

Summary of Product Characteristics

1. Name of the Medicinal Product

Clotrimazole Vaginal Inserts USP 500mg

2. Qualitative and Quantitative Composition

For list of excipients, see section 6.1

3. Pharmaceutical form

Vaginal Tablets.

4. Clinical particulars

4.1 Therapeutic indication

Clotrimazole 500mg Vaginal Tablets are recommended for the treatment of candidal vaginitis.

4.2 Posology and method of administration

The vaginal tablet should be inserted into the vagina, as high as possible, using the applicator provided.

Adults: One 500mg Vaginal Tablets should be inserted at night. Using the applicator provided, the vaginal tablet should be inserted as high as possible into the vagina. This is best achieved when lying back with legs bent up. A second treatment may be carried out if necessary.

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

Generally:

Treatment during the menstrual period should not be performed due to the risk of the vaginal tablet 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: As the product is used with an applicator, paediatric usage is not recommended.

4.3 Contraindications

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

4.4 Special warning and precaution 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 Tablets, 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 Tablets 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 500mg Vaginal Tablets. Clotrimazole 500mg Vaginal Tablets 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.

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 vaginal clotrimazole 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 overdosage, if necessary by determination of the respective plasma levels.

4.6 Fertility, 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. 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 Tablets should be inserted without using an applicator.

Lactation

Available pharmacodynamic/toxicological data in animals have shown excretion of clotrimazole/metabolites in milk after intravenous administration. A risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from clotrimazole therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines

The medication has no or negligible influence on the ability to drive or use machinery.

4.8 Undesirable effect

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

Immune system disorders: allergic reaction (syncope, hypotension, dyspnea, urticaria, pruritus).

Reproductive system and breast disorders: genital peeling, pruritus, rash, oedema, erythema, discomfort, burning, irritation, pelvic pain, vaginal haemorrhage.

Gastrointestinal disorders: abdominal 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.

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.

However, in the event of accidental oral ingestion, routine measures such as gastric lavage should be performed 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 antiinfectives and antiseptics – imidazole derivatives

ATC code: G01A F02

Mechanism of Action

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 concentrations of clotrimazole after vaginal application of a 500mg dose were less than 10 ng/ml, reflecting that clotrimazole applied intravaginally does not lead to measurable systemic effects or side effects.

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 fetal 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

Lactose monohydrate, Maize Starch, Methyl paraben, Propyl paraben, Sodium Starch Glycolate, Talc, Magnesium stearate, Colloidal Silicon Dioxide, Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

48 months

6.4 Special precaution for storage

Store below 30°C. Protect from moisture and light

6.5 Nature and contents of container

A printed carton containing a leaflet, an applicator packed in polypropylene bag and a printed aluminium strip containing 1 white biconvex vaginal uncoated tablet with G logo on one side and plain on other side

6.6 Special precautions for disposal and other handling

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

7. Marketing authorization holder

Glenmark Pharmaceuticals Limited

8. Marketing authorization number (s)

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9. Date of first authorization/renewal of the authorization

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10. Date of revision of the text

Aug 2020