1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC):

1. NAME OF THE MEDICINAL PRODUCT:

TRIDERMIX-G CREAM (Betamethasone Valerate, Neomycin Sulphate, Tolnaftate and Clioquinol Cream)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Composition:
- Betamethasone Valerate BP (0.05 % W/W)
- Neomycin Sulphate BP (0.5 % W/W)
- Tolnaftate USP (1 % W/W)
- Iodochlorohydoroxyquinoline (Clioquinol) BP (1 % W/W)
- Cream Base (- QS)

3. PHARMACEUTICAL FORM : TOPICAL CREAM

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications

Betamethasone valerate, Neomycin sulphate, Tolnaftate, Clioquinol cream indicated for treatment of following condition

- Atopic dermatitis (including infantile atopic dermatitis)
- Nummular dermatitis (discoid eczema)
- Prurigo nodularis
- Psoriasis (excluding widespread plaque psoriasis)
- Adjunct to systemic steroid therapy in generalised erythroderma
- Insect bite reactions
- Eczema in Adults and children (age 2 years and over)
- Dermatitis and contact sensitivity reaction.
- seborrhoea Dermatitis
- Genital intertrigo
- fungal infection
- Bacterial infections
- Skin infections

4.2 Posology and Method of Administration

Creams are especially appropriate for moist or weeping surfaces.

Apply thinly and gently rub in using only enough to cover the entire affected area once or twice daily for up to 4 weeks until improvement occurs, then reduce the frequency of application or change the treatment to a less potent preparation.

Allow adequate time for absorption after each application.

4.3 Contraindications

Rosacea; acne vulgaris perioral dermatitis; perianal and gental pruritus; primary cutaneous viral infection. Primary infected skin lesions caused by fungi or bacteria; primary or secondary infections due to yeast; secondary infection due to Pseudomonas or Proteus sp; dermatoses in children (aged 2 years and over), Dermatitis and napkin eruptions, Perforated otitis externa, Prolonged use, Prolonged use, Pregnancy and lactation, Infants& children (aged 2 years and over)

4.4 Special warnings and precautions

If a reaction suggesting hypersensitivity or chemical irritation should occur, use of the medication should be discontinued. Long term, continuous topical therapy. Face may exhibit atrophic changes on prolonged treatment. Avoide contact with eyes, Psoriasis, Renal impairment. Bacterial infection, contact sensitization, extension of infection, potential for ototoxicity and nephrotoxicity.

Systemic absorption may be increased by various factors such as application over a large skin surface area, application to damaged skin, application under occlusive skin dressings and prolonged uration of therapy.

4.5 Interaction with other medicinal products and other form of interactions:

Co-administered drugs that can inhibit CYP3A4 (e.g. ritonavir, 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.

4.6 Pregnancy and Lactation

Pregnancy:

If your doctor says you can use Betamethasone Valerate, Neomycin Sulphate, Tolnaftate and Clioquinol cream while pregnant or breastfeeding you should not use it on large areas of skin, underneath airtight dressings, or for prolonged periods of time. This will minimise any absorption of the medicine.

Ask your doctor or pharmacist for further information.

4.7 Effects on Ability to Drive and Use Machines

Not applicable.

4.8 Undesirable effects:

Skin reactions occur rarely and may include irritation and contact dermatitis.

4.9 Overdose

Topically applied Betamethasone valerate, Neomycin sulphate, Tolnaftate, Clioquinol cream may be absorbed in sufficient amounts to produce systemic effects.

Acute overdosage is very unlikely to occur; however, in the case of chronic overdosage or misuse the features of hypercortisolism may occur.

5. PHARMACOLOGICAL PROPERTIES:

5.1Pharmacodynamic Properties:

Pharmacotherapeutic group: Anti-inflammatory, Antibiotic, Antifungal.

ATC Code: D07XC01

Betamethasone Valerate: Betamethasone valerate has anti-inflammatory, antipruritic, and vasoconstrictive properties. The mechanism of the anti-inflammatory activity of the topical steroids, in general, is unclear. However, corticosteroids are thought to act by the induction of phospholipase A2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A2.

Neomycin Sulphate: Neomycin is bactericidal in action. Similar to other aminoglycosides, it inhibits bacterial protein synthesis through irreversible binding to the 30 S ribosomal subunit of susceptible bacteria. Neomycin is actively transported into the bacterial cell where it binds to receptors present on the 30 S ribosomal subunit. This binding interferes with the initiation complex between the messenger RNA (mRNA) and the subunit. As a result, abnormal, Non-functional proteins are formed due to misreading of the bacterial DNA. Eventually, susceptible bacteria die because of the lack of functional proteins.

Tolnaftate: Tolnaftate is a topical fungicide. Though its exact mechanism unknown, it is believed to prevent ergosterol biosynthesis by inhibiting squalene epoxidase. It has also been reported to distort the hyphae and to stunt mycelial growth in susceptible organisms.

Clioquinol: Clioquinol is bacteriostatic, however, the precise mechanism of its action is unknown. Topical absorption is rapid and extensive, especially when the skin is covered with an occlusive dressing or if the medication is applied to extensive or eroded areas of the skin. Clioquinol is absorbed through the skin in sufficient amounts to affect thyroid function tests.

5.2 Pharmacokinetic properties:

Betamethasone Valerate

Absorption: Topical corticosteroids can be systemically absorbed from intact healthy skin. The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Occlusion, inflammation and/or other disease processes in the skin may also increase percutaneous absorption.

Distribution: The use of pharmacodynamic endpoints for assessing the systemic exposure of topical corticosteroids is necessary because circulating levels are well below the level of detection.

Metabolism: Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. They are metabolised, primarily in the liver.

Elimination: Topical corticosteroids are excreted by the kidneys. In addition, 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.

Clioquinol: Oral administration of clioquinol to rats during pregnancy was associated with reduced fetal body weight at doses ≥ 120 mg/kg/day and delays in ossification at doses ≥ 300 mg/kg/day.

5.3 Preclinical safety data
Non-clinical data reveal no special hazard for humans based on studies of repeated dose toxicity, genotoxicity and carcinogenicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients
Cetomacrogol 1000 INH
Cetostearyl Alcohol BP
White Soft Paraffin BP
Sodium Acid Phosphate BP
Chlorocresol BP
Light Liquid Paraffin BP
Propylene Glycol BP
Purified Water BP

6.2 Incompatibilities
Not known

6.3 Shelf Life
36 months

6.4 Special precaution for storage
Store at temperature not exceeding 30°C. Do not Freeze. Protect from Light.

6.5 Nature and content of container
The cream is filled into lami tubes enclosed in an outer carton. Pack sizes available are 30g.

6.6 Special precautions for disposal and other handling
Not applicable.

7. MARKETING AUTHORISATION HOLDER
Kremoint Pharma Pvt. Ltd.,
B-8 Additional MIDC, Ambernath, Ambernath (E). Thane 421506

8. Marketing authorisation number(s)
KD-146

9. Date of first authorisation/renewal of the authorisation
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10. Date of revision of the text
