SUMMARY OF PRODUCT CHARACTERISTICS

(SmPC)

OPRALIX®, Cream (2.5%+2.5%) w/w

1. **NAME OF MEDICINAL PRODUCT**

   OPRALIX®

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION (active substances)**

   Lidocaine + Prilocaine 2.5% + 2.5% w/w.

3. **PHARMACEUTICAL FORM**

   Cream.

4. **CLINICAL PARTICULARS**

4.1. Therapeutic indications

Topical anaesthesia of the skin in connection with:

- needle insertion, e.g. intravenous catheters or blood sampling,
- superficial surgical procedures on the genital skin for the removal of warts, circumcision or removal of foreskin.

4.2. Posology and method of administration

OPRALIX® cream causes anesthesia of skin. The depth and duration of anesthesia depends upon the application time, the dose and the application site.

Application site/ Age group	Procedure	Application
Skin		A thick layer of cream should be applied to the skin, under an occlusive dressing.
Adults		Recommended dose: approximately 1.5 g/10cm^2 of skin area.
	Minor procedures, e.g. needle insertion and surgical treatment of localised lesions.	2 g (approximately half a 5 g tube). Minimum application time 1 hour – maximum 5 hours (1).
	Dermal surgical procedures on larger areas in a hospital setting, e.g. split-skin grafting.	Approximately 1.5-2 g/10 cm^2. Minimum application time 2 hours – maximum 5 hours (1).
Children **Infants 3-11 months** (2) **Children 1-5 years** **Children 6-11 years**	Minor procedures, e.g. needle insertion and surgical treatment of localised lesions.	Approximately 1.0 g/10cm^2. Application time 30 minutes to 1 hour. Up to 2.0 g and up to 20 cm^2 (3) Up to 10.0 g and up to 100 cm^2 Up to 20.0 g and up to 200 cm^2
Genital skin **Adults**	Surgical treatment of localised lesions, e.g. removal of genital warts (condylomata acuminata), circumcision or removal of foreskin.	Approximately 5-10 g of cream for 5-10 minutes. No occlusive dressing is required. The procedure should be commenced immediately after removal of the cream.

(1) After longer application time anaesthesia decreases.

(2) OPRALIX® should not be used in infants 3 to 12 months of age who are being treated with medicines that may cause methaemoglobinaemia, because of safety concerns.

(3) No clinically significant increase in methaemoglobin levels has been observed after an application time of up to 4 hours on 16 cm^2 skin area.

4.3. Contraindications

- Hypersensitivity to local anaesthetics of the amide type or to any of the excipients of the product.
- Hereditary, idiopathic or poisoning-induced methaemoglobinaemia.
- Atopic dermatitis.
- Newborn infants/infants younger than 3 months.

4.4. Special warnings and precautions for use

- OPRALIX® should not be applied to open wounds or skin ulcers because the absorption of its ingredients increases.
- Caution should be exercised when OPRALIX® is applied to patients with dermatitis and patients with G6PD deficiency.
- Due to insufficient data on absorption, OPRALIX® should not be used on the genital mucosa of the children. However, it has been proved to be safe when it used in children for circumcision and applied to the foreskin.
- The application of OPRALIX® near eyes should be avoided, since it may cause corneal irritation.
- It should not be applied to the ear in cases of perforation or rupture of the tympanic membrane, because its penetration in the middle ear is ototoxic.
- Patients with severe liver disease are at increased risk of developing toxic plasma concentrations of lidocaine and prilocaine due to the decreased capacity of the liver to metabolized them.

OPRALIX® should not be used:

- In infants aged 3 to 12 months, who are being treated with medicines that may cause methaemoglobinaemia, such as sulphonamides, antimalarials *(see also "Undesirable effects")*.
- Before intracutaneous injection of vaccines with live microorganisms e.g. BCG vaccine, because the interaction between the active ingredients of OPRALIX® and the vaccine cannot be ruled out.

4.5. Interaction with other medicinal products and other forms of interactions

- In patients taking medications which may cause methaemoglobinaemia e.g. sulphonamides, antimalarials, OPRALIX® may cause an increase in methaemoglobin levels *(see "Undesirable effects")*.
- OPRALIX® should be used with caution in patients receiving class I antiarrhythmic drugs (quinidine, procainamide, mexiletine, etc.).

4.6. Pregnancy and lactation

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.

Pregnancy

OPRALIX® should be used during pregnancy only if it is absolutely necessary and the expected benefits to the mother outweigh any potential risk to the foetus.

Lactation

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. Generally, it should be used with caution in breast-feeding women.

4.7. Effects on ability to drive and use machines

None reported when used at the recommended doses.

4.8. Undesirable effects

➔ *Common (> 1%)*

Skin: Local reactions such as paleness, erythema and oedema caused by OPRALIX® at the application site are transient and usually mild.

➔ *Less common (> 1% and <1%)*

An initially mild sensation of burning or itching is observed lees frequently.

➔ *Rare (<1%)*

Allergic reactions (which in rare cases may develop into anaphylactic shock) to amide-type local anaesthetics and an increase in methaemoglobin levels are rare.

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 directly at the National Organization for Medicines, Mesogeion 284, GR-15562, Holargos, Athens, Tel: +30 21 32040380/337, Fax: +30 21 06549585, Website http://www.eof.gr.

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 conjunction with methaemoglobin-inducing agents (e.g. sulphonamides).

However, should other symptoms of systemic toxicity occur after application of OPRALIX® to the skin , 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.

Clinically significant methaemoglobinaemia should be treated with a slow intravenous injection of methylene blue.

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

OPRALIX® when it is applied to intact skin under an occlusive dressing, 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.

The time needed to achieve reliable anaesthesia of intact skin is approximately ½ to 2 hours, depending on the type of procedure.

The duration of anaesthesia following the application of cream for 1 to 2 hours is at least 2 hours after removal of the dressing.

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

OPRALIX® cream produces a biphasic vascular response involving initial vasoconstriction followed by vasodilatation at the application site *(see section 4.8 "Undesirable effects").*

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 "Special warnings and precautions for use").*

5.2. **Pharmacokinetic properties**

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

Following application to the thigh in adults (60 g cream/400 cm^2 for 3 hours), the extent of absorption was approximately 5% of lidocaine and prilocaine. Maximum plasma concentrations (mean 0.12 and 0.07 µg/ml) were reached approximately 2-6 hours after application.

The extent of systemic absorption was approximately 10% following application to the face (10 g/100 cm^2 for 2 hours). Maximum plasma concentrations (mean 0.16 and 0.06 µg/ml) were reached after approximately 1.5-3 hours.

After the application of 10 g 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.

Lidocaine is metabolised in the liver in various metabolites, including 2,6 xylidine. Prilocaine is metabolised in the liver and kidneys in various metabolites, including ortho-toluidine and N-n-propylalanine.

In infants 3-12 months of age, after the application of 2 g OPRALIX® cream with an area of 10 cm^2 for 4 hours, maximum plasma concentrations of lidocaine and prilocaine were 0.155 µg/ml and 0.131 µg/ml respectively. In children 2-3 years of age, after the application of 10 g OPRALIX® cream with an area of 100 cm^2 for 2 hours, maximum plasma concentrations of lidocaine and prilocaine were 0.135 µg/ml and 0.215 µg/ml respectively. In children 6-8 years of age, after the application of 10 - 16 g OPRALIX® cream with an area of 100 - 160 cm^2 for 2 hours,

maximum plasma concentrations of lidocaine and prilocaine were 0.299 μg/ml and 0.110 μg/ml respectively.

5.3. Preclinical safety data

Lidocaine and prilocaine have been extensively used for many years, and therefore their applications in therapeutics are well known.

Preclinical studies on laboratory animals have shown that metabolites of lidocaine and prilocaine at multiple doses of those used with OPRALIX® cream had carcinogenic activity. The same metabolites have shown mild mutagenic activity in certain microbial and in vitro experimental arrangements. No teratogenic or embryotoxic effects have been observed.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

- Poloxyl 40 Hydrogenated castor oil
- Carbomer
- Sodium hydroxide
- Water purified

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

18 (eighteen) months, provided that the product is kept in its original packaging in accordance with the storage instructions.

6.4. **Special precautions for storage**

Do not store above 25°C.

6.5. **Nature and contents of container**

1) Cardboard box that contains 10 aluminium tubes of 5 g, along with 24 occlusive dressings and a patient information leaflet.

2) Cardboard box that contains 5 aluminium tubes of 5 g, along with 12 occlusive dressings and a patient information leaflet.

3) Cardboard box that contains 1 aluminium tube of 5 g and a patient information leaflet.

Not all pack sizes may be marketed.

6.6. **Instructions for use/handling**

Not required.

6.7. **Marketing Authorisation Holder**

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7. **MARKETING AUTHORISATION NUMBER(S)**

6666/16/11.01.2017.

8. **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

25.09.2009.

8. **DATE OF REVISION OF THE TEXT**

11.01.2017.