## 1. Name of the Medicinal Product

(a) Product Name : Fexoskin Cream
(b) Pharmaceutical Dosage Form : Cream

## 2. Quality and Quantitative Composition

(a) Qualitative Declaration, the active substance should be declared by its recommended INN. Accompanied by its salt or hydrate form if relevant.

**Composition:**
Each tube contains:

| | |
|---|---|
| Clotrimazole USP | 1.0%w/w |
| Betamethasone Dipropionate USP Eq. to Betamethasone | 0.05%w/w |
| Neomycin sulphate USP | 0.5%w/w |
| Preservative: | |
| Cream base | q.s. |

(b) Quantitative Declaration, the quantity of the active substance must be expressed per dosage unit

| Sr. No. | Name of the Materials | Specification | Label Claim | Qty/gm | Active/ Inactive |
|---|---|---|---|---|---|
| 1. | Clotrimazole | U.S.P. | 1.0% w/w | 10 mg | Active |
| 2. | Betamethasone Dipropionate Eq. to Betamethasone | U.S.P. | 0.05%w/w | 0.5 mg | Active |
| 3. | Neomycin sulphate | U.S.P. | 0.55w/w | 5.5 mg | Active |

## 3. Pharmaceutical Form Visual description of the appearance of the product (colour, markings, etc.) e.g.:

White Colour Semi Solid Cream Filled in Printed Lami Tube.

## 4. Clinical Particulars

### 4.1 Therapeutic Indications:

Fexoskin Cream is indicated in patients 17 years and older for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris and tinea corporis due to Epidermophyton floccosum, Trichophyton mentagrophytes, and Trichophyton rubrum. Effective treatment without the risks associated with topical corticosteroid use may be obtained using a topical antifungal agent that does not contain a corticosteroid, especially for non-inflammatory tinea infections. The efficacy of Fexoskin Cream for the treatment of infections caused by zoophilic dermatophytes (e.g., Microsporum canis) has not been established. Several cases of treatment failure of Fexoskin Cream in the treatment of infections caused by Microsporum canis have been reported. Neomycin sulfate is a broad –spectrum antibiotic agent effective against gram-

negative & gram-positive organisms, although it is not effective against Pseudomonas aeruginosa

**4.2 Posology and method of administration:**

**Posology**

Posology
Adults and children over the age of 12 years.

Paediatric population
Fexoskin Cream is not recommended for children under the age of 12 years

**Method of administration**
Topical administration twice daily for two weeks (tinea cruis, tinea corporis and candidiasis)
Or for four weeks (tinea pedis).

**4.3 Contraindications:**
Use of Betamethasone + Clotrimazole + Neomycin is considered to be harmful for patients with known allergy to any of the components or excipients of this medicine. Avoid its use in case of any fungal infections (ringworm or athlete's foot), viral infections (herpes or chickenpox) or for treatment of acne or rosacea. Consult your doctor before using it for any condition.

**4.4 Special warning and precautions for use:**

Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment.

Conditions which augment systemic absorption include use over large surface areas, prolonged use, and use under occlusive dressings. Use of more than one corticosteroid- containing product at the same time may increase total systemic glucocorticoid exposure. Patients applying Fexoskin Cream to a large surface area or to areas under occlusion should be evaluated periodically for evidence of HPA-axis suppression. This may be done by using the ACTH stimulation, morning plasma cortisol, and urinary free cortisol tests.

If HPA-axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent corticosteroid. Recovery of HPA-axis function is generally prompt upon discontinuation of topical corticosteroids. Infrequently, signs and symptoms of glucocorticosteroid insufficiency may occur, requiring supplemental systemic corticosteroids.

In a small study, Fexoskin Cream was applied using large dosages, 7gm daily for 14 days (BID) to the crural area of normal adult subjects. Three of the eight normal subjects on whom Fexoskin Cream was applied exhibited low morning plasma cortisol levels during treatment. One of these subjects had an abnormal Cortrosyn test. The effect on morning plasma cortisol was transient and subjects recovered one week after discontinuing dosing. In addition, two separate studies in pediatric patients demonstrated adrenal suppression as determined by cosyntropin testing.

Pediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios.

If irritation develops, Fexoskin Cream should be discontinued and appropriate therapy instituted.

**4.5 Interaction with other medicinal products and other forms of interactions:**

Fexoskin Cream may cause damage to latex contraceptives as the effectiveness of such contraceptives may be reduced. Consequently, patient should be advised to use alternative precautions for at least five days after using this product.

**4.6 Pregnancy and lactation:**

Pregnancy Category C: There have been no teratogenic studies performed in animals or humans with the combination of clotrimazole and betamethasone dipropionate. Corticosteroids are generally teratogenic in laboratory animals when administered at relatively low dosage levels.

Studies in pregnant rats with intravaginal doses up to 100 mg/kg (15 times the maximum human dose) revealed no evidence of fetotoxicity due to clotrimazole exposure.

No increase in fetal malformations was noted in pregnant rats receiving oral (gastric tube) clotrimazole doses up to 100 mg/kg/day during gestation days 6-15. However, clotrimazole dosed at 100 mg/kg/day was embryotoxic (increased resorptions), fetotoxic (reduced fetal weights) and maternally toxic (reduced body weight gain) to rats. Clotrimazole dosed at 200 mg/kg/day (30 times the maximum human dose) was maternally lethal, and therefore fetuses were not evaluated in this group. Also in this study, doses up to 50 mg/kg/day (8 times the maximum human dose) had no adverse effects on dams or fetuses. However, in the combined fertility, teratogenicity, and postnatal development study described above, 50 mg/kg clotrimazole, was associated with reduced maternal weight gain and reduced numbers of offspring reared to 4 weeks.

Oral clotrimazole doses of 25, 50, 100, and 200 mg/kg/day (2-15 times the maximum human dose) were not teratogenic in mice. No evidence of maternal toxicity or embryotoxicity was seen in pregnant rabbits dosed orally with 60, 120, or 180 mg/kg/day (18-55 times the maximum human dose).

Betamethasone dipropionate has been shown to be teratogenic in rabbits when given by the intramuscular route at doses of 0.05 mg/kg. This dose is approximately one-fifth the maximum human dose. The abnormalities observed included umbilical hernias, cephalocele and cleft palates. Betamethasone dipropionate has not been tested for teratogenic potential by the dermal route of administration. Some corticosteroids have been shown to be teratogenic after dermal application to laboratory animals.

There are no adequate and well-controlled studies in pregnant women of the teratogenic effects of topically applied corticosteroids. Therefore, Fexoskin Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Breastfeeding**

Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroids production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, caution should be exercised when Fexoskin Cream is administered to a nursing woman.

**4.7 Effects on ability to drive and use machine:**

There have been no studies to investigate the effect of Betamethasone + Clotrimazole + Neomycin on driving performance or the ability to operate machinery. A detrimental effect on such activities would not be anticipated from the adverse reaction profile of topical Betamethasone + Clotrimazole + Neomycin.

**4.8 Undesirable effects:**

Burning, tingling, dry skin, or stinging may occur. If any of these effects persist or worsen, notify your doctor or pharmacist promptly.

Remember that your doctor has prescribed this medication because he or she has judged that the benefit to you is greater than the risk of side effects. Many people using this medication do not have serious side effects.

Tell your doctor right away if any of these unlikely but serious side effects occur: extreme hair growth, skin thinning/discoloration, acne, stretch marks, "hair bumps" (folliculitis).

Rarely, it is possible this medication will be absorbed from the skin into the bloodstream. This can lead to side effects of too much corticosteroid. These side effects are more likely in children, and in people who use this medication for a long time or over large areas of the skin. Tell your doctor right away if any of the following side effects occur: unusual/extreme tiredness, weight loss, headache, swelling ankles/feet, increased thirst/urination, vision problems.

A very serious allergic reaction to this drug is rare. However, seek immediate medical attention if you notice any of the following symptoms of a serious allergic reaction: rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing.

**4.9 Overdose:**

Amounts greater than 45g/week of Fexoskin Cream should not be used. Acute overdosage with topical application of Fexoskin Cream is unlikely and would not be expected to lead to life-threatening situation. Fexoskin Cream should not be used for longer than the prescribed time period. Topically applied corticosteroids, such as the one contained in Fexoskin Cream can be absorbed in sufficient amounts to produce systemic effects.

**5. Pharmacological Properties**

**5.1 Pharmacodynamic Properties:**

Cream contains the dipropionate ester of betamethasone, a glucocorticoid exhibiting the general properties of corticosteroids, and clotrimazole which is an imidazole antifungal agent. Topical

corticosteroids are effective in the treatment of a range of dermatoses because of their anti-inflammatory anti-pruritic and vasoconstrictive actions. Clotrimazole is a broad-spectrum antifungal agent with activity against Trichomones, Staphylococci and Bacteroides. Neomycin is an aminoglycoside antibiotic that primarily exerts its effect on bacterial cells by inhibiting polypeptide assembly and synthesis on the ribosome.

**5.2 Pharmacokinetic Properties:**

Cream intended for treatment of skin conditions and is applied topically. Thus there are minimal pharmacokinetic aspects related to bioavailability at the site of action.

Clotrimazole penetrates the epidermis after topical administration but there is little, if any, systemic absorption.

The extent of percutaneous absorption of topical corticosteroids is determined by many factors including vehicle, integrity of skin and use of occlusion.

Systemically absorbed topical corticosteroids are bound to plasma proteins metabolised in the liver and excreted by the kidneys. Some corticosteroids and their metabolites are also excreted in the bile.

Neomycin is poorly absorbed from the gastrointestinal tract and after topical administration an insufficient amount is absorbed to produce systemic effects. Absorption has been reported to occur from wounds and inflamed skin. After absorption neomycin is rapidly excreted by the kidneys in active form.

**5.3 Preclinical Safety Data:**
Not applicable

**6 Pharmaceutical Particulars**

**6.1 List of excipients:**

| S. No. | Excipients | Specification |
|---|---|---|
| **1** | Ceto-Stearyl Alcohol | B.P. |
| **2** | Cetomacragol-1000 | B.P. |
| **3** | Liquid Parafin Light | B.P. |
| **4** | Chlorocresol | USPNF |
| **5** | Methyl Paraben Sodium | B.P. |
| **6** | Propyl Paraben Sodium | B.P. |
| **7** | Propylene Glycol | B.P. |
| **8** | Sodium Di-Hydrogen Ortho Phosphate | B.P |

**6.2 Incompatibilities:**
Not applicable

**6.3 Shelf life:**
36 Months

**6.4 Special precautions for storage:**
Store in a cool place. Protect from light
Keep all medicines out of reach of children

**6.5 Nature and contents of container:**
30 gm Lami tube pack in a unit carton

**6.6 Special precaution for disposal**
Patients should be advised to wash their hands after applying Cream unless it is the hands that are being treated

**7. Applicant/Manufacturer**


| | | |
|---|---|---|
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