Professional Information for Oramico Gel

SCHEDULING STATUS S2

1. NAME OF THE MEDICINE

Oramico Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of **Oramico Gel** contains 20 mg miconazole.

Excipients with known effect:

Contains alcohol: 7,6 mg ethanol (96 %) per gram.

Contains sweetener: 1 mg sodium saccharin per gram.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral gel.

White to off-white homogenous translucent oral gel, with pineapple taste and free from any gritty particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Oramico Gel is indicated for the treatment of fungal infections of the mouth (e.g. thrush in babies four months and older and oral candidiasis in other age groups) and for fungal stomatitis occurring in association with dentures.

4.2 Posology and method of administration

Posology

Full term infants: 4 – 24 months: 1,25 mL (¼ measuring spoon) of gel, applied four times a day after meals. Each dose is to be divided into smaller portions and the gel applied to the affected

area(s) with a clean finger. The gel is not to be swallowed immediately, but kept in the mouth as long as possible.

Adults and children 2 years and older: 2,5 mL (½ measuring spoon) of gel, applied four times a day after meals. The gel is not to be swallowed immediately, but kept in your mouth as long as possible.

The application of **Oramico Gel** must be repeated three to four times daily, depending upon the severity of the infection.

Apply the gel regularly until all signs of the infection have disappeared. Continue using for another two days after the infection has cleared.

Application of the gel is preferably done after meals.

In fungal stomatitis, associated with dentures, apply **Oramico Gel** to the lesions in the evening and leave on overnight.

For oral candidiasis, dental prostheses should be removed at night and brushed with **Oramico Gel**.

Method of administration

For oral administration.

Oramico Gel should be spread evenly over the affected areas of the oropharyngeal mucosa and tongue, taking care to properly cover oral ulcerations and other lesions.

Instructions for use and handling:

To open the tube, unscrew the cap. Then pierce the seal of the tube by means of the pin on the top of the cap.

4.3 Contraindications

Oramico Gel is contraindicated in the following situations:

- in patients with known hypersensitivity to miconazole, other imidazole derivatives or to any of the excipients listed in section 6.1 (see section 4.4)

- in infants less than 4 months of age or in those with swallowing reflex not yet fully developed and prematurely born infants less than six months of age
- in patients with impaired liver function
- co-administration of the following medicine that are subject to metabolism by CYP3A4 (see section 4.5):
  - substrates known to prolong QT interval e.g. astemizole, bepridil, cisapride, dofetilide, halofantrine, mizolastine, pimozide, quinidine, sertindole and terfenadine
  - ergot alkaloids
  - HMG-CoA reductase inhibitors such as simvastatin and lovastatin
  - triazolam and midazolam.
- in combination with warfarin (metabolised by CYP2C9) (see section 4.5).

4.4 Special warnings and precautions for use

Avoid contact with the eyes.

Miconazole, as in **Oramico Gel**, is systemically absorbed and is known to inhibit CYP2C9 and CYP3A4 (see section 5.2) which can lead to prolonged effects of warfarin. Bleeding events, some with fatal outcomes, have been reported with concurrent use of **Oramico Gel** and warfarin (see sections 4.5 and 4.8). If the concomitant use of miconazole, as in **Oramico Gel** with an oral anticoagulant, such as warfarin is planned, caution should be exercised, and the anticoagulant effect must be carefully monitored and titrated (see section 4.5).

Patients should be advised that if they experience unexpected bleeding or bruising, nosebleeds, coughing up blood, blood in the urine, black tarry stools or coffee ground vomit, to stop treatment with **Oramico Gel** and seek medical advice.

Severe hypersensitivity reactions, including anaphylaxis and angioedema, have been reported during treatment with miconazole, as in **Oramico Gel** and with other miconazole formulations (see section 4.8). If a reaction suggesting hypersensitivity or irritation should occur, the treatment should be discontinued (see section 4.3).

It is advisable to monitor miconazole, as in **Oramico Gel**, and phenytoin levels, if these two medicines are used concomitantly.

In patients using certain oral hypoglycaemics, such as sulphonylureas, an enhanced therapeutic effect leading to hypoglycaemia may occur during concomitant treatment with **Oramico Gel** and appropriate measures should be considered (see section 4.5).

Choking in infants and young children

Particularly in infants and young children (aged 4 months – 2 years), caution is required, to ensure that **Oramico Gel** does not obstruct the throat. Hence, **Oramico Gel** should not be applied to the back of the throat. Each dose should be divided into smaller portions and applied into the mouth with a clean finger. Observe the patient for possible choking. Also due to the risk of choking, **Oramico Gel** must not be applied to the nipple of a breastfeeding woman for administration to an infant.

It is important to take into consideration the variability of the maturation of the swallowing function in infants, especially when giving **Oramico Gel** to infants between the ages of 4 – 6 months. The lower age limit should be increased to 5 – 6 months of age for infants who are pre-term, or infants exhibiting slow neuromuscular development.

Serious skin reactions (e.g. toxic epidermal necrolysis and Stevens-Johnson syndrome) have been reported in patients using miconazole, as in **Oramico Gel** (see section 4.8). It is recommended that patients be informed about the signs of serious skin reactions, and that the use of **Oramico Gel** be discontinued at the first appearance of skin rash.

Oramico Gel contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially “sodium-free”.

Oramico Gel contains 0,0076 g of alcohol (ethanol) in each 1 g which is equivalent to 0,0076 mg/mg (0,76 % *m/m*). The amount in 1 g is equivalent to less than 1 mL beer or 1 mL wine. The small amount of alcohol in **Oramico Gel** will not have any noticeable effects.

4.5 Interaction with other medicines and other forms of interaction

When using any concomitant medicine, the corresponding professional information should be consulted for information on the route of metabolism. Miconazole can inhibit the metabolism of medicines metabolised by the CYP3A4 and CYP2C9 enzyme systems. This can result in an increase and/or prolongation of their effects, including adverse effects.

Oramico Gel is contraindicated with the co-administration of the following medicines that are subject to the metabolism by CYP3A4 (see section 4.3):

- substrates known to prolong the QT interval e.g. astemizole, cisapride, dofetilide, mizolastine, pimozide, quinidine, sertindole and terfenadine
- ergot alkaloids
- HMG-CoA reductase inhibitors such as simvastatin and lovastatin
- triazolam and oral midazolam.

When **Oramico Gel** is co-administered with the following medicines, caution should be used, because of a possible increase or prolongation of the therapeutic outcome and/or adverse events. If necessary, their dosage should be reduced and, where appropriate, plasma levels monitored:
Medicines subject to metabolism by CYP2C9 (see section 4.4):

- oral anticoagulants such as warfarin (see section 4.3)
- oral hypoglycaemics such as sulphonylureas
- phenytoin.

Other medicines subject to metabolism by CYP3A4:

- HIV protease inhibitors, such as ritonavir and saquinavir
- certain antineoplastic medicines, such as vinca alkaloids, busulfan and docetaxel

- certain calcium channel blockers, such as dihydropyridines and verapamil
- certain immunosuppressive medicines: ciclosporin, tacrolimus, sirolimus (also known as rapamycin)
- others: carbamazepine, cilostazol, disopyramide, buspirone, alfentanil, sildenafil, alprazolam, brotizolam, midazolam IV, rifabutin, methylprednisolone, trimetrexate, ebastine and reboxetine.

4.6 Fertility, pregnancy and lactation

Pregnancy

Oramico Gel should not be used during pregnancy, as safety has not been demonstrated.

Breastfeeding

It is not known whether miconazole, as in **Oramico Gel**, is excreted in human milk. **Oramico Gel** should not be used in patients who are breastfeeding their infants.

4.7 Effects on ability to drive and use machines

Oramico Gel should not affect alertness or driving ability.

4.8 Undesirable effects

Description of selected adverse reactions

Increases in international normalised ration (INR) and bleeding events such as epistaxis, contusion, haematuria, melaena, haematemesis, haematoma and haemorrhages have been reported in patients treated with oral anticoagulants such as warfarin in association with miconazole oral gel, such as **Oramico Gel** (see sections 4.3, 4.4 and 4.5). Some events had fatal outcomes.

System organ class	**Adverse drug reactions**		
	Frequency category		
	Frequent	**Less frequent**	**Frequency unknown**

Immune system disorders			Anaphylactic reaction, hypersensitivity
Nervous system disorders		Dysgeusia	
Respiratory, thoracic and mediastinal disorders			Choking (see section 4.3)
Gastrointestinal disorders	Dry mouth, nausea, oral discomfort, vomiting, regurgitation		Diarrhoea, stomatitis, tongue discolouration
Hepatobiliary disorders			Hepatitis
Skin and subcutaneous tissue disorders			Angioedema, toxic epidermal necrolysis, Stevens-Johnson syndrome, urticaria, rash, acute generalised exanthematous pustulosis, drug reaction with eosinophilia and systemic symptoms
General disorders and administration site conditions	Abnormal product taste		

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of **Oramico Gel** is important. It allows continued monitoring of the benefit/risk balance of **Oramico Gel**. Health care providers are

requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Symptoms

In the event of accidental overdose, vomiting and diarrhoea may occur.

Treatment

Treatment is symptomatic and supportive. A specific antidote is not available.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 20.2.2 Antimicrobial (chemotherapeutic) agents. Fungicides.

ATC code: A01A B09 and A07A C01

Miconazole possesses an antifungal activity against the common dermatophytes and yeasts as well as an antibacterial activity against certain Gram-positive bacilli and cocci.

Its activity is based on the inhibition of the ergosterol biosynthesis in fungi and the change in the composition of the lipid components in the membrane, resulting in fungal cell necrosis.

5.2 Pharmacokinetic properties

Absorption

Miconazole is systemically absorbed after administration as the oral gel. Administration of a 60 mg dose of miconazole as the oral gel results in peak plasma concentrations of 31 to 49 ng/mL, occurring approximately two hours post-dose.

Distribution

Absorbed miconazole is bound to plasma proteins (88,2 %), primarily to serum albumin and red blood cells (10,6 %).

Biotransformation

The absorbed portion of miconazole is largely metabolised; less than 1 % of an administered dose is excreted unchanged in the urine. The terminal half-life of plasma miconazole is 20 to 25 hours in most patients.

Elimination

The elimination half-life of miconazole is similar in renally impaired patients. Plasma concentrations of miconazole are moderately reduced (approximately 50 %) during haemodialysis. About 50 % of an oral dose may be excreted in the faeces partly metabolised and partly unchanged.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polysorbate 20

Pregelatinised potato starch

Glycerine

Sodium saccharin

Ethanol 96 %

Pineapple flavour

Purified water.

6.2 Incompatibilities

None known.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 30 °C. Protect from light.

Keep the tube tightly closed until required for use.

6.5 Nature and contents of container

Aluminium tube containing 30 g gel, with white HDPE piercing screw cap, packed in an outer carton.

6.6 Special precautions for disposal and other handling

Each tube of the gel is sealed – use the cap to pierce the seal.

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

LeBasi Pharmaceuticals (Pty) Ltd

San Domenico Building, Unit 6

10 Church Street

Durbanville

7551

8. REGISTRATION NUMBER

57/20.2.2/0035

9. DATE OF FIRST AUTHORISATION

4 February 2025

10. DATE OF REVISION OF THE TEXT