## 1. Summary of Product Characteristics

**Invented Name of the Medicinal Product**

**KETORAL CREAM**

Ketoconazole Cream 2%

**Strength**

Ketoconazole USP 20 mg

**Dosage Form**

Topical Semi Solid Dosage Form

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gm contains:

Ketoconazole USP…….20 mg

Cream Base……. q.s.

## 3. PHARMACEUTICAL FORM

White color smooth Cream.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

For the treatment of the following mycotic infections of the skin: tinea pedis, tinea cruris and candidal intertrigo.

### 4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Ketoconazole cream is for use in adults.

For the treatment of tinea pedis (athlete's foot) and tinea cruris (dhobie itch) and candidal intertrigo (sweat rash).

For tinea pedis, Ketoconazole Cream should be applied to the affected areas twice daily. The usual duration of treatment for mild infections is 1 week. For more severe or extensive infections (eg involving the sole or sides of the feet), treatment should be continued for 2–3 days after all signs of infection have disappeared to prevent relapse.

For tinea cruris and candidal intertrigo, apply cream to the affected areas once or twice daily until 2-3 days after all signs of infection have disappeared to prevent relapse. Treatment for up to 6 weeks may be necessary. If no improvement in symptoms is experienced after 4 weeks treatment, a doctor should be consulted.
Method of administration: Topical use.

## 4.3 CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients listed.

## 4.4 WARNING AND PRECAUTIONS

Ketoconazole Cream is not for ophthalmic use.
To prevent a rebound effect after stopping a prolonged treatment with topical corticosteroids it is recommended to continue applying a mild topical corticosteroid in the morning and to apply Ketoconazole Cream in the evening, and to subsequently and gradually withdraw the steroid therapy over a period of 2-3 weeks.

## 4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

None known.

## 4.6 PREGNANCY AND LACTATION

There are no adequate and well-controlled studies in pregnant or lactating women. To date, no other relevant epidemiological data are available. Data on a limited number of exposed pregnancies indicate no adverse effects of topical ketoconazole on pregnancy or on the health of the foetus/newborn child. Animal studies have shown reproductive toxicity at doses that are not relevant to the topical administration of ketoconazole.

Plasma concentrations of ketoconazole are not detectable after topical application of Ketoconazole Cream to the skin of non-pregnant humans (See Pharmacokinetic properties. There are no known risks associated with the use of Ketoconazole Cream in pregnancy or lactation.

## 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

None.

## 4.8 UNDESIRABLE EFFECTS

The safety of ketoconazole cream was evaluated in 1079 subjects who participated in 30 clinical trials. Ketoconazole cream was applied topically to the skin.

Based on pooled safety data from these clinical trials, the most commonly reported (≥1% incidence) ADRs were (with % incidence): application site pruritus (2%), skin burning sensation (1.9%), and application site erythema (1%). Including the above-mentioned adverse drug reactions (ADRs), the following table displays ADRs that have been reported with the use of ketoconazole cream from either clinical trial or postmarketing experiences. The displayed frequency categories use 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 clinical trial data). | | |
| **System Organ Class** | **Adverse Drug Reactions** | | |
| | **Frequency Category** | | |
| | **Common** (≥1/100 to <1/10) | **Uncommon** (≥1/1,000 to <1/100) | **Not Known** |
| **Immune System Disorders** | | Hypersensitivity | |
| **Skin and Subcutaneous Tissue Disorders** | Skin burning sensation | Bullous eruption<br>Dermatitis contact<br>Rash<br>Skin exfoliation<br>Sticky skin | Urticaria |
| **General Disorders and** | Application site | Application site | |

| | | | |
|---|---|---|---|
| **Administration Site Conditions** | erythema<br>Application site pruritus | bleeding<br>Application site discomfort<br>Application site dryness<br>Application site inflammation<br>Application site irritation<br>Application site paraesthesia<br>Application site reaction | |

## 4.9 OVERDOSE

Topical application

Excessive topical application may lead to erythema, oedema and a burning sensation, which will disappear upon discontinuation of the treatment.

Ingestion In the event of accidental ingestion, supportive and symptomatic measures should be carried out.

# 5. PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Imidazole and triazole derivatives; ATC code: D01 AC08

Ketoconazole has a potent antimycotic action against dermatophytes and yeasts. Ketoconazole cream acts rapidly on the pruritus, which is commonly seen in dermatophyte and yeast infections. This symptomatic improvement often occurs before the first signs of healing are observed.

A study in 250 patients has shown that application twice daily for 7 days of ketoconazole 2% cream vs clotrimazole 1% cream for 4 weeks on both feet demonstrated efficacy in patients with tinea pedis (athlete's foot) presenting lesions between the toes.

The primary efficacy endpoint was negative microscopic KOH examination at 4 weeks. Ketoconazole 2% treatment showed equivalent efficacy to 4 weeks clotrimazole 1% treatment. There was no evidence of relapse following treatment with ketoconazole cream at 8 weeks.

### 5.2 Pharmacokinetic properties

Plasma concentrations of ketoconazole were not detectable after topical administration of ketoconazole cream in adults on the skin. In one study in infants with seborrhoeic dermatitis (n = 19), where approximately 40 g of ketoconazole cream was applied daily on 40 % of the body surface area, plasma levels of ketoconazole were detected in 5 infants, ranging from 32 to 133 ng/mL.

### 5.3 Preclinical safety data

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

| |
|---|
| White Soft Paraffin |
| Cetostearyl Alcohol |
| Cetomacrogol –1000 |
| Light Liquid Paraffin |
| Chlorocresol |
| Propylene Glycol |
| Propyl Paraben |
| Purified Water |

**6.2 Incompatibilities:** Not applicable.

**6.3 Shelf life:** 36 Months.

**6.4 Special precautions for storage:** Store below 30°C. Protected from light.

**6.5 Nature and contents of container**

Available in 30 gm tube in monocarton along with insert & such 10 monocarton in an outer carton.

**6.6 Special precautions for disposal and other Special handling**

None

**7. Marketed by:**

**EMBASSY**

**PHARMACEUTICAL & CHEMICALS LTD.**

41, Ademola Street, South West Ikoyi,

Lagos, Nigeria.

**8. Manufactured by:**

**M/S. YASH MEDICARE PVT. LTD.**

Nr. Sabar Dairy, Talod Road, Po. Hajipur,

Ta. Himatnagar-383 006, Gujarat, India.