions]

This product may exacerbate the formation of methemoglobin in patients receiving other medications that cause methemoglobinemia, e.g., sulfonamide.

When this product is given at a high dose, systemic toxicities should be considered for patients who are receiving other local anesthetics or other medications with similar molecular structure to local anesthetics, e.g., tocaine. [Overdose]

There is no case report of systemic toxic symptoms associated with this product except for a foreign case of methemoglobinemia. In the case of symptom of systemic toxicity, its signs are similar to those noted when local anesthetics is given by other routes of administration. The toxicities of local anesthetics are excitatory symptoms of nervous system, and central nervous system and cardiovascular depression in severe cases.

Severe neurogenic symptoms (convulsion, central nervous system depression) must be treated symptomatically with respiratory support and anticonvulsants. Methemoglobinemia can be treated by slow intravenous injection of methylene blue.

[Pharmacology and Toxicology]

This product is applied on intact skin surface and covered with sealed coating, releasing lidocaine and prilocaine to subcutaneous layer and derma, accumulating lidocaine and prilocaine in dermal pain receptor and nerve endings to achieve dermal anesthesia. Lidocaine and prilocaine are amide local anesthetics, both stabilizing nerve cell membrane by blocking ionic flow required in generation of nerve impulses and conduction, thereby achieving local anesthetic effect.

[Pharmacokinetics]

The systemic absorption of lidocaine and prilocaine in this product depends on dose, application duration, skin thickness at different parts of the body, and other skin conditions.
Intact skin: When the cream is applied to adult thigh (60 g/400 cm2), approximately 5% of lidocaine and prilocaine can be absorbed in 3 hours; plasma drug concentration peaked at 2 - 6 hours, with an average level of lidocaine and prilocaine of 0.12 and 0.07 μg/mL, respectively.

Face: When applied at a dose of 10 g/100 cm2, approximately 10% can be systemically absorbed in 2 hours; plasma drug concentration peaked at 1.5 - 3 h , with an average level of lidocaine and prilocaine of 0.16 and 0.6 μg/mL, respectively.

Genital mucosa: When 10 g of this product is applied on vaginal mucosa; plasma drug concentration peaked at 20

- 45 min, with an average level of lidocaine and prilocaine of 0.18 and 0.15 μg/mL, respectively. [Storage] Tightly-closed, preferably stored below 25°C. Do not freeze.

7. MARKETING AUTHORIZATION HOLDER

[Packaging] Aluminium tube for medicinal ointment. [Shelf Life] 24 months [Quality Standard] YBH02032006 [Approval No.] GYZZ H20063466 [Manufacturer] Name: Tongfang Pharmaceuticals Group Co., Ltd
Manufacturing Site: Badaling Industrial Development Zone, Yanqing County, Beijing Postal Code: 102101

Tel: 010-61162229 61162206

8. MARKETING AUTHORIZATION NUMBER

H2022/CTD9054/18894

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

2022 June 23

10. DATE OF REVISION OF THE TEXT

01/08/2026