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SYNCOM FORMULATIONS INDIA LIMITED
256-257, Sector-1, Pithampur, Dist.-Dhar, (M.P) 454775
Email: info@sfil.in

Bringing a smile on every face..

Product Name : NCI FUNGIBAN TRIPLE ACTION CREAM 30 gm
Generic Name : Betamethasone Valerate, Gentamicin Sulphate, Tolnaftate, Iodochlorohydroxyquinoline & Chlorocresol Cream

1.3.1 Summary of Product Characteristics (SmPC)

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1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

NCI FUNGIBAN TRIPLE ACTION CREAM 30 gm

2. Composition

Each g contains:

Betamethasone Valerate BP 0.61 mg

Gentamicin Sulfate BP eq. to gentamicin BP 1.0 mg

Tolnaftate USP 15.0 mg

Iodochlorohydroxyquinoline 15.0 mg

Chlorocresol BP 1.0 mg

Component and grade	Function	Quantity mg/g
Betamethasone Valerate BP	Active Ingredient	0.61 mg
Gentamicin Sulphate eq. to Gentamicin base BP	Active Ingredient	1.0 mg
Tolnaftate USP	Active Ingredient	15.0 mg
Iodochlorohydroxyquinoline IH	Active Ingredient	15.0 mg
Chlorocresol BP	Preservative	1.0 mg
Sodium edetate (Sodium EDTA) (Injectable Grade) BP	Chelating agent	1.0 mg
Light Liquid Paraffin BP	Preservative	160.0 mg
Polysorbate-60 BP	Emulsifier	10.0 mg
Polysorbate-80 BP	Emulsifier	10.0 mg
Cetyl Alcohol (Ginol-16) BP	Thickening agent	60.0 mg
Glycerol Mono Stearate BP	Emulsifier	60.0 mg
Propylene Glycol BP	Moisturizing agent	70.0 mg
Cetomacrogol Emulsifying Wax (Cetomacrogol 1000 IHT) BP	Solubilizer	10.0 mg
Purified Water BP	Solvent	Q.S. to 1 g

3. Pharmaceutical Form:

Cream

4. Clinical Particulars:

4.1 Therapeutic Indications

Betamethasone Valerate, Gentamicin Sulphate, Tolnaftate, Iodochlorohydroxyquinoline & Chlorocresol Cream is indicated for the relief of the inflammatory manifestations of corticosteroidresponsive dermatoses when complicated by secondary infection caused by organisms sensitive to the components of this dermatologic preparation or when the possibility of such infection is suspected.

Such disorders include: inguinal dermatosis, chronic dermatitis of the extremities, erythrasma, balanoposthitis, herpes zoster, eczematoid dermatitis, contact dermatitis, follicular dermatitis, dyshidrosis, paronychia, anal pruritus, seborrheic eczema, intertrigo, seborrheic dermatitis, pustular acne, impetigo, neurodermatitis, angular stomatitis, photosensitivity dermatitis, licheni- fied inguinal dermatophytosis and tinea infections such as tinea pedis, tinea cruris and tinea corporis.

4.2 Posology and method of administration

A thin film of Betamethasone Valerate, Gentamicin Sulphate, Tolnaftate, Iodochlorohydroxyquinoline & Chlorocresol Cream should be applied to cover completely the affected area two or three times daily, or as prescribed by the physician. Frequency of application should be determined according to severity of the condition.

Duration of therapy should be determined by patient response. In cases of tinea pedia, longer therapy (2-4 weeks) may be necessary.

Method of Administration

Topical Use only.

4.3 Contraindications

Betamethasone Valerate, Gentamicin Sulphate, Tolnaftate, Iodochlorohydroxyquinoline & Chlorocresol Cream is contraindicated in those patients with a history of sensitivity reactions to any of its components.

4.4 Special warnings and precautions for use

Any of the side effects that are reported following systemic use of corticosteroids, including adrenal suppression, may also occur with topical corticosteroids, especially in infants and children.

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Systemic absorption of topical corticosteroids will be increased if extensive body surface areas are treated or if the occlusive technique is used. Suitable precautions should be taken under these conditions or when long-term use is anticipated, particularly in infants and children.

Systemic absorption of topically applied gentamicin may be increased if extensive body surface areas are treated, especially over prolonged time periods or in the presence of dermal disruption.

In these cases, the undesirable effects which occur following systemic use of gentamicin may potentially occur.

Cautious use is recommended under these conditions, particularly in infants and children.

Prolonged use of topical antibiotics occasionally may result in overgrowth of non-susceptible organisms. If this occurs or if irritation, sensitization or superinfection develops, treatment with EMI Cream should be discontinued and appropriate therapy instituted. Systemic absorption of Iodochlorhydroxyquinolin may interfere with thyroid function tests. Therapy should be discontinued one month before these tests are conducted. The ferric chloride test for phenylketonuria can yield a false-positive result if Iodochlorhydroxyquinolin is present in the urine. Slight staining of linens or clothing due to Iodochlorhydroxyquinolin may occur. EMI Cream is not for ophthalmic use.

Pediatric Use: Pediatric patients may demonstrate greater susceptibility to topical corticosteroidinduced hypothalamic-pituitary-adrenal (HPA) axis suppression and to exogenous corticosteroid effects than mature patients because of greater absorption due to a large skin surface area to body weight ratio.

HPA axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids.

Manifestations of adrenal suppression in children include low plasma cortisol levels and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include a bulging fontanelle, headaches and bilateral papilledema.

4.5 Interaction with other medicinal products and other forms of interaction

CYP3A4 inhibitors Co-administered drugs that can inhibit CYP3A4 (e.g. ritonavir and itraconazole) have been shown to inhibit the metabolism of corticosteroids leading to increased systemic exposure. The extent to which this interaction is clinically relevant depends on the dose and route of administration of the corticosteroids and the potency of the CYP3A4 inhibitor.

Systemic aminoglycoside therapy

Possibility of cumulative toxicity should be considered when gentamicin sulphate is applied topically in combination with systemic aminoglycoside therapy.

4.6 Pregnancy and Lactation Pregnancy

Since safety of topical corticosteroid use in pregnant women has not been established, drugs of this class should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively in large amounts or for prolonged periods of time in pregnant patients.

Since it is not known whether topical administration of corticosteroids can result in sufficient systemic absorption to produce detectable quantities in breast milk, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

4.7 Effects on the ability to drive and use machines

There have been no studies to investigate the effect of Betamethasone Valerate with gentamicin, Tolnaftate and Iodochlorohydroxyquinoline 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 EMI Cream.

4.8 Undesirable effects

Local adverse reactions reported with the use of topical corticosteroids, especially under occlusive dressings, include: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae and miliaria. Rash, irritation and hypersensitivity have been reported with the topical usage of gentamicin sulfate, Iodochlorohydroxyquinoline and rarely with tolnaftate.

4.9 Overdose

Symptoms

Excessive or prolonged use of topical corticosteroids can suppress pituitary-adrenal function, resulting in secondary adrenal insufficiency, and produce manifestations of hypercorticism, including Cushing's disease.

A single overdose of gentamicin would not be expected to produce symptoms.

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Excessive or prolonged use of topical antibiotics may lead to over-growth of lesions by nonsusceptible organisms.

Systemically, tolnaftate is pharmacologically inactive.

Iodochlorohydroxyquinoline rarely produces iodism.

Treatment

Appropriate symptomatic treatment is indicated. Acute hyper corticoid symptoms are usually reversible. Treat electrolyte imbalance, if necessary. In case of chronic toxicity, slow withdrawal of corticosteroids is advised.

If overgrowth by nonsusceptible organisms occurs, stop treatment with EMI Cream and institute appropriate therapy.

5. Pharmacological Particulars:

5.1 Pharmacodynamics properties

Betamethasone Valerate - D07XC01 (Anti-inflammatory)

Gentamicin Sulphate- J01GB03 (Aminoglycoside antibiotic.)

Tolnaftate- D01AE18 (Antifungal.)

Iodochlorohydroxyquinoline- P01AA02 (Antiprotozoal)

Betamethasone Valerate, Gentamicin Sulphate, Tolnaftate, Iodochlorohydroxyquinoline & Chlorocresol Cream combines the anti-inflammatory, antipruritic and vasoconstrictive agent betamethasone valerate, the wide-spectrum antibiotic gentamicin sulfate, the fungicidal agent tolnaftate and Iodochlorohydroxyquinoline, an antibacterial and antifungal agent.

The corticosteroids are a class of compounds comprising steroid hormones, secreted by the adrenal cortex and their synthetic analogs. In pharmacologic doses corticosteroids are used primarily for their anti-inflammatory and/or immunosuppressive effects.

Topical corticosteroids, such as betamethasone dipropionate, are effective in the treatment of corticosteroid-responsive dermatoses primarily because of their anti-inflammatory, antipruritic, and vasoconstrictive actions. However, while the physiologic, pharmacologic, and clinical effects of the corticosteroids are well known, the exact mechanisms of their actions in each disease are uncertain.

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Betamethasone dipropionate, a corticosteroid, has been shown to have topical (dermatologic) and systemic pharmacologic and metabolic effects characteristic of this class of drugs.

Gentamicin sulphate is mixture of antibiotic substances produced by the growth of micromonospora purpurea. It is a bactericidal antibiotic which acts by inhibiting protein synthesis. It has greater antibacterial activity than streptomycin, neomycin or kanamycin.

Gentamicin exerts a number of effects on cells of susceptible bacteria. It affects the integrity of the plasma membrane and the metabolism of RNA, but it's most important effect is inhibition of protein synthesis at the level of the 30s ribosomal subunit.

Iodochlorohydroxyquinoline is a broad spectrum anti-bacterial and anti-fungal agent. Its precise mechanism of action is unknown.

Tolnaftate is a potent fungicidal agent against Trichophyton mentagrophytes, Trichophyton rubrum, Microsporum canis, Epidermophyton floccosum and Malassezia furfur. Clinical studies have shown the excellent fungicidal effect of tolnaftate in a large number of patients with superficial fungal infections.1 Therapy with tolnaftate has been notable for lack of recurrence.

Each component of EMI Cream makes a significant contribution to the efficacy of the product in treating infections of mixed etiology.

5.2 Pharmacokinetic properties

The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids. Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

Sixty-three pediatric patients ages 1 to 12 years, with atopic dermatitis, were enrolled in an open-label, hypothalamic-pituitary-adrenal (HPA) axis safety study. Betamethasone dipropionate cream was applied

twice daily for 2 to 3 weeks over a mean body surface area of 40% (range 35% to 90%). In 10 of 43 (23%) evaluable patients, adrenal suppression was indicated by either a less than or equal to 5 mcg/dL pre-stimulation cortisol, or a cosyntropin post-stimulation cortisol less than or equal to 18 mcg/dL and/or an increase of less than 7 mcg/dL from the baseline cortisol.

Gentamicin sulphate

Absorption:

Topical application of gentamicin can result in some systemic absorption. Treatment of large areas can result in plasma concentrations of up to 1µg/ml.

Gentamicin is 70-85% bound to plasma albumin following administration.

Effective plasma concentration is 4 - 8ug/ml.

The volume of distribution (VD) is 0.31/kg.

Elimination

> 90% Gentamicin is excreted unchanged in the urine by glomerular filtration.

T½ = 2 - 3 hours in individuals with normal kidney function, but can be increased in cases of renal insufficiency.

The elimination rate constant is;

0.02 Hr-1 for anuric patients*

0.30 Hr-1 normal

*Therefore, in those with anuria, care must be exercised.

Up to 4% Iodochlorohydroxyquinoline applied to the skin may be absorbed. Excretion is mainly as conjugated metabolites in the urine.

5.3 Pre-clinical Safety:

There are no preclinical data of relevance to the prescriber which are additional to that in other sections of the SmPC.

6. Pharmaceutical particulars

6.1 List of excipients

- Betamethasone Valerate BP

- Gentamicin Sulphate eq. to Gentamicin base BP
- Tolnaftate USP
- Iodochlorohydroxyquinoline IH
- Chlorocresol BP
- Sodium edetate (Sodium EDTA) (Injectable Grade) BP
- Light Liquid Paraffin BP
- Polysorbate-60 BP
- Polysorbate-80 BP
- Cetyl Alcohol (Ginol-16) BP
- Glycerol Mono Stearate BP
- Propylene Glycol BP
- Cetomacrogol Emulsifying Wax (Cetomacrogol 1000 IHT) BP
- Purified Water BP

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store in a temperature not exceeding 30ºC.

6.5 Nature and contents of container

Collapsible aluminium tube of 30 g cream packed in a unit carton with an insert.

6.6 Special precautions for disposal and other handling

Not applicable

7. Marketing authorization holder:

NCI Pharmchem Ind. Ltd.

8. Marketing authorization number(s)

Yet to receive

9. Date of first authorization/renewal of the authorization

Not applicable

10. Date of revision of the text

Not applicable