

## 1 NAME OF THE MEDICINAL PRODUCT

SKINFIX CREAM 20 GM (KETOCONAZOLE CREAM BP 2% w/w)

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gm contains:

Ketoconazole BP ..... 2% w/w

Cream Base.....QS

| Sr. No. | Ingredients            | Specification | Label claim (in %w/w) | Over-ages added (in %) | Qty./ 20 g Tubes (in g) | Qty./ Batch (in kg) | Reason for inclusion             |
|---------|------------------------|---------------|-----------------------|------------------------|-------------------------|---------------------|----------------------------------|
| 1.      | Ketoconazole*          | BP            | 2 %                   | ---                    | 0.84                    | 3.15                | Active Pharmaceutical Ingredient |
| 2.      | White Soft Paraffin    | BP            | --                    | --                     | 6.4                     | 24                  | Emollient                        |
| 3.      | Cetostearyl Alcohol    | BP            | --                    | --                     | 4                       | 15.00               | Emulsion stabilizer              |
| 4.      | Cetomacrogol 1000      | BP            | --                    | --                     | 1.00                    | 3.75                | Non-Ionic Emulsifying agent      |
| 5.      | Methyl Hydroxybenzoate | BP            | --                    | --                     | 0.003                   | 0.225               | Antimicrobial Preservative       |
| 6.      | Propyl Hydroxybenzoate | BP            | --                    | --                     | 0.022                   | 0.075               | Antimicrobial Preservative       |
| 7.      | Di-sodium Edetate      | BP            | --                    | --                     | 0.04                    | 0.15                | Chelating agent                  |
| 8.      | Propylene Glycol       | BP            | --                    | --                     | 0.09                    | 9.00                | Co-solvent                       |
| 9.      | Glycerol               | BP            | --                    | --                     | 0.09                    | 9.00                | Solvent                          |
| 10.     | Light Liquid Paraffin  | BP            | --                    | --                     | 0.75                    | 3.75                | Emollient                        |
| 11.     | Purified Water         | BP            | --                    | --                     | Q.S.                    | Q.S.                | Vehicle                          |

Cream Base ..... q.s.

## 3 PHARMACEUTICAL FORMS

Topical Cream

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indication.

The topical application of SKINFIX is used in the treatment of dermatophyte infections of the skin such as Tinea corporis, Tinea cruris, Tinea manus and Tinea pedis infections due to Trichophyton spp, Microsporon spp and Epidermophyton spp.

SKINFIX cream is also indicated for the treatment of cutaneous candidosis (including vulvitis), tinea (pityriasis) versicolor and seborrhoeic dermatitis caused by Malassezia (previously called Pityrosporum) spp.

#### **4.2 Posology and method of administration.**

SKINFIX cream is for use in adults.

##### Tinea pedis:

SKINFIX 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 until a few days after all signs and symptoms have disappeared in order to prevent relapse.

For other infections:

SKINFIX cream should be applied to the affected areas once or twice daily, depending on the severity of the infection.

The treatment should be continued until a few days after the disappearance of all signs and symptoms. The usual duration of treatment is: Tinea versicolor 2–3 weeks, Tinea corporis 3–4 weeks.

The diagnosis should be reconsidered if no clinical improvement is noted after 4 weeks. General measures in regard to hygiene should be observed to control sources of infection or reinfection.

Seborrhoeic dermatitis is a chronic condition and relapse is highly likely.

Method of administration: Cutaneous administration.

Paediatrics

There are limited data on the use of SKINFIX cream in paediatric patients.

#### **4.3 Contraindications**

SKINFIX cream is contra-indicated in patients with a known hypersensitivity to any of the ingredients or to Ketoconazole itself.

#### **4.4 Special warnings and precaution for use.**

SKINFIX cream is not for ophthalmic use.

If coadministered with a topical corticosteroid, 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 KETOCANAZOLE2% cream in the evening, and to subsequently and gradually withdraw the topical corticosteroid therapy over a period of 2- 3 weeks.

#### **4.5 Interaction with other medicinal product and other forms of interaction.**

No interaction studies have been performed.

#### **4.6 Pregnancy and Lactation.**

There are no adequate and well-controlled studies in pregnant or lactating women. 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 SKINFIX Cream to the skin of non-pregnant humans. (See Pharmacokinetic properties, section 5.2)  
There are no known risks associated with the use of SKINFIX Cream in pregnancy or lactation.

#### **4.7 Effect on the ability to drive and use machine.**

SKINFIX cream has no influence on the ability to drive and use machines.

#### **4.8 Undesirable effect.**

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 ( $\geq 1\%$  incidence) adverse reactions were (with % incidence): application site pruritus (2%), skin burning sensation (1.9%), and application site erythema (1%).

Including the above-mentioned adverse reactions, the following table displays adverse reactions 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 ( $\geq 1/10$ )

Common ( $\geq 1/100$  to  $< 1/10$ )

Uncommon ( $\geq 1/1,000$  to  $< 1/100$ )

Rare ( $\geq 1/10,000$  to  $< 1/1,000$ )

Very rare ( $< 1/10,000$ )

Not Known (cannot be estimated from the available clinical trial data).

| System Organ Class | Adverse Reactions  |
|--------------------|--------------------|
|                    | Frequency Category |
|                    |                    |

|   | <b>Common</b><br>(≥1/100 to 1/10)                      | <b>Uncommon</b><br>(≥1/1,000 to <1/100)   | <b>Not Known</b> |
|---|--|---|------------------|
| <b>Immune System Disorders</b>                              |  | Hypersensitivity  |                  |
| <b>Skin and Subcutaneous Tissue Disorders</b>               | Skin burning sensation                                 | Bullous eruption<br>Dermatitis<br>contact Rash<br>Skin exfoliation<br>Sticky skin   | Urticaria        |
| <b>General Disorders and Administration Site Conditions</b> | Application site erythema<br>Application site pruritus | Application site bleeding<br>Application site discomfort<br>Application site dryness<br>Application site inflammation<br>Application site irritation<br>Application site paresthesia<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.

#### ATC Code: D01AC08

Usually Ketoconazole cream acts rapidly on pruritus, which is commonly seen in dermatophyte and yeast infections, as well as skin conditions associated with the presence of *Malassezia* spp. This symptomatic improvement is observed before the first signs of healing are observed.

Ketoconazole, a synthetic imidazole dioxolane derivative, has a potent antimycotic activity against dermatophytes such as *Trichophyton* spp., *Epidermophyton floccosum* and *Microsporum* spp. and against yeasts, including *Malassezia* spp. and *Candida* spp. The effect on *Malassezia* spp. is particularly pronounced.

A study in 250 patients has shown that application twice daily for 7 days of KETOCANAZOLE 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. SKINFIX Cream 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 SKINFIX Cream in adults on the skin. In one study in infants with seborrhoeic dermatitis (n = 19), where approximately 40 g of SKINFIX cream was applied daily on 40% of the body surface area, plasma levels of SKINFIX 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    | BP |
| Cetostearyl Alcohol    | BP |
| Cetomacrogol 1000      | BP |
| Methyl Hydroxybenzoate | BP |
| Propyl Hydroxybenzoate | BP |
| Di-sodium Edetate      | BP |
| Propylene Glycol       | BP |
| Glycerol               | BP |
| Light Liquid Paraffin  | BP |
| Purified Water         | BP |

## **6.2 Incompatibilities**

unknown

## **6.3 Shelf-life**

36 months

## **6.4 Special precautions for storage**

Do not store above 30°C. Store in a dry place.

## **6.5 Nature and composition of immediate packaging**

20 gm cream packed in a printed lami tube. such 1 blister are packed in a carton along with a leaflet.

## **6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials**

None.

## **7 Manufacture / applicant**

### **MANUFACTURER**

#### **OHAD PHARMACEUTICALS PVT. LTD.**

Plot no. 222 & 223, GIDC, Industrial  
Estate, Palej – 392220, District:  
Bharuch, Gujarat, India.

### **MARKETED BY**

#### **EVERDESTINY PHARMACEUTICALS LTD.**

Lagos, Nigeria.