1. NAME OF THE MEDICINAL PRODUCT

MAUREEN CREAM

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gm cream contains:
Clotrimazole,
Beclomethasone Dipropionate
Clobetasol Propionate
Gentamycin Sulphate

3. PHARMACEUTICAL FORM

Topical dosage form.

A white semi-solid cream filled in 20 gm white rubber tube

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Kemi Plus Cream is indicated for wide range of eczemas and other inflammatory and allergic infections of the skin caused by various fungi and bacteria including Tineacapitis, Tineafaciei, Tineacorporis, Tineapedis, Candida spp.,Tineaversicolor as well as both Gram-positive and Gram-negative bacteria.

These infections include contact and/ or follicular dermatitis, impetigo, intertrigo, eczema,psoriasis, otitis externa and non-specific pruritus.

4.1 Posology and method of administration

Urea 5% w/w Cream is applied topically. Wash affected areas well, rinse off all traces of soap, dry, and apply sparingly twice daily. Occlusive dressings may be used but are usually unnecessary because of the self-occlusive nature of the cream.

4.3 Contraindications:

Since MAUREEN CREAM contains a steroid, Beclomethasone Dipropionate, the risk of systemic absorption should be considered when applying the cream. Kemi Plus cream should not be applied with an occlusive dressing to large areas of the body. It should not be used indiscriminately for pruritus. It should not be applied to ulcers of the leg and long term topical use is best avoided, especially in children.

4.4 Special warnings and precautions for use:

For topical use only. Avoid contact with eyes, lips or mucous membranes.

This medication is to be used as directed by a physician and should not be used to treat any condition other than that for which it was prescribed. If redness or irritation occurs, discontinue use and consult a physician.

4.5 Pregnancy and lactation

No report exists on the topical use to establish any adverse effect to pregnant or nursing mothers

4.6 Effects on ability to drive and use machines

Adverse effects on the ability to drive or operate machinery have not been observed.

4.7 Undesirable effects

The following adverse reactions have been reported with the use of Clotrimazole: Erythema, Stinging, Blistering, Oedema, Pruritus, Burning and general irritation to the skin. Corticosteroids have anti-proliferative effects on keratinocytes and fibroblasts (leading to skin thinning and atrophy. Skin thinning is more likely if corticosteroid preparations are applied under occlusion.

4.8 Overdose

Excessive use of Kemi Plus cream may result in the following because of the corticosteroid content, thinning of the skin which may be restored over a period of time, increased hair growth, acne at the site of application in some cases.

5 Pharmacological properties

5.1 Pharmacodynamic properties

Mechanism of Action of Clotrimazole

Clotrimazole is an imidazole antifungal agent. Imidazoles inhibit 14-α-demethylation of lanosterol in fungi by binding to one of the cytochrome P-450 enzymes. This leads to the accumulation of 14-α-methylsterols and reduced concentrations of ergosterol, a sterol essential for a normal fungal cytoplasmic membrane. The methylsterols may affect the electron transport system, thereby inhibiting growth of fungi.

Clotrimazole is fungicidal or fungistatic depending on the drug concentrations. It inhibits the conversion of Lanosterol to 14 demethylLanosterol by inhibiting the cytochromeP450 enzyme 14 alpha demethylase and impair ergosterol synthesis which is an essential constituent of cell membrane. Inhibition of ergosterol synthesis will alter the membrane permeability of the susceptible fungus and kill or inhibit them.

Mechanism of Action of Gentamicin

Gentamicin exerts its bactericidal action against gram negative organisms & some of gram positive organisms by inhibiting bacterial protein synthesis. The process involves

1. Penetration of bacterial cell membrane & binding directly to the bacterial ribosome,
2. Misleading of m-RNA codon by bacterial ribosome,
3. Formation of peptide chains with wrong amino acid sequence which gets incorporated into bacterial cell membrane and alters its permeability,
4. Bacterial cell lysis. Some bacterial strains resistant to other amino glycosides are sensitive to Gentamicin.

Mechanism of Action of Beclomethasone dipropionate

Mechanism of action: The drug exerts its pharmacological action by penetrating and binding to cytoplasmic receptor protein and causes a structural change in steroid receptor complex. This structural change allows it`s migration in to the nucleus and then binding to specific sites on the DNA which leads to transcription of specific m-RNA and which ultimately regulates protein synthesis. It exerts highly selective glucocorticoid action. It stimulates the enzymes needed to decrease the inflammatory response.The drug exerts anti-inflammatory and immunosuppressant actions as follows: -

1) Induce lipocortins in macrophages, endothelium, and fibroblasts which inhibits Phospholipase A2 and thus decreases the production of Prostaglandins, leukotrienes (LT), and platelet activating factor,

2) Causes negative regulation of genes for cytokines in macrophages, endothelial cells and lymphocytes and thus decreases the production of interleukins (IL-1, IL-2, IL-3, IL-6), TNF-alpha, GM-CSF (granulocyte macrophage colony stimulating factor), Gama interferon and suppresses fibroblast proliferation and T-lymphocyte functions and interferes chemo taxis.

3) Decreases the production of acute phase reactants from macrophages and endothelial cells and interferes complement function.

4) Decreases the production of ELAM-1(Endothelial leukocyte adhesion molecule-1) and ICAM-1(intracellular adhesion molecule-1) in endothelial cells.

5) Inhibit IgE mediated histamine and LT-C4 release from basophiles and the effects of antigen-antibody reaction is not mediated 6) Reduces the production of collagenase and stromolysin and thus prevents tissue destruction.

Mechanism of Action of Clobetasol propionate

Like other topical corticosteroids, Clobetasol propionate 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.

5.2 Pharmacokinetic properties

Pharmacokinetics of Clotrimazole

Absorption: Absorption is minimal after topical administration.

Pharmacokinetics of Gentamicin

Metabolism:Not metabolized

Excretion: Excreted mainly through urine.

Absorption: Poorly absorbed orally

Distribution: Distributed extracellularly. CSF penetration and intraocular penetration poor.

Pharmacokinetics of Beclomethasone dipropionate

Absorption: It enters in to the systemic circulation after topical administration.

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 may increase percutaneous absorption of topical corticosteroids. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids.

Once absorbed through the skin, the pharmacokinetics of topical corticosteroids is 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.

Studies performed with Clotrimazole and Betamethasone Dipropionate Cream indicates that these topical combination anti-fungal/corticosteroids may have vasoconstrictor potencies in a range that is comparable to high potency topical corticosteroids. Therefore use is not recommended in patients less than 17 years of age, in diaper dermatitis, and under occlusion.

Pharmacokinetics of Clobetasol propionate

The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Occlusive dressings with hydrocortisone for up to 24 hours have not been demonstrated to increase penetration; however,

occlusion of hydrocortisone for 96 hours markedly enhances penetration. Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin may increase percutaneous absorption. Greater absorption was observed for the Clobetasol propionate gel formulation as compared to the cream formulation in in vitro human skin penetration studies. Studies performed with Clobetasol propionate gel, cream and ointment indicate that they are in the super-high range of potency as compared with other topical corticosteroids.

5.3 Preclinical safety data

Long-term animal studies for carcinogenic potential have not been performed on this product to date. Studies on reproduction and fertility also have not been performed.

6 Pharmaceutical particulars

6.1 List of excipients

Cetostearyl Alcohol BP

Liquid Paraffin

Chlorocresol

Chlorocresol

Sodium dihydrogen Phosphate

Butylated Hydroxyl Toluene

Cetomacrogol 1000 BP

Benzyl Alcohol

Sodium EDTA

White Petroleum Jelly

Purified Water BP

6.2 Incompatibilities

None

6.3 Shelf life

3 years

6.4 Special precautions for storage

Preserve in tight containers. Protect from light.

6.5 Nature and contents of container

20 gm white rubber tube

7 MARKETING AUTHORISATION HOLDER

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8 MANUFACTURED BY:

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