REGAL PHARMACEUTICALS LIMITED
NAIROBI, KENYA

SUMMARY OF PHARMACEUTICAL CHARACTERISTICS (SmPC)

UNISTEN COMBI PACK QUERY RESPONSE
REF. NO.: DFAR/HMDAR/018/FDA/2023
RWANDA FOOD AND DRUGS AUTHORITY (RFDA)

UNISTEN COMBI PACK

Summary of Product Characteristics

Contents

1. Name of The Medicinal Product

Unisten combi pack

2. Qualitative and Quantitative Composition

The Unisten combi pack contains 1 tablet and 20gms cream.

Each tablet contains clotrimazole 500mg.

Excipient with known effect: Each tablet contains lactose.

Each gram of cream contains Clotrimazole 1% w/w

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Vaginal tablet

Bullet shaped tablets impressed UNISTEN V1 on one side and REGAL on the other side, free from visible impurities.

Cream

A white thick mass, free from visible impurities

4. Clinical particulars

4.1 Therapeutic indications

Unisten V-1 tablets are indicated for the treatment of C*andida vaginitis.*

The Unisten cream is indicated for:

(i) All dermatomycoses due to moulds and other fungi, (e.g. *Trichophyton* species).

(ii) All dermatomycoses due to yeasts (*Candida* species).

(iii) Skin diseases showing secondary infection with these fungi.

(iv) Candida nappy rash, vulvitis and balanitis.

4.2 Posology and method of administration

Posology

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

Unisten Cream should be applied thinly 2 or 3 times daily and rubbed in gently.

Method of administration

- The tablet is placed into the holder of the applicator provided. The applicator is inserted into the vagina as deeply as is 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.

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

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.

- Unisten Cream should be applied thinly 2 or 3 times daily and rubbed in gently. Treatment should be continued for at least one month for dermatophyte infections and at least two weeks for candidal infections.

  There is no separate dosage schedule for the young or elderly.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

4.4 Special warnings and precautions for use
Unisten cream contains cetostearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis).

Before using Unisten V-1 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 imidazole's or other vaginal antifungal products.

Unisten V-1 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 Unisten V-1 tablet. Unisten V-1 tablet can be used again if the candida infection returns after 7 days. However, if the candida 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
Clotrimazole reduces the efficacy of other drugs which are used for the treatment of fungal diseases (amphotericin and other polyene antibiotics, e.g. nystatin).

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 Unisten V-1 tablet and oral tacrolimus (FK-506; immunosuppressant) might lead to increased tacrolimus plasma levels. 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:

In animal studies, 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.

There is limited amount of data from the use of clotrimazole in pregnant women.

Clotrimazole can be used during pregnancy, but only under the supervision of a physician or midwife.

During pregnancy, the vaginal tablet can be inserted without using an applicator.

Breast-feeding:

Available pharmacodynamic/toxicological data in animals have shown excretion of clotrimazole/metabolites in milk after intravenous administration (see section 5.3). 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
This 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.

Immune system disorders:

allergic reaction (syncope, hypotension, dyspnea, urticaria, pruritus)

Rarely patients may experience local mild burning or irritation immediately after applying the vaginal tablet. Very rarely, the patient may find this irritation intolerable and stop treatment. Hypersensitivity reactions may occur.

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. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard

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. Pharmacological properties

5.1 Pharmacodynamic properties
ATC Code: G01A F02

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

The antimycotic effect of clotrimazole is primarily fungistatic, and at high concentrations also fungicidal. Clotrimazole is only effective against proliferating fungi; fungal spores are only slightly sensitive, in-vitro; Current knowledge indicates that the antimycotic effect of clotrimazole is due to inhibition of 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.

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
Absorption of Clotrimazole from the vagina following administration as a vaginal tablet is 3-10%. Fungicidal concentrations of clotrimazole are found in the vaginal fluid up to 3 days after the application of one 500 mg vaginal tablet. In contrast plasma levels of clotrimazole up to 72 hours after application are lower than 0.01 μg/ml, demonstrating that clotrimazole is rapidly metabolised 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 hydroxy derivatives occur. These agents are mainly excreted via the gallbladder with the faeces.

The elimination half-life of clotrimazole is 3.5-5 hours.

5.3 Preclinical safety data
Toxicity studies in rats, dogs and monkeys showed changes in the liver and adrenal glands after long term administration. However, these changes were reversible after administration ended.

There is no evidence of mutagenicity or teratogenicity in animals, and experience of topical application in pregnant women gives no evidence of embryotoxic or foetotoxic effects.

6. Pharmaceutical particulars

6.1 List of excipients

- Unisten V-1 tablet

Lactose
Starch
Sodium starch Glycolate type A
Magnesium stearate
Starch
Gelatin

- Unisten cream

Chlorocresol
Cetomacrogol
Emulsifying wax
Liquid Paraffin
Propylene glycol
Polysorbate 80 (Tween 80)
Disodium Hydrogen Phosphate Dodecahydrate
Citric Acid
White soft paraffin

6.2 Incompatibilities
None known.

6.3 Shelf life
36 months

6.4 Special precautions for storage
Store at room temperature below 30°C. Store in the original package.in order to protect from moisture.

7. Registrant

Name and address of holder of a registration.

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8. Manufacturer

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