1. NAME OF THE MEDICINAL PRODUCT

Clotrimazole, Betamethasone and Neomycin Gel

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition:

Clotrimazole BP……1.0 % w/w

Neomycin Sulfate USP ……..0.50 % w/w

Equivalent to Neomycin Base…….0.35 % w/w

Betamethasone Dipropionate USP

Equivalent to Betamethasone……..0.05 % w/w

In a Gel base.

3. PHARMACEUTICAL FORM

Topical, Semi-solid Dosage Form – Gel

4. Clinical particulars

4.1 Therapeutic indications

Clotrimazole + Betamethasone + Neomycin Gel is indicated for the relief of the inflammation manifestations of corticosteroid response dermatoses when complicated by secondary infection caused by organism sensitive to this components or dermatological preparation or when the possibility of such infection is suspected.

Such disorders include: Chrome dermatitis of the extremities, balanoposthitis, eczematoid dermatitis, contact dermatitis, follicular dermatitis, parakeratosis. anal pruritis. Intertigo, Impetigo neurodermatitis, angular stomatitis, photosensitivity dermatitis, dermatitis. Lichenfied inguinal dermatophytosis and linea infections such as tinea pedis, tinea cruns and tinea corporis. As with other highly active corticosteroids. Therapy should be discontinued when control has been achieved If no improvement is seen within 2 weeks, reassessment of the diagnosis may be necessary.

4.2 Posology and method of administration

It 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 pedis, longer therapy (2-4 weeks) may be necessary.

Or As directed by the physician.

Route of administration: Topical.

4.3 Contraindications

It is contraindicated in those patients with a history of sensitivity reactions to any of its components. Use in paediatric patients under 12 years of age is not recommended.

4.4 Special warnings and precautions for use

If irritation or hypersensitivity develops with the use of the drug, Treatment should be dis continued and appropriate therapy instituted. The use of neomycin may result in overgrowth of no susceptible organisms including fungi. If super infection occurs during neomycin therapy, the drug should be discontinued and appropriate therapy instituted.

General systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestation of Cushing's syndrome, hyperglycemia, and glycosuria in some patients. The use of Gel for longer than 4 weeks is not recommended.

4.5 Interaction with other medicinal products and other forms of interaction

Betamethasone

Betamethasone is known to interact with other drugs like Amphotencin B. carbamazepine lofexidine, metyrosine, oxandrolone, perindopril, phenytoin (Na), rifampicin. Always consult your physician for the change of dose regimen or an alternative drug of choice that may strictly be required.

Clotrimazole

Clotrimazole is known to interact with other drugs like aliskiren. Always consult your physician for the change of dose regimen or an alternative drug of choice that may strictly be required.

Neomycin

Neomycin is known to interact with other drugs like acarbose, atracurium (Besylate), cyanocobalamine digoxin Doxacurium, Fluorouracil, gentamicin, gestodene. hydroxocobalamin, mecobalamine, Methotrexate, pancuronium (Br). Always consult your physician for the change of dose.

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

foetus. Drugs of this class should not be used extensively in large amounts or for prolonged periods of time in pregnant patients.

Lactation

Since it is not known whether topical administration of corticosteroids can result in suficient 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. It is not for ophthalmic use. Systemic absorption of topical corticosteroid can produce reversible HPA axis suppression with the potential for Glucocorticosteroid insufficiency after withdrawal from treatment. Patients applying a topical steroid to a large surface area or to areas under occlusion should be evaluated for evidence of HPA axis suppression.

Manifestations of Cushing syndrome, hyperglycemia, and glucosuna can also be produced in some patients by systemic absorption of topical corticosteroids while on therapy Paediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratio. Irritation or sensitization develops with the use of this Gel. Treatment should be discontinued and appropriate therapy instituted. Prolonged use of topical antibiotics occasionally may result in overgrowth or non-susceptible organisms. If this occurs or irritation, sensitization or super infection develops, treatment with this Gel should be discontinued and appropriate therapy instituted.

4.7 Effects on ability to drive and use machines

Not available.

4.8 Undesirable effects

The most frequent adverse reactions reported were burning irritation, latching, and stinging sensation, less frequent adverse reactions were skin atrophy, cracking and fissuring of the skin, erythema and folliculitis, numbness of fingers, skin atrophy and telangiectasia.

The following additional local adverse reactions have been reported occasionally with topical corticosteroids, dryness. Acneiform eruptions, hypo pigmentation, allergic contact dermatitis, secondary infections, stnae and miliaria. Neomycin occasionally causes skin sensitization. Ototoxicity nephrotoxicity have been reported with oral administration..

4.9 Overdose

Symptoms: Excessive or prolonged use of topical Corticosteroids can suppress hypothalamic-pitutary-adrenal function resulting in secondary adrenal insufficiency and produce

manifestations of hypercorticism including Cushing disease. Excessive or prolonged use of topical antibiotics may lead to overgrowth of non-susceptible organisms in lesions. 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 non susceptible organisms occurs, stop treatment with this Gel and institute appropriate therapy.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Antifungal, Antibiotic and Anti-inflammatory.

ATC code: Betamethasone Dipropionate: D07AC01, Clotrimazole: D01AC01, Neomycin Sulfate : D06AX04

Betamethasone is a glucocorticosteroids receptor agonist. This leads to changes in genetic expression once this complex binds to the GRE. The anti-inflammatory actions of corticosteroids are thought to involve lipocortins phospholipase A2 inhibitory proteins which, through inhibits Arachidonic acid, control the biosyntehesis of prostaglandins and leukotrienes.

Clotrimazole exerts antifungal effects by inhibition of fungal sterol synthesis. lt appears to inhibit the enzymatic conversion of 2,4-methylenedihydrolanosterol to demethylsterol. the precursor to ergosterol, which is an essential building block of cytoplasmic membrane of the fungi. Clotrimazole is a broad spectrum antifungal agent that inhibits the growth of most fungi pathogenic to man. Including the candida and dermatophytes (Trichophyton, microsporum and epidermophyton).

Neomyicn acts on bacteria by interfering with bacterial protein synthesis by binding to 30s ribosomes. The antibacterial spectrum of neomycin includes specific organisms which are susceptible to it and generally includes all Medically important aerobic gram negative bacilli except pseudomonas aeruginosa. Aerobic bacteria are Resistant. Staphylococcus aureus and Staph. Epidermidis are highly sensitive. But all streptococci are relatively resistant.

5.2. Pharmacokinetics

Topical corticosteroids can be absorbed from normal intact skin. The extent of percutaneous absorption of topical corticosteroids is determined by many factors. including the vehicle and the integrity of the epidermal barrier. Inflammation and/or other disease processes in the skin may increase percutaneous absorption. Systemic absorption following use of topical Clotrimazole preparations is very low Estimated bioavailability is less than 0.5% Clotrimazole concentrations achieved in the epidermal layers exceed the minimal inhibitory concentrations (MICs) for almost

all pathogenic fungi.

5.3. Preclinical safety data

Not Available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cetyl alcohol, Light liquid paraffin, Polyoxy-40 hydrogenated castor oil, Isopropyl myristate, Benzyl alcohol, polysorbate 60, Glycerol, Polyacrylate crosspolymer – 6, Xanthan Gum, propylene glycol, colour erythrosine supra, Flavour engloish lavender comp P4154, Purified water

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

36 months from the date of Manufacture.

6.4 Special precautions for storage

Do not store above 30°C. Do not freeze.

Do not accept if seal is broken.

Keep the medicine out of reach of children.

For external use only.

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

30gm Lami tube in a printed carton along with insert.

6.6 Special precautions for disposal <and other handling>

Any unused product or waste material should be disposed of in accordance with local requirements

7. APPLICANT/MANUFACTURER>

M/S SAI SAGAR PHARMA LIMITED

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LAGOS, LAGOS STATE NIGERIA

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