SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Clotrimazole 500 mg Vaginal Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vaginal tablet contains clotrimazole 500 mg.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Vaginal tablet

White coloured, Oblong shaped Uncoated tablets having “500” embossed on one side and Plain on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Clotrimazole vaginal tablets are indicated for the treatment of candidal vaginitis.

4.2 Posology and method of administration

Posology:

The treatment consists of one vaginal tablet to be inserted in the evening.

Method of administration

Adults:

One 500mg vaginal tablet should be inserted as a single dose at night. Using the applicator provided, the tablet should be inserted as high as possible into the vagina. The vaginal tablet is placed into the holder of the applicator provided. The applicator is inserted into the vagina as deeply as comfortable. This is best achieved when lying on the back with the legs slightly bent. 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. 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 vaginal tablet might crumble out of the vagina. Pieces of undissolved vaginal tablet may be noticed by women who experience vaginal dryness. To help prevent this it is important that the vaginal tablet is inserted as high as possible into the vagina at bedtime.

As a matter of practicality the treatment should not be undertaken during menstruation. 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.

If the external symptoms of the disease (e.g. discharge, itching) have not subsided completely within three days after termination of therapy, treatment should be continued only after consulting the attending doctor.

Children:

Not for use in children under 16

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4.3 Contraindications

Hypersensitivity to clotrimazole 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:

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

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

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

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

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.

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 tablet and oral tacrolimus (FK506; 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

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.

Lactation:

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.

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.

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

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

The frequency of adverse events listed below is defined using the following convention: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000), not known (cannot be estimated from the available data).

Tabulated summary of adverse reactions

System Organ Class	**Frequency**	**Adverse reaction**
Reproductive system and breast disorders	Not known	vaginal exfoliation, vaginal discharge, vaginal haemorrhage, vulvovaginal discomfort, vulvovaginal erythema, vulvovaginal burning sensation, vulvovaginal pruritus, vulvovaginal pain.
Immune system disorders	Not known	allergic reaction (syncope, hypotension, dyspnea, urticaria, pruritus, anaphylactic reaction, angioedema, hypersensitivity)
Vascular disorder	Not known	syncope, hypotension
Respiratory, thoracic and mediastinal disorders	Not known	dyspnea
Gastrointestinal disorders	Not known	abdominal pain,

		Nausea
Skin and Subcutaneous Tissue Disorders	Not known	rash, urticaria, pruritus
General disorders and administration site conditions	Not known	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 via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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, routine measures such as gastric lavage should be performed only if clinical symptoms of overdose become apparent (e.g. dizziness, nausea or vomiting). It should be carried out only if the airway can be protected adequately.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Gynaecological antiinfectives and antiseptics – imidazole derivatives

ATC Code: G01A F02

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 microgram/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

Adipic acid

Pregelatinised Maize Starch

Maize Starch

Microcrystalline Cellulose

Sodium Hydrogen Carbonate

Magnesium Stearate

Stearic Acid

Colloidal Silicon Dioxide

Polysorbate 80

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

5 Years

6.4 Special precautions for storage

Store at room temperature below 25°C. Store in the original package to protect from moisture.

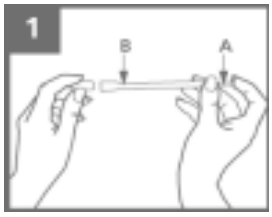
6.5 Nature and contents of container

Each vaginal tablet is packed in an aluminum foil blister. The blister pack along with leaflet and applicator are enclosed in a carton.

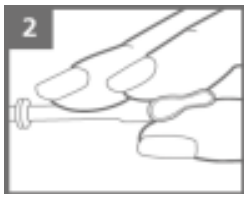
6.6 Special precautions for disposal and other handling

Wash your hands before handling the applicator and the foil blister pack and again

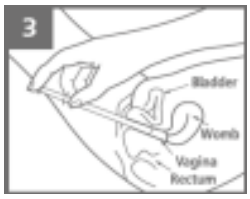
afterwards when you have used the applicator.



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



The disposable applicator is to be inserted into the vagina as deep as possible. By carefully pushing the inner plunger as far as it will go, the vaginal 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 MARKETING AUTHORISATION HOLDER

Special Concept Development (UK) Limited T/A RxFarma
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Watford, Hertfordshire,
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8 MARKETING AUTHORISATION NUMBER(S)

PL 36722/0140

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11/05/2023

10 DATE OF REVISION OF THE TEXT

28/05/2026