PACKAGE INSERT TEMPLATE FOR CLOTRIMAZOLE VAGINAL TABLET

Brand or Product Name
[Product name] Vaginal Tablet 100mg
[Product name] Vaginal Tablet 500mg

Name and Strength of Active Substance(s)
Clotrimazole 100mg
Clotrimazole 500mg

Product Description
[Visual description of the appearance of the product (eg colour, viscosity etc)
eg Biconvex white-pale yellow pessary with 1 rounded end

Pharmacodynamics
Clotrimazole is an imidazole derivative with a broad spectrum of antimycotic activity.

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 primarily 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.

In addition to its antimycotic action, clotrimazole also acts on gram-positive microorganisms (Streptococci /Staphylococci / Gardnerella vaginalis), and gram-negative microorganisms (Bacteroides). In vitro clotrimazole inhibits the multiplication of Corynebacteria and grampositive cocci - with the exception of Enterococci - in concentrations of 0.5-10 µg/ml substrate. 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.

Pharmacokinetics
Pharmacokinetic investigations after vaginal application have shown that only a small amount of clotrimazole (3-10%) is absorbed.

Due to the rapid hepatic metabolization 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, suggesting that clotrimazole applied intravaginally is unlikely to lead to measurable systemic effects or side effects.

Indication
Infections of the genital region (vaginitis) caused by fungi (usually Candida) and superinfections caused by Clotrimazole-sensitive bacteria.

Recommended Dosage
1 vaginal tablet to be introduced each evening on 6 successive days. Alternatively, 2 vaginal tablets may be inserted into the vagina at bedtime for 3 consecutive nights. The vaginal tablet 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. Clotrimazole vaginal tablets need moisture in the vagina to dissolve

completely, otherwise undissolved pieces of the vaginal tablet might crumble out of the vagina. To prevent this it is important to insert the medication as deeply as possible into the vagina at bedtime. Should the vaginal tablet not dissolve completely within one night the use of a vaginal cream should be considered.

If symptoms persist for more than 7 days the patient may have a medical condition that requires treatment by a doctor. The treatment can be repeated if necessary, however, recurrent infections may indicate an underlying medical cause. Patient should seek medical advice if symptoms return within 2 months. lf the labia and adjacent areas are simultaneously infected, local treatment with an external cream should also be given in addition to the intravaginal treatment (combination treatment). The sexual partner should also undergo local treatment if symptoms, e.g. pruritus, inflammation, etc. are present. Treatment during the menstrual period should not be performed. 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. Avoidance of vaginal intercourse is recommended in case of vaginal infection and while using this product the partner could become infected.

During pregnancy, the vaginal tablets should be used and should be inserted without using an applicator.

Not for use in children under 16.

Mode of Administration
Intravaginal

Contraindications
Hypersensitivity to clotrimazole or to any other component of the product.

Warnings and Precautions
If the patient has a fever (temperature of 38°C or above), lower abdominal pain, back pain, foul smelling vaginal discharge, nausea, vaginal haemorrhage, and/or associated shoulder pain the patient should consult a doctor.

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.

Effects on the ability to drive and use machines
Clotrimazole vaginal tablet has no or negligible influence on the ability to drive or use machinery.

Interactions with Other Medicaments
Concomitant medication with vaginal clotrimazole and oral tacrolimus might lead to increased tacrolimus plasma levels and similarly with sirolimus. Patients should be thoroughly monitored for symptoms of tacrolimus or sirolimus overdosage, if necessary by determination of the respective plasma levels.

Statement on Usage During Pregnancy and Lactation
Pregnancy
Experimental and clinical investigations give no indication that clotrimazole has any harmful effects on the mother and child when administered during pregnancy. Sanitation of the birth canal should be ensured particularly during the last 4-6 weeks of pregnancy. During pregnancy the clotrimazole vaginal tablet should be inserted without using an applicator. Administration during the first trimester of pregnancy should be used with clear indication.

Lactation
Available pharmacodynamic/toxicological data in animals have shown excretion of clotrimazole/ metabolites in milk. Breast-feeding should be discontinued during treatment with clotrimazole.

Adverse Effects / Undesirable Effects
Immune system disorders: allergic reaction (syncope, hypotension, dyspnea, urticaria)

Reproductive system and breast disorders: genital peeling, pruritis, rash, edema, erythema, discomfort, burning, irritation, pelvic pain & vaginal haemorrhage.

Gastrointestinal disorders: abdominal pain.

Overdose and Treatment
No risk of acute intoxication is seen as it is unlikely to occur following a single vaginal application of an overdose. There is no specific antidote.

Storage Conditions
[eg Store below….°C]

Dosage Forms and Packaging Available
[Packaging type & pack size]

Name and Address of Manufacturer
[Name & full address of manufacturer]

Name and Address of Marketing Authorization Holder
[Name & full address of marketing authorization holder]

Date of Revision of Package Insert
[day/month/year]