SCHEDULING STATUS

S1

1. NAME OF THE MEDICINE

FUNGISTOP VAGINAL 1 % *m/m* cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 g of cream contains 10 mg clotrimazole.

Excipients with known effect:

Preservatives:

Nipastat 0,275 % *m/m*

Imidurea 0,300 % *m/m*

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream.

A soft white cream.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Infections of the genital region (vaginitis) caused by candida.

4.2 Posology and method of administration

Posology

FUNGISTOP VAGINAL should be inserted as deeply as possible into the vagina in the evening before going to bed. Insertion is best achieved when lying back with the legs slightly drawn up. The content of 1 applicator of FUNGISTOP VAGINAL (about 5 g) should be inserted each evening on 6 successive days.

For candida vulvitis or vulvo-vaginitis the vaginal cream should be applied thinly to the external genitalia 2 - 3 times a day for 1 - 2 weeks.

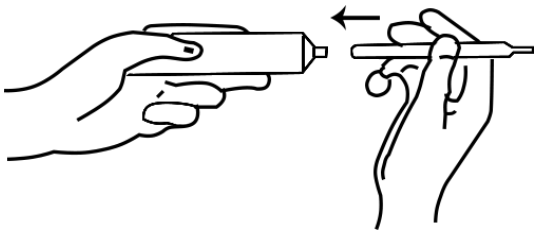
For the prevention of re-infection, the partner should be treated locally with clotrimazole cream at the same time. This preparation does not stain the underwear.

Method of administration

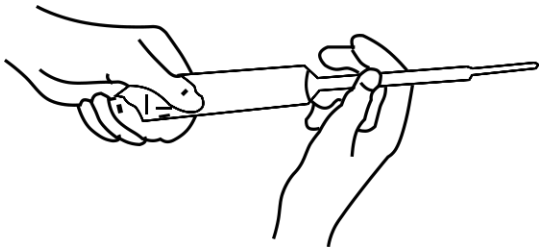
Preparation of the applicator:

1. Wash hands thoroughly.

2. Screw the open end of one of the applicators over the opening of the tube of cream.



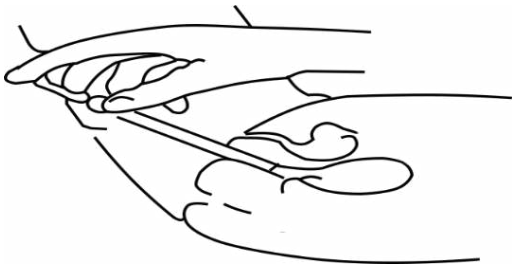
3. Gently squeeze the bottom of the tube so that the cream fills the applicator to the top, pushing the plunger out to almost its full extent.



4. Unscrew the tube of cream and replace its cap.

Inserting the applicator:

5. Carefully insert the end of the applicator as deeply as possible into the vagina. (Making sure the plunger does not fall out). This is best achieved when lying on the back with the legs pulled in a little towards the body.



6. Slowly push the plunger with the forefinger until it stops.

7. Remove the applicator from the vagina and discard it.

Each applicator is for single use only:

The surplus cream may be used to treat any inflammation of the vulva (outer vaginal area) and nearby areas. The cream should be applied thinly and rubbed in gently two to three times a day.

4.3 Contraindications

Hypersensitivity to clotrimazole or any of the excipients of FUNGISTOP VAGINAL (see section 6.1).

4.4 Special warnings and precautions for use

Use only if you have already had a vaginal yeast infection diagnosed by a medical practitioner and you have the same symptoms now, otherwise consult your doctor. These symptoms include itching and burning of the vagina and sometimes a white discharge.

Patients should be advised to consult their medical practitioner if there is no improvement within 3 days or if the symptoms have not disappeared within one week of using FUNGISTOP VAGINAL.

Patients should be advised to consult a medical practitioner in the event of abdominal pain, fever or a foul-smelling vaginal discharge before or during the use of FUNGISTOP VAGINAL.

Recurrent infections may indicate an underlying medical cause. Patients should seek medical advice if symptoms return within 2 months.

Treatment during the menstrual period should not be performed. The treatment should be completed before the onset of menstruation.

Tampons, intravaginal douches, spermicides or other vaginal preparations should not be used while using FUNGISTOP VAGINAL.

Avoidance of vaginal intercourse is recommended in case of vaginal infection and while using FUNGISTOP VAGINAL.

As FUNGISTOP VAGINAL may reduce the effectiveness of condoms and diaphragms, patients should be advised to refrain from sexual intercourse to prevent transmission of HIV and sexually transmitted diseases (STD's) during treatment until the symptoms of candidiasis infection have resolved (see section 4.5).

If skin rash or new irritation occurs, discontinue use.

Contact with eyes should be avoided.

Excipients

FUNGISTOP VAGINAL contains cetostearyl alcohol which may cause local skin reactions (e.g. contact dermatitis).

Paediatric population

FUNGISTOP VAGINAL is intended for use by adults and children 12 years of age and older.

4.5 Interaction with other medicines and other forms of interaction

FUNGISTOP VAGINAL may cause damage to latex contraceptives, such as condoms and diaphragms, when applied on the genital area (women: intravaginally, labia and adjacent area of the vulva; men: prepuce and glans of

the penis). Consequently, the effectiveness and safety of such contraceptives may be reduced. Patients should be advised to use alternative precautions for at least five days after using FUNGISTOP VAGINAL.

Concomitant use of FUNGISTOP VAGINAL with oral tacrolimus (FK-506; immunosuppressant) might lead to increased tacrolimus plasma levels and similarly with sirolimus. Patients should thus be closely monitored for signs and symptoms of tacrolimus or sirolimus overdosage, if necessary, by determination of the respective plasma levels.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety and efficacy of FUNGISTOP VAGINAL in pregnancy has not been established.

There is limited amount of data from the use of FUNGISTOP VAGINAL in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of FUNGISTOP VAGINAL during the first trimester of pregnancy.

Breastfeeding

Available pharmacodynamic/toxicological data in animals have shown excretion of clotrimazole and its metabolites in milk. Breastfeeding should be discontinued during treatment with FUNGISTOP VAGINAL.

Fertility

No human studies of the effects of clotrimazole on fertility have been performed, however, animal studies have not demonstrated any effects of clotrimazole on fertility.

4.7 Effects on ability to drive and use machines

FUNGISTOP VAGINAL has no or negligible influence on the ability to drive a vehicle or use machinery.

4.8 Undesirable effects

The following adverse reactions have been identified during post-approval use. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to estimate their frequency.

Tabulated list of adverse reactions

MedDRA System Organ Class	**Frequency**	**Description**
Immune system disorders	*Frequency unknown*	Allergic reaction, anaphylactic reaction, angioedema, hypersensitivity.
Vascular disorders	*Frequency unknown*	Syncope, hypotension.
Respiratory, thoracic and mediastinal disorders	*Frequency unknown*	Dyspnoea.
Gastrointestinal disorders	*Frequency unknown*	Abdominal pain, lower abdominal cramps, nausea.
Skin and subcutaneous tissue disorders	*Frequency unknown*	Skin rash, urticaria, pruritus, contact allergic dermatitis
Renal and urinary disorders	*Frequency unknown*	Increase in urinary frequency.
Reproductive system and breast disorders	*Frequency unknown*	Genital peeling*, vulvovaginal pruritus, rash, vulvovaginal erythema, vulvovaginal discomfort, vulvovaginal burning sensation, pelvic pain, vaginal haemorrhage, vaginal exfoliation, vaginal discharge, vulvovaginal pain. ** This is a result of the natural exfoliation process of removing damaged vaginal epithelium.*
General disorders and administration site	*Frequency unknown*	Application site irritation, oedema, pain.

conditions

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/ risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

See section 4.8. In case of accidental ingestion, gastrointestinal disturbances and central nervous system depression may occur. Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 20.2.2 Fungicides.

Pharmacotherapeutic group: Gynaecological anti-infectives and antiseptics – imidazole derivatives

ATC code: G01AF02

Clotrimazole acts against fungi by inhibiting ergosterol synthesis. Inhibition of ergosterol synthesis leads to structural and functional impairment of the fungal cytoplasmic membrane.

Clotrimazole has a broad antimycotic spectrum of action *in vitro* and *in vivo*, which includes dermatophytes, yeasts and moulds.

5.2 Pharmacokinetic properties

Pharmacokinetic investigations after vaginal application have shown that only a small amount of clotrimazole (3 – 10 % of the dose) is absorbed. Due to the rapid hepatic metabolism of absorbed clotrimazole into pharmacologically

inactive metabolites, the resulting peak plasma concentrations of clotrimazole after vaginal application of a 500 mg dose were less than 10 ng/mL, reflecting that clotrimazole applied intravaginally does not lead to measurable systemic effects or side effects.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol

Purified water

Imidurea

Nipastat

Liquid paraffin

Cremophor A25

Cremophor A6

Cetostearyl alcohol.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C in a well closed container, protected from light.

6.5 Nature and contents of container

30 g printed aluminium tube with 1 vaginal applicator, placed in an outer carton.

50 g printed aluminium tube with 6 or 8 vaginal applicators, placed in an outer carton.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Biotech Laboratories (Pty) Ltd

Ground Floor, Block K West, Central Park

400 16th Road, Randjespark, Midrand 1685

South Africa

8. REGISTRATION NUMBER

27/20.2.2/0338

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 December 1992

10. DATE OF REVISION OF THE TEXT

29 September 2023