National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) TEMPLATE

1. NAME OF THE MEDICINAL PRODUCT

Clotrimazole 500mg Vaginal Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains clotrimazole 500mg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solid-Vaginal Tablet

4. Clinical particulars

4.1 Therapeutic indications

1. Clotrimazole vaginal tablets are indicated for the treatment of candidal vaginitis.
2. The treatment consists of one vaginal tablet to be inserted at night, using the applicator provided.

4.2 Posology and method of administration

One 500mg tablet should be placed into the holder of the applicator. The applicator should be inserted as high as possible into the vagina. This is bestachieved 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 shouldthen be removed from the vagina and disposed of carefully, out of the reach of children. A second treatment may be carried out if necessary.Treatment should not be performed during menstrual period due to the risk of the tablets being washed out by the menstrual flow. The treatment shouldbe 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.

Do not use this product to treat nail or scalp infections.

4.4 Special warnings and precautions for use

None Known

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.

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 is a 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 topical 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.

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

Clotrimazole has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

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

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

Skin and subcutaneous tissue disorders: blisters, discomfort/pain, oedema, erythema, irritation, peeling/exfoliation, pruritus, rash, stinging/burning.

Reporting of suspected adverse reactions

Reporting suspected adverse reaction after authorization 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 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, gastric lavage is rarely required and should be considered only if a life-threatening amount of clotrimazole has been ingested within the preceding hour or 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 Pharmacodynamics properties

Pharmacotherapeutic group: Antifungals for topical use – imidazole and triazole derivatives
ATC Code: D01A C01

Mechanism of Action
Clotrimazole acts against fungi by inhibiting ergosterol synthesis. Inhibition of ergosterol synthesis leads to structural and functional impairment of the 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 gram-positive 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.

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 tothe rapid hepatic metabolism of absorbed clotrimazole into pharmacologically inactive metabolites the resulting peak plasma levels of clotrimazole up to72 hours after vaginal application of a 500mg dose were less than 10 ng/ml, demonstrating that clotrimazole applied intravaginally is rapidlymetabolised 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 hydroxyderivatives occur. These agents are mainly excreted via the gallbladder with the faeces.

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

Microcrystalline cellulose, Pregelatinised maize starch, Sodium hydrogen carbonate, Stearic acid, Lactose, Polysorbate, Magnesium stearate, Maize starch, Colloidal silicon dioxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

48 Months

6.4 Special precautions for storage

Store below 30°C. Protect from light.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

Original package contains 1 vaginal tablet with a disposable applicator. Each vaginal tablet is packed in an aluminium foil blister

6.6 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. Unused product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT

Glenmark Pharmaceutical Nigeria Limited,
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8. MANUFACTURER

M/S Glenmark Pharmaceutical Ltd,
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9. NAFDAC REGISTRATION NUMBER(S)

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