	<b>Module 1 Administrative and Product Information</b>
	<b>KANDORAL PLUS</b>
	<b>Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream</b>

### 1.3 PRODUCT INFORMATION

#### 1.3.1 Summary of Product Characteristics (SmPC)

##### 1. Name of the Medicinal Product

Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream.

##### 2. Qualitative and Quantitative Composition

###### Composition:

Ketoconazole USP ..... 1 % w/w

Clobetasol Propionate USP ..... 0.025 % w/w

Neomycin Sulfate USP ..... 0.50 % w/w

Vitamin E USP..... 1 % w/w

Cream Base..... Q.S.

##### 3. Pharmaceutical Form

Cream.

##### 4. Clinical Particulars

###### 4.1 Therapeutic Indications

Ketoconazole, Clobetasol Propionate and Neomycin Sulfate and Vitamin E Cream is indicated for the topical treatment of fungal infections of the skin including:

Tinea Cruris, Tinea Corporis, Tinea Manus, Tinea Pedis and so on.

###### 4.2 Posology and Method of Administration

Topical Application.


Apply to the affected area two or three times daily. Generally the duration of application depends on the type of infecting organism. Treat as below for the following:

Tinea Corporis: 2 Weeks

Tinea Cruris: 2 Weeks

Tinea Manus: 4 Weeks

Tinea Pedis: 4 Weeks

	<b>Module 1 Administrative and Product Information</b>
	<b>KANDORAL PLUS</b>
	<b>Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream</b>


#### **4.3 Contraindications**

Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream., is contraindicated in the patients with known hypersensitivity to any of its active ingredients. Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream. is for topical use only and cannot be used for internal or ophthalmic use. Vitamin E, Hypersensitivity to white soft paraffin, light liquid paraffin and anhydrous lanolin or to any of the excipients listed.

#### **4.4 Special Warnings and Precautions for Use**

Avoid contacting with eyes.

- Patients with tinea cruris avoid wearing underwear that is tight-fitting or made from synthetic materials (e.g. rayon, nylon). Instead wear loose-fitting, cotton underwear.
- Patient with tinea pedis avoids wearing socks made from wool or synthetic materials (for example rayon or nylon). Instead wear clean cotton socks and change them daily or more often if your feet sweat a lot. Wear well-ventilated shoes.
- If your skin problem does not improve within 2-4 weeks for cutaneous candidiasis, pityriasis versicolor, tinea corporis or tinea cruris or 4 weeks for seborrheic dermatitis or if it becomes worse check with your doctor.
- Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream. contains Clobetasol Propionate. If the product is administered for long term in large area or used with banding treatment it may induce the reversibility restraint of PHA axis. Cushing syndromes, hyperglycosenua, urinary glucose etc. can be occurred on some patients. So long term and large area using the product is not recommended. Banding treatments is not recommended too.
- The product can be used in the cockled skin of the face, armpit and groin under the supervision of a medical doctor.
- Combing with other skin infection the anti-infective drugs should be administrated. If the infection has not been controlled, stop using the product until the infection is controlled.

	<b>Module 1 Administrative and Product Information</b>
	<b>KANDORAL PLUS</b>
	<b>Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream</b>

- When the local ulcer and damage occur, Neomycin Sulfate is absorbed increasingly. The adverse reaction of aminoglycoside drug should be observed.

#### **4.5 Interaction with Other Medicinal Products and Other Forms of Interaction**

Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream. is a topical cream Hence, does not interacts with any other products.

Vitamin E: The absorption of topical minoxidil can be increased by concurrent topical soft paraffin. This could potentiate the hypotensive effects of vasodilators.

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

Pregnant and lactation women should be used with caution.

Large area and long term using is not recommended.

#### **4.7 Effects on Ability to Drive and Use Machines**

Not known.

#### **4.8 Undesirable Effects**

Erythema, burning, itch, sharp pain or other stimulus symptom, folliculitis, skin atrophy, capillarectais, etc are commonly seen.

- Skin dryness, pilosis polytrichis, striae atrophicae and infectious susceptibility increasing can be observed.


- Adrenocortical hyperfunction can be induced by long term using. The symptom includes pilosis polytrichia, acne, moon face, osteoporosis, etc.

- Allergic contact dermatitis can be seen on occasion.

Vitamin E:

Occasionally, hypersensitivity reactions, otherwise adverse effects are unlikely. Should this occur, use of the product should be discontinued.

Adverse events which have been associated with white soft paraffin, light liquid paraffin and anhydrous lanolin are given below, tabulated by system organ class and frequency. Frequencies are defined as: Very common ( $\geq 1/10$ ); Common ( $\geq 1/100$  and

	<b>Module 1 Administrative and Product Information</b>
	<b>KANDORAL PLUS</b>
	<b>Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream</b>


<1/10); Uncommon ( $\geq 1/1000$  and <1/100); Rare ( $\geq 1/10,000$  and <1/1000); Very rare (< 1/10,000); Not known (cannot be estimated from the available data). Within each frequency grouping, adverse events are presented in order of decreasing seriousness.

<b>System Organ Class</b>	<b>Frequency</b>	<b>Adverse Events</b>
Immune System Disorders	Not known	Hypersensitivity, Dermatitis allergic
Skin and Subcutaneous Tissue Disorders	Not known	Acne

#### **4.9 Overdose**

Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream., is well tolerated, no adverse effect has been observed in the event of over dosage.

Vitamin E cream is of low toxicity. If accidental ingestion occurs, conservative treatment only is required. There have been no reports of over dosage with use of this product.

	<b>Module 1 Administrative and Product Information</b>
	<b>KANDORAL PLUS</b>
	<b>Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream</b>

## 5. Pharmacological Properties

### 5.1 Pharmacodynamic Properties

The active ingredient of Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream. is Ketoconazole, a Pyrrolidone antifungal agent. It has extremely potent anti- mycotic actions against dermatophytes and yeasts (Candidiasis, Pityrosporum Sabour, Torulopsis, Cryptococcus), histoplasmosis capsulalum, eumycetes. However the product has weak inhibitory action to aspergillus, sporothrix schenckii, dermatiaceous fungi and mucor except for entomophyhorales.

Vitamin E Cream:


Vitamin E is a collective term used to describe 8 separate fat soluble antioxidants, most commonly alpha-tocopherol. Vitamin E acts to protect cells against the effects of free radicals, which are potentially damaging by-products of the body's metabolism. Vitamin E deficiency is seen in persons with abetalipoproteinemia, premature, very low birth weight infants (birth weights less than 1500 grams, or 3½ pounds), cystic fibrosis, and cholestasis and severe liver disease. Preliminary research suggests vitamin E may help prevent or delay coronary heart disease and protect against the damaging effects of free radicals, which may contribute to the development of chronic diseases such as cancer. It also protects other fat-soluble vitamins (A and B group vitamins) from destruction by oxygen. Low levels of vitamin E have been linked to increased incidence of breast and colon cancer.

### Mechanism of Action

**Ketoconazole:** It can selectively inhibit the cytochromes P-450 activity of fungi. Therefore, the biosynthesis of Ergosterol on the cell membrane inhibited.

**Clobetasol propionate:** It is a hormone of the cortex that is highly effective anti0inflammatory and cause capillary contraction.

**Neomycin sulfate:** It is external use aminoglycoside antibiotics, can treat local infection.

	<b>Module 1 Administrative and Product Information</b>
	<b>KANDORAL PLUS</b>
	<b>Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream</b>

#### **Vitamin E Cream:**

The mechanism of action for most of vitamin E's effects are still unknown. Vitamin E is an antioxidant, preventing free radical reactions with cell membranes. Though in some cases vitamin E has been shown to have pro-oxidant activity.

One mechanism of vitamin E's antioxidant effect is in the termination of lipid peroxidation. Vitamin E reacts with unstable lipid radicals, producing stable lipids and a relatively stable vitamin E radical. The vitamin E radical is then reduced back to stable vitamin E by reaction with acrobats or glutathione.

### **5.2 Pharmacokinetic Properties**

**Ketoconazole:** It is applied to the chest, back and buttocks of the healthy volunteers cannot be inspected in blood (Detectable Limit is less than 5 mg/ml) during the first 7 hours.


**Clobetasol Propionate:** It can be completely absorbed by dermal. The administered dose is metabolized, primarily in the liver and is excreted by kidney.

**Neomycin Sulfate:** It can be rarely absorbed by derma. However when the skin is ulcer and breakage it can be absorbed increasingly.

**Vitamin E:** Vitamin E is an antioxidant, preventing free radical reactions with cell membranes. Though in some cases vitamin E has been shown to have pro-oxidant activity. One mechanism of vitamin E's antioxidant effect is in the termination of lipid peroxidation.

### **5.3 Preclinical Safety Data**

Not known.

	<b>Module 1 Administrative and Product Information</b>
	<b>KANDORAL PLUS</b>
	<b>Ketoconazole, Clobetasol Propionate, Neomycin Sulfate and Vitamin E Cream</b>

## **6. Pharmaceutical Particulars**

### **6.1 List of Excipients**

Benzyl Alcohol, Cetostearyl Alcohol, Self-Emulsifying Glyceryl Monostearate, Cetomacrogol Emulsifying Wax, Silicone Oil, White Soft Paraffin, Light Liquid Paraffin, Methyl Paraben, Propyl Paraben, Propylene Glycol, Disodium Edetate, Sodium Acid Phosphate, Sodium Phosphate, Rose Flavor, Purified Water.

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf Life**

36 months

### **6.4 Special Precautions for Storage**

Store in cool and dry place, Protect from light.

### **6.5 Nature and Contents of Container**

1 KANDORAL PLUS (30 gm Lamitube) packed in inner carton with a packaging insert.

### **6.6 Special Precautions for Disposal and Other Handling**

Not applicable.