



SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

Mycoten® Vaginal Tablets

(Clotrimazole 100mg)

1. NAME OF THE MEDICINAL PRODUCT

Mycoten® Vaginal Tablets (Clotrimazole 100mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains clotrimazole 100mg.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Vaginal tablet.

4. Clinical particulars

4.1 Therapeutic indications

Clotrimazole vaginal tablets are indicated for the treatment of patients with vaginal yeast infections such as *Candida albicans*, other *Candida* species and vaginal infections caused by *Trichomonas vaginalis*.

4.2 Posology and method of administration

Posology

The treatment consists of one vaginal tablet to be inserted at night, using the applicator provided.

Method of Administration

Mycoten® (Clotrimazole 100mg) Vaginal tablet should be placed into the holder of the applicator. The applicator should be inserted as high as possible into the vagina. This is best achieved when lying back with legs bent up. The plunger is slowly pushed in as far as it will go depositing the tablet in the vagina. The applicator should then be removed from the vagina and disposed of carefully, out of the reach of children. Mycoten Vaginal tablet is effective when applied for 3 or 6 or 14 days.

Clotrimazole vaginal tablets need moisture in the vagina in order to dissolve completely, otherwise undissolved pieces of the tablets might crumble out of the vagina. Pieces of undissolved tablets may be noticed by women who experience vaginal dryness. To help prevent this it is important that the tablet is inserted as high as possible into the vagina at bedtime.

Treatment should not be performed during menstrual period due to the risk of the tablets being washed out by the menstrual flow. The treatment should be finished before the onset of menstruation.

Do not use tampons, intravaginal douches, spermicides or other vaginal products while using this product.

Vaginal intercourse should be avoided in case of vaginal infection and while using this product because the partner could become infected.

Children: Not for use in children under 16 years of age.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Medical advice should be sought if this is the first time the patient has experienced symptoms of candidal vaginitis.

Before using Clotrimazole vaginal tablet, medical advice must be sought if any of the following are applicable:

- more than two infections of candidal vaginitis in the last 6 months.
- previous history of sexually transmitted disease or exposure to partner with sexually transmitted disease.
- pregnancy or suspected pregnancy.
- aged under 16 or over 60 years.
- known hypersensitivity to imidazoles or other vaginal antifungal products.

Clotrimazole vaginal tablet should not be used if the patient has any of the following symptoms where upon medical advice should be sought:

- irregular vaginal bleeding.
- abnormal vaginal bleeding or a blood-stained discharge.
- vulval or vaginal ulcers, blisters or sores.
- lower abdominal pain or dysuria.
- any adverse events such as redness, irritation or swelling associated with the treatment.
- fever or chills.
- nausea or vomiting.
- diarrhoea.
- foul smelling vaginal discharge.

Patients should be advised to consult their physician if the symptoms have not been relieved within one week of using Clotrimazole vaginal tablet. Clotrimazole vaginal tablet can be used again if the candidal infection returns after 7 days. However, if the candidal

infection recurs more than twice within six months, patients should be advised to consult their physician.

When used in pregnancy, the vaginal tablet should be inserted without using an applicator (see "Pregnancy").

Keep out of reach of children.

4.5 Interaction with other medicinal products and other forms of interaction

Laboratory tests have suggested that, when used together, this product may cause damage to latex contraceptives. Consequently the effectiveness of such contraceptives may be reduced. Patients should be advised to use alternative precautions for at least five days after using this product.

Concomitant medication with Clotrimazole vaginal tablet and 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 overdose, if necessary by determination of the respective plasma levels.

4.6 Pregnancy and Lactation

Fertility:

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

Pregnancy:

There are limited amount of data from the use of clotrimazole in pregnant women. Animal studies with clotrimazole have shown reproductive toxicity at high oral doses (see section 5.3). At the low systemic exposures of clotrimazole following vaginal treatment, harmful effects with respect to reproductive toxicity are not predicted.

Clotrimazole can be used during pregnancy, but only under the supervision of a physician or midwife.

During pregnancy, the vaginal tablet should be inserted without using an applicator.

Breast-feeding:

There are no data on the excretion of clotrimazole into human milk. However, systemic absorption is minimal after administration and is unlikely to lead to systemic effects. Clotrimazole may be used during lactation.

4.7 Effects on ability to drive and use machines

No or negligible influence.

4.8 Undesirable effects

Frequency not known. As the listed undesirable effects are based on spontaneous reports, assigning accurate frequency of occurrence for each is not possible.

Immune system disorders:

Anaphylactic reaction, angioedema, hypersensitivity.

Vascular disorder:

syncope, hypotension.

Respiratory, thoracic and mediastinal disorders:

dyspnea.

Gastrointestinal disorders:

abdominal pain, nausea

Skin and Subcutaneous Tissue Disorders:

Rash, urticaria, pruritus.

Reproductive system and breast disorders:

Vaginal exfoliation, vaginal discharge, vaginal haemorrhage, vulvovaginal discomfort, vulvovaginal erythema, vulvovaginal burning sensation, vulvovaginal pruritus, vulvovaginal pain.

General disorders and administration site conditions: application site irritation, oedema, pain.

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 to the appropriate authorities.

4.9 Overdose

No risk of acute intoxication is seen as it is unlikely to occur following a single vaginal or dermal application of an overdose (application over a large area under conditions favourable to absorption) or inadvertent oral ingestion. There is no specific antidote.

In the event of accidental oral ingestion, gastric lavage is rarely required and should be considered only if clinical symptoms of overdose become apparent (e.g. dizziness, nausea or vomiting). Gastric lavage should be carried out only if the airway can be protected adequately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Gynaecological anti-infectives and antiseptics - imidazole derivatives **ATC code:** G01AF02

Mechanism of action

Azoles (e.g. clotrimazole) are usually recommended for the local treatment of vulvovaginal candidosis that is characterized by vulvovaginal symptoms such as itching, burning, discharge, redness, swelling and soreness.

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, moulds etc.

Under appropriate test conditions, the MIC values for these types of fungi are in the region of less than 0.062-8.0 µg/ml substrate. The mode of action of clotrimazole is fungistatic or fungicidal depending on the concentration of clotrimazole at the site of infection. *In-vitro* activity is limited to proliferating fungal elements; fungal spores are only slightly sensitive.

Primarily resistant variants of sensitive fungal species are very rare; the development of secondary resistance by sensitive fungi has so far only been observed in very isolated cases under therapeutic conditions.

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 levels of clotrimazole up to 72 hours after vaginal application of a 100mg dose were less than 10 ng/ml, demonstrating that clotrimazole applied intravaginally is rapidly metabolised and does not lead to measurable systemic effects or side effects.

Binding of clotrimazole to blood serum proteins is about 98% in the undiluted serum, due to its highly hydrophobic properties.

Clotrimazole is metabolised in the liver via oxidation and degradation of the imidazole cycle (desamination, O-desalkylation). Thus inactive hydroxy derivatives occur. These agents are mainly excreted via the gallbladder with the faeces.

The elimination half-life of clotrimazole is 3.5-5 hours.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of repeated dose toxicity, genotoxicity and carcinogenicity.

Clotrimazole was not teratogenic in reproductive toxicity studies in mice, rats and rabbits. In rats high oral doses were associated with maternal toxicity, embryotoxicity, reduced foetal weights and decreased pup survival.

In rats clotrimazole and/or its metabolites were secreted into milk at levels higher than in plasma by a factor of 10 to 20 at 4 hrs after administration, followed by a decline to a factor of 0.4 by 24 hrs.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Clotrimazole powder
Lactose monohydrate
Corn starch
Corn starch for paste

Incompatibilities

None known.

6.2 Shelf life

48 months

6.3 Special precautions for storage

Store below 30°C in tight container protected from light and moisture. Keep this medicine out of sight and reach of children.

6.4 Nature and contents of container and special equipment for use, administration or implantation

Original package contains 6 vaginal tablets in an aluminium foil blister with a disposable applicator.

6.5 Special precautions for disposal and other handling

The vaginal tablet is to be taken out of the aluminium package and inserted into the holder of the disposable applicator.

The disposable applicator is to be inserted into the vagina as high as possible.

By carefully pushing the inner plunger as far as it will go, the tablet is placed in the vagina.

After usage, the disposable applicator is to be removed from the vagina and safely disposed of, out of the reach of children.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT/MANUFACTURER

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