Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Clotrimazole Vaginal Tablets BP 100 mg

2. Qualitative and quantitative composition

Each uncoated vaginal tablet contains:
Clotrimazole BP 100 mg
Excipients QS
For excipients see section 6.1.

3. Pharmaceutical form

Vaginal Tablet. A white, bullet concave, biconvex, uncoated tablet having one side embossed with VG & plain on other side.

4. Clinical particulars

4.1 Therapeutic indications

Clotrimazole 100mg Vaginal Tablets are recommended for the treatment of candidal vaginitis.

4.2 Posology and method of administration

These tablets should be inserted into the vagina, as high as possible, using the applicator provided. This is best achieved when lying back with legs bent up.

Adults:

Two tablets should be inserted daily (preferably at night) for three consecutive days. Alternatively, one tablet may be inserted daily for six days, preferably at night. There is no separate dosage schedule for the elderly.

Clotrimazole 100mg Vaginal Tablets need moisture in the vagina in order to dissolve completely; otherwise, undissolved pieces of the tablet might crumble out of the vagina. Pieces of undissolved tablet 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.

Generally:

Treatment during the menstrual period should not be performed due to the risk of the 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:

Not for use in children under 16.

4.3 Contraindications

Hypersensitivity to clotrimazole or any other ingredient in this medicine

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 100mg Vaginal Tablets, medical advice

must be sought if any of the following are applicable:
- more than two infections of candidal vaginitis in the last six months.
- previous history of a 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 100mg Vaginal Tablets should not be used if the patient has any of the following symptoms whereupon 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 100mg Vaginal Tablets. The 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

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 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 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 tablet 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 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: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

- **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 anti-infectives 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 8.0µg/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

Magnesium Stearate, Purified Talc, Crospovidone, Croscarmellose Sodium, Hydroxypropyl Cellulose, Colloidal Anhydrous Silica, Lactose, Mannitol, Microcrystalline Cellulose and Dummy.

6.2 Incompatibilities

Not applicable.

6.3 Shelf-Life

36 months

6.4 Special Precautions for storage

Stored at a temperature not exceeding 30°C, in a cool and dark place, protect from direct sunlight.

6.5 Nature and Content of container

1 x 6 pack: 6 tablets packed in a blister and such 1 blister is packed in single carton along with pack insert and applicator.

6.6 Special precautions for disposal and other handling

Not applicable.

7. Marketing Authorization Holder

GALAXY PHARMACEUTICAL LTD.
1st Floor, Doctors Park, 3rd Parkland Avenue,
P.O.BOX 39107 - 00623, Nairobi (Kenya)

8. Marketing Authorization Number

CTD8499/18675

9. Date of first authorization/renewal of the authorization

22/06/2023

10. Date of revision of the text