1. NAME OF THE MEDICINAL PRODUCT

Econazole Nitrate, Triamcinolone Acetonide and Gentamicin Sulfate Cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition:

Econazole Nitrate BP……..……..…1% w/w

Triamcinolone Acetonide BP…….0.1% w/w

Gentamicin Sulfate BP equivalent to Gentamicin……..…0.1% w/w

In a cream base……q.s.

For complete list of excipients refer section 6.1

3. PHARMACEUTICAL FORM

Topical, Semi-solid Dosage Form – Cream.

A White soft cream.

4. Clinical particulars

4.1 Therapeutic indications

For topical treatment of antiinflammatory and other dermatomycoses caused by fungi and bacteria:

- vulvovaginal candidiasis, tricomonas, vaginitis, Tricophytosis (tinea corpis, tinea face, tinea capitis etc),
- Trychophytosis (tinea corpis, tinea pedis etc)
- Contact dermatitis,eczema, impetigo etc

Bacterial skin infections caused by susceptible strains of gentamicin.

4.2 Posology and method of administration

Apply 2-3 times daily to the affected areas and rubbed gently.

OR

As directed by the physician.

Route of administration: Topical.

4.3 Contraindications

- Patients with hypersensitivity to any of the components of Econazole Nitrate, Triamcinolone Acetonide and Gentamicin Sulfate Cream.
- Patents with tuberculosis, varicella, herpes simplex, herpes zoster, vaccinnia and syphilis.
- Patients with eczematous otitis externa and perforated eardrum.
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4.4 Special warnings and precautions for use

Avoid prolonged use especially in pregnant patients.

4.5 Interaction with other medicinal products and other forms of interaction

Econazole is a known inhibitor of CYP3A4/2C9. Due to limited systemic availability after vaginal application, clinically relevant interactions are unlikely to occur but have been reported with oral anticoagulants. In patients taking oral anticoagulants, such as warafarin are acenocoumarol, caution should be exercised and the anticoagulant effect should be monitored more frequently.

Adjustment of the oral anticoagulant dosage may be necessary during and after the treatment with econazole. Contact between latex products such as contraceptive diaphragms or condoms and this product must be avoided since the constituents of the product may damage the latex. Patients using spermicidal contraceptives should consult their physician since any local vaginal treatment may inactivate the spermicidal contraceptive.

Gentamicin Sulfate should not be used concurrently with other potentially nephrotoxic or ototoxic drug substances unless considered essential by the physician. The potential nephrotoxicity of other aminoglycosides, vancomycin and some cephalosporins, ciclosporin, cisplatin, fludarabine and amphotericin may be increased in the presence of gentamicin and monitoring of renal function is therefore recommended.

Furosemide (frusemide) and piretanide may potentiate the ototoxicity of gentamicin, and ethacrynic acid, which is ototoxic in its own right, should be avoided with gentamicin. Aminoglycosides, including gentamicin, may induce neuromuscular blockade and respiratory paralysis and should therefore only be used with great caution in patients receiving curare-type muscle relaxants. Aminoglycosides antagonise the effects of cholinergic agents such as neostigmine and pyridostigmine. Indometacin has been reported to increase the plasma concentrations of aminoglycosides when given concomitantly. Bacteriostatic antibiotics may give an antagonistic interaction, but in some cases (e.g. with clindamycin and lincomycin) the disadvantage of antagonism may be outweighed by the addition of activity against anaerobic organisms. Synergistic action has been demonstrated with penicillin. However, if penicillins (such

as ticarcillin) are used with gentamicin the drugs should not be physically mixed and patients with poor renal function should be monitored for effectiveness of the gentamicin. Cross-sensitivity with aminoglycosides may occur.

4.6 Pregnancy and Lactation

Pregnancy

Not the Econazole but the Triamcinolone Acetonide crosses the placenta and topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. The relevance of this finding to human beings has not been established. However, topical steroids in large amounts or for prolonged periods should not be used in pregnancy.

Lactation

Negligible amount of econazole and to some extent Triamcinolone may be excreted in small amounts in breast milk. So, this cream should not be prescribed to the lactating mother or if prescribed lactation should be withheld during treatment.

4.7 Effects on ability to drive and use machines

Not available.

4.8 Undesirable effects

Information on side effects according to the body system is as follows:

System Organ Class Adverse Reaction

Immune system disorders: Hypersensitivity

Skin and subcutaneous

Tissue disorders:

Application site reactions, including contact dermatitis, skin atrophy, steroid purpura, striae, skin fragility, exfoliative dermatitis, burning sensation, acneiform eruption, folliculitis, rosacea, periocular and perioral dermatitis, delayed wound healing, granulomas, telangiectases, erythema, hypopigmentation, hypertrichosis, masking or aggravation of dermatophyte infection and secondary infection or aggravation of existing infection, photosensitivity, rash, urticaria, pruritus.

A few patients may be allergic to any of the components. If an adverse reaction occurs, medication should be discontinued.

Use of topical corticosteroids, such as triamcinolone, in the per orbital region may result in ocular complications. Under certain circumstances sufficient amounts of topical corticosteroids, such as triamcinolone, can be absorbed to cause systemic corticosteroid effects including adrenal

suppression and Cushing's syndrome. Cessation of topical steroid therapy after an extended treatment period can result in Addisonian crisis.

4.9 Overdose

Econazole Nitrate, Triamcinolone Acetonide & Gentamicin Sulfate Cream is intended for topical use. If accidental ingestion of large quantities of the product occurs, an appropriate method of gastric emptying may be used if considered desirable.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Econazole prevents fungal organisms from producing vital substances required for growth and function. This medication is effective only for infections caused by fungal organisms.

Triamcinolone and its derivatives are synthetic glucocorticoids that are used for their anti-inflammatory or immunosuppressive properties.

Gentamicin is a broad spectrum amino glycoside antibiotic.

Aminoglycosides work by binding to the bacterial 30S ribosomal subunit, causing misreading of t-RNA, leaving the bacterium unable to synthesize proteins vital to its growth.

5.2. Pharmacokinetics

Econazole nitrate:

Econazole interacts with 14-α demethylase, a cytochrome P-450 enzyme necessary to convert lanosterol to ergosterol. As ergosterol is an essential component of the fungal cell membrane, inhibition of its synthesis results in increased cellular permeability causing leakage of cellular contents. Econazole may also inhibit endogenous respiration, interact with membrane phospholipids, inhibit the transformation of yeasts to mycelial forms, inhibit purine uptake, and impair triglyceride and/or phospholipid biosynthesis. After topical application to the skin of normal subjects, systemic absorption of Econazole nitrate is extremely low. Although most of the applied drug remains on the skin surface, drug concentrations were found in the stratum corneum which, by far, exceeded the minimum inhibitory concentration for dermatophytes.

Triamcinolone Acetonide:

The anti-inflammatory actions of corticosteroids are thought to involve lipocortins, phospholipase A2 inhibitory proteins which, through inhibition of arachidonic acid, control the biosynthesis of prostaglandins and leukotrienes. The immune system is suppressed by corticosteroids due to a decrease in the function of the lymphatic system, a reduction in immunoglobulin and complement

concentrations, the precipitation of lymphocytopenia, and interference with antigen-antibody binding. Rapid absorption following oral administration

Gentamicin:

Aminoglycosides like gentamicin "irreversibly" bind to specific 30S-subunit proteins and 16S rRNA. Specifically gentamicin binds to four nucleotides of 16S rRNA and a single amino acid of protein S12. This interferes with decoding site in the vicinity of nucleotide 1400 in 16S rRNA of 30S subunit. This region interacts with the wobble base in the anticodon of tRNA. This leads to interference with the initiation complex, misreading of mRNA so incorrect amino acids are inserted into the polypeptide leading to nonfunctional or toxic peptides and the breakup of polysomes into nonfunctional monosomes. Injections lead to peak serum concentrations in 30-60 minutes. Topical gentamicin is readily absorbed from large burned, denuded, or granulating areas but not through intact skin. Absorption of gentamicin is faster and greater with the cream compared to the ointment. Gentamicin is absorbed in small quantities following topical application to the eye. Gentamicin is also absorbed in small amounts following topical application to the ear (especially if the eardrum is perforated or if tissue damage is present).

5.3.Preclinical safety data

Not Available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Chlorocresol, Cetomacrogol-1000, Cetostearyl Alcohol, Light Liquid Paraffin, White Soft Paraffin, Sodium Dihydrogen Phosphate Dihydrate, Disodium Hydrogen Phosphate (Dihydrate), Disodium Edetate, Sodium Metabisulfite, Propylene Glycol, 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 Alu 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

Sai Sagar Pharma Limited
No. 2, Kaara Street, Off Osolo way,
Ajao Estate, Isolo, Lagos, Nigeria.

Manufacturer:

S Kant
HEALTHCARE Ltd.

1802-1805, G.I.D.C., Phase III,

Vapi - 396 195. Gujarat, INDIA.