REGAL PHARMACEUTICALS LIMITED
NAIROBI, KENYA

SUMMARY OF PHARMACEUTICAL CHARACTERISTICS (SmPC)

UNISTEN CREAM QUERY RESPONSE
REF. NO.: DFAR/HMDAR/017/FDA/2023
RWANDA FOOD AND DRUGS AUTHORITY (RFDA)

Contents

Summary of Product Characteristics

UNISTEN CREAM

1. Name of the medicinal product
Unisten Cream
2. Qualitative and quantitative composition
Clotrimazole 1% w/w. For excipients, see 6.1.
3. Pharmaceutical form
Cream. A thick white mass, free from visible impurities.
4. Clinical particulars
4.1 Therapeutic indications For the treatment of:

(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) Candidal nappy rash, vulvitis and balanitis.

4.2 Posology and method of administration

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.

If the feet are infected, they should be washed and dried, especially between the toes, before applying the cream.

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

This product contains cetostearyl alcohol, which may cause local skin reactions (e.g. contact dermatitis).

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 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 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 (see section 5.3). 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 (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.

Clotrimazole cream 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 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 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 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: Antifungals for topical use – imidazole and triazole derivatives

ATC Code: **D01AC01**

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 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 dermal application have shown that clotrimazole is minimally absorbed from the intact or inflamed skin into the human blood circulation. The resulting peak serum concentrations of clotrimazole were below the detection limit of 0.001 µg/ml, suggesting that clotrimazole applied topically is unlikely to 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
Chlorocresol
Cetomacrogol
Emulsifying wax
Liquid Paraffin
Propylene glycol
Polysorbate 80 (Tween 80)
Disodium Hydrogen Phosphate Dodecahydrate
Citric Acid
White soft paraffin

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Store below 30°C, in a dry place. Protect from light. Keep out of reach of children.

7. Registrant

Name and address of holder of a registration.

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Registration number. H98/086

Date of first registration- 03/19/1998

8. Manufacturer

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