**Professional Information for VARI MICONAZOLE 2 % *m/m* ORAL GEL**

**SCHEDULING STATUS:** S2

## 1. NAME OF THE MEDICINE

**VARI MICONAZOLE 2 % *m/m* ORAL GEL**

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains 20 mg miconazole.

*Excipients with known effects:*

Contains sweetener: 3,06 mg sodium saccharin in each gram.

Contains preservatives: 0,2 % *m/m* methyl paraben and 0,02 % *m/m* propyl paraben.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Oral gel.

A translucent, homogeneous gel, free from any visible contaminants, with a pineapple flavour.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

**VARI MICONAZOLE 2 % *m/m* ORAL GEL** is indicated for the treatment of fungal infections of the mouth (oral candidiasis or thrush) and for fungal stomatitis occurring in association with dentures.

### 4.2 Posology and method of administration

*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 of age 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 the mouth as long as possible.

**VARI MICONAZOLE 2 % *m/m* ORAL 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. Apply after meals.

The application of **VARI MICONAZOLE 2 % *m/m* ORAL GEL** should 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.

For the treatment of oral lesions, **VARI MICONAZOLE 2 % *m/m* ORAL GEL** must be kept in contact with the affected areas as long as possible. This can be achieved by retaining the gel in the mouth for the maximum time possible before swallowing.

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

For oral candidiasis, dental prostheses should be removed at night and brushed with the gel.

*Instructions for use and handling:*

To open the tube, unscrew the cap and pierce the seal of the tube with the pin on top of the cap.

### 4.3 Contraindications

- Hypersensitivity to miconazole or to any of the excipients listed in section 6.1.
- Infants less than 4 months of age, in cases where the swallowing reflex has not fully developed yet or in prematurely born infants under the age of 6 months.
- Patients with impaired liver function.
- Co-administration with the following medicines metabolised by CYP3A4 (see section 4.5):

- Substrates that prolong QT-interval including 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.

- Use of **VARI MICONAZOLE 2 % *m/m* ORAL GEL** in combination with warfarin (metabolised by CYP2C9).

## 4.4 Special warnings and precautions for use

Avoid contact with the eyes.

*Choking in infants and young children*

It is important to take into consideration the variability of the maturation of the swallowing function in infants, especially when giving **VARI MICONAZOLE 2 % *m/m* ORAL GEL** to infants between the ages of 4 – 6 months. The lower age limit should be increased to 6 months of age for infants who are pre-term, or infants exhibiting slow neuromuscular development.

Caution should be exercised, particularly in infants and young children (aged 4 months – 2 years), that the gel does not obstruct the throat. The gel should therefore not be applied to the back of the throat. The full dose should be divided into smaller doses and applied into the mouth with a clean finger. Observe the patient for possible choking. Also, due to the risk of choking, the gel must not be applied to the nipple of a breastfeeding woman for administration to an infant.

*Oral anti-coagulants*

Miconazole 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 **VARI MICONAZOLE 2 % *m/m* ORAL GEL** and warfarin (see section 4.3 and section 4.5).

*Phenytoin*

Phenytoin levels should be monitored when used concomitantly with **VARI MICONAZOLE 2 % *m/m* ORAL GEL** (see section 4.5).

*Oral hypoglycaemics*

**VARI MICONAZOLE 2 % *m/m* ORAL GEL** may cause an enhanced hypoglycaemic effect when used with oral hypoglycaemics (e.g. sulfonylureas). Appropriate measures should be taken (see section 4.5).

Severe hypersensitivity reactions, including anaphylaxis and angioedema, have been reported during treatment with **VARI MICONAZOLE 2 % *m/m* ORAL GEL** and with other miconazole formulations (see section 4.8). If a reaction suggesting hypersensitivity or irritation should occur, the treatment should be discontinued.

Serious skin reactions (e.g. toxic epidermal necrolysis and Stevens-Johnson syndrome) have been reported in patients receiving **VARI MICONAZOLE 2 % *m/m* ORAL GEL** (see section 4.8). It is recommended that patients be informed about the signs of serious skin reactions, and that use of **VARI MICONAZOLE 2 % *m/m* ORAL GEL** be discontinued at the first appearance of skin rash.

## 4.5 Interaction with other medicines and other forms of interaction

When using any concomitant medicine, the corresponding label should be consulted for information on the route of metabolism. **VARI MICONAZOLE 2 % *m/m* ORAL GEL** can inhibit the metabolism of medicines metabolised by the CYP3A4 and CYP2C9 enzyme systems. This can result in prolongation or increase of the effect of these medicines, including an increase in side effects.

Refer to section 4.3 for co-administration of certain medicines that are subject to metabolism by CYP3A4.

Concomitant use of **VARI MICONAZOLE 2 % *m/m* ORAL GEL** is contraindicated with the

following (see section 4.3):

- Substrates that prolong QT-interval including astemizole, dofetilide, halofantrine, mizolastine, pimozide, quinidine, sertindole and terfenadine.
- Ergot alkaloids.
- HMG-CoA reductase inhibitors such as simvastatin and lovastatin.
- Triazolam and midazolam.

Caution is advised with concomitant use of **VARI MICONAZOLE 2 % *m/m* ORAL GEL** and the following medicines because of a possible increase or prolongation of the therapeutic outcome and/or adverse effects. If necessary, their dosage should be reduced and, where appropriate, plasma levels monitored:

*Medicines subject to metabolism by CYP2C9 (see section 4.4)*

- Oral anti-coagulants (e.g. warfarin) (see section 4.3).
- Oral hypoglycaemics (e.g. sulfonylureas).
- Phenytoin.

*Other medicines subject to metabolism by CYP3A4:*

- HIV protease inhibitors (e.g. ritonavir and saquinavir).
- Certain antineoplastic medicines (e.g. the vinca alkaloids, busulfan and docetaxel).
- Certain calcium channel blockers (e.g. dihydropyridines and verapamil).
- Certain immunosuppressants (e.g. ciclosporin, tacrolimus, sirolimus).
- Other medicines including alfentanil, alprazolam, brotizolam, buspirone, carbamazepine, cilostazol, disopyramide, ebastine, methylprednisolone, midazolam IV, reboxetine, rifabutin, sildenafil and trimetrexate.

## 4.6 Fertility, pregnancy and lactation

### Pregnancy

**VARI MICONAZOLE 2 % *m/m* ORAL GEL** should not be used during pregnancy as the safety and efficacy have not been established.

**Breastfeeding**

There are no data available on the excretion of miconazole in human milk; therefore, **VARI MICONAZOLE 2 % *m/m* ORAL GEL** should not be used in patients who are breastfeeding.

**Fertility**

There are no fertility data available.

## 4.7 Effects on ability to drive and use machines

**VARI MICONAZOLE 2 % *m/m* ORAL GEL** has no influence on the ability to drive vehicles or use machines.

## 4.8 Undesirable effects

***Immune system disorders:***

*Less frequent:* Allergic conditions, including angioneurotic oedema and anaphylactic reactions.

***Nervous system disorders:***

*Frequent:* Dysgeusia.

***Respiratory, thoracic and mediastinal disorders:***

*Less frequent*: Choking.

***Gastrointestinal disorders:***

*Frequent:* Nausea, regurgitation of food, vomiting, diarrhoea, dry mouth, oral discomfort.

***Hepato-biliary disorders:***

*Frequent:* Hepatitis.

***Skin and subcutaneous tissue disorders:***

*Less frequent*: Lyell syndrome (toxic epidermal necrolysis), Stevens-Johnson syndrome, urticaria, rash.

***General disorders and administration site conditions:***

*Frequent*: Product taste abnormal.

***Post-marketing experience:***

*Immune system disorders:* Hypersensitivity reactions.

*Gastrointestinal disorders:* Stomatitis, tongue discolouration.

*Skin and subcutaneous tissue disorders:* Angioedema, acute generalised exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS).

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of **VARI MICONAZOLE 2 % *m/m* ORAL GEL** is important. It allows continued monitoring of the benefit/risk balance of **VARI MICONAZOLE 2 % *m/m* ORAL GEL**. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

## 4.9 Overdose

***Symptoms:***

Overdoses may lead to gastrointestinal symptoms such as vomiting and diarrhoea.

***Treatment:***

Treatment is symptomatic and supportive.

No specific antidote for **VARI MICONAZOLE 2 % *m/m* ORAL GEL** is available.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

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

Pharmacotherapeutic group: Antifungals for dermatological/topical use; imidazole derivative.

ATC code: A01A B09 and A07A C01.

Miconazole is an imidazole antifungal with *in vitro* antifungal activity against dermatophytes and yeasts as well as antibacterial activity against certain Gram-positive bacilli and cocci. Miconazole inhibits the ergosterol biosynthesis in fungi. This change in the composition of the lipid components in the membrane, results in fungal cell necrosis.

### 5.2 Pharmacokinetic properties

*Absorption:*

Miconazole is systemically absorbed after oral administration and results in a peak plasma concentration of 31 to 49 ng/mL after administration of a 60 mg dose. Peak plasma concentrations occur two hours after administration.

*Distribution:*

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

*Biotransformation and elimination:*

Miconazole is metabolised to a large extent. Less than 1 % is excreted unchanged in the urine. The terminal half-life of miconazole is between 20 and 25 hours in the broader population. The plasma elimination half-life is similar in renally impaired patients. Plasma concentrations of miconazole are reduced approximately 50 % during haemodialysis.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Glycerol

Methyl paraben

Pineapple essence

Polysorbate 80

Pregelatinised potato starch

Propyl paraben

Purified water

Sodium saccharin.

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

2 years.

### 6.4 Special precautions for storage

Store at or below 25 °C.

Do not freeze.

Keep the tube tightly closed.

### 6.5 Nature and contents of container

**VARI MICONAZOLE 2 % *m/m* ORAL GEL** is supplied in aluminium tubes with white plastic caps, containing 30 g or 40 g gel.

### 6.6 Special precautions for disposal and other handling

No special requirements.

## 7. HOLDER OF CERTIFICATE OF REGISTRATION

BARRS PHARMACEUTICAL INDUSTRIES (PTY) LTD

10 Inyoni Street,

Ndabeni, 7405

Cape Town

South Africa

## 8. REGISTRATION NUMBER

36/20.2.2/0233

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

December 2017

## 10. DATE OF REVISION OF THE TEXT

24 August 2023