For the use only of Registered Medical Practitioner or a Hospital or a Laboratory.

Beclomethasone Dipropionate & Gentamicin

क्लोमिरेट

CLOMIRET®

Clotrimazole 1% w/w + Beclomethasone Dipropionate 0.025% w/w

COMPOSITION:
CLOMIRET Cream: Each tube contains Clotrimazole USP 1.0% w/w & Beclomethasone Dipropionate USP 0.025% w/w

THERAPEUTIC CLASS:
Topical Anti-Infective (anti-fungal) with Corticosteroids

CLINICAL PHARMACOLOGY:
CLOMIRET Cream has been shown to be at least as effective as Clotrimazole alone in a different Cream vehicle. Use of corticosteroid in the treatment of a fungal infection may lead to suppression of host inflammation leading to worsening or decreased cure rate.

PHARMACODYNAMICS:
BECLOMETHASONE:
Beclomethasone Dipropionate is a potent glucocorticoid which has anti-inflammatory, antipruritic and vasoconstrictive properties. Corticosteroids are hormones that produced naturally by the adrenal glands, and have many important functions, including control of inflammatory responses. CLOMIRET Cream is a synthetic corticosteroid with anti-infective (antifungal) and used to decrease inflammation in the skin. As a cream, it is used to treat severe inflammatory skin disorders (e.g. eczema) unresponsive to less potent steroids, but is generally avoided in the treatment of psoriasis due to the risk of rebound on withdrawal. CLOMIRET Cream is also used to treat the inflammation caused by a number of conditions such as allergic reactions, eczema, fungal infections and psoriasis.

CLOTRIMAZOLE:
An imidazole derivative with a broad spectrum of antimycotic activity. Clotrimazole is a broad-spectrum antifungal agent that is used for the treatment of dermal infections caused by various species of pathogenic dermatophytes, yeasts, and Malassezia furfur. The primary action of clotrimazole is against dividing and growing organisms.
In vitro, clotrimazole exhibits fungistatic and fungicidal activity against isolates of Trichophyton rubrum,Trichophyton mentagrophytes, Epidermophyton floccosum, Microsporum canis and Candida species including Candida albicans. In general, the in vitro activity of clotrimazole corresponds to that of tolnaftate and griseofulvin against the mycelia of dermatophytes (Trichophyton, Microsporum, and Epidermophyton), and to that of the polyenes (amphotericin B and nystatin) against budding fungi (Candida).

MODE OF ACTION:
BECLOMETHASONE: Unbound corticosteroids cross cell membranes and bind with high affinity to specific cytoplasmic receptors. The result includes inhibition of leukocyte infiltration at the site of inflammation, interference in the function of mediators of inflammatory response, suppression of humoral immune responses, and reduction in edema or scar tissue. The antiinflammatory actions of corticosteroids are thought to involve phospholipase A2 inhibitory proteins, lipocortins, which control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes. For the investigated use in the treatment of GvHD or Crohn's, beclometasone acts by binding to interleukin-13 to inhibit cytokines, which in turn inhibits inflammatory chemicals downstream.

CLOTRIMAZOLE:
Clotrimazole interacts with yeast 14-α demethylase, a cytochrome P-450 enzyme that converts lanosterol to ergosterol, an essential component of the membrane. In this way, clotrimazole inhibits ergosterol synthesis, resulting in increased cellular permeability. Clotrimazole may also inhibit endogenous respiration, interact with membrane phospholipids, inhibit the transformation of yeasts to mycelial forms and the uptake of purine, impair triglyceride and/or phospholipid biosynthesis, and inhibit the movement of calcium and potassium ions across the cell membrane by blocking the ion transport pathway known as the Gardos channel.

INDICATIONS & USAGE:
Fungal infections of skin with eczematous features in hairy or intertriginous areas & Dandruff with severe pruritus; *Tinea Capitis, Tinea Corporis, Tinea Barbae, Tinea Cruris, Tinea Manum, Tinea Unguium, Tinea Pedis, Tinea Versicolor, Vulvovaginal Candidiasis, Candidal Nappy Rash, Candidal Paronychia*.

***CLOMIRET cream** is suitable for both adults and children of at least 3 years of age.

USE IN SPECIAL POPULATIONS:
Pregnancy: This medicine should not be used during pregnancy unless considered essential by your doctor. If it is prescribed by your doctor it should not be used on large areas of skin, underneath airtight dressings, or for prolonged periods of time. Consult your doctor for further information.
Lactation: This medicine should not be used during breastfeeding unless considered essential by the doctor. If it is prescribed by your doctor it should not be used on large areas of skin, underneath airtight dressings or for prolonged periods of time. If it is applied to the breasts it should be washed off carefully before breastfeeding and then reapplied afterwards.

DOSAGE & APPLICATION:
Apply to affected areas 2-3 times daily.

CONTRAINDICATIONS:
- Hypersensitivity to any of the ingredients.
- Rosacea, Acne, Peri-Oral Dermatitis, Tuberculosis of the skin and varicose ulcers.
- Skin lesions caused by infections with viruses (e.g. Herpes Simplex, Vaccinia or Varicella), fungi (e.g. Candida, Tinea) or bacteria (e.g. Impetigo), syphilitic skin lesions.
- Corticosteroids have been shown to be teratogenic in animals following dermal application. As these agents are absorbed percutaneously, teratogenicity following topical application cannot be excluded. Therefore **CLOMIRET Cream** should not be used during pregnancy.
- The use of **CLOMIRET Cream** is not recommended during breast feeding.

SPECIAL PRECAUTIONS AND WARNING:
- Do not ingest **CLOMIRET Cream**.
- Do not apply this cream to any damaged skin. This includes skin which has been burnt, scraped, or cut in any way.
- Never share this cream with anybody else, even if they are suffering from the same condition as you.
- Before you begin using this cream always inform your prescribing physician if you are pregnant, breastfeeding, trying to conceive, are taking any other medication, or if you suffer from any other kind of medical condition or disease.
- Should be used for short courses only, as prolonged and intensive treatment may cause local atrophic changes in the skin such as stria, thinning, loss of elasticity, dilatation of the superficial blood vessels, telangiectasia and ecchymosis.
- Topical corticosteroid preparations should be used with caution near the eyes; application to the eyelids may cause glaucoma.
- This medicine should not be used for longer than five days on the face or in children.
- For external use only; do not use in or around the eye.
- Before administering **CLOMIRET Cream** wash hands and the area of skin to be treated, allowing both to dry.

OVERDOSE & TREATMENT:
Excessive or prolonged use of **CLOMIRET Cream** may result in systemic absorption of steroid and complications of steroid therapy, especially growth retardation in children, suppression of pituitary adrenal function, increased susceptibility to infection, hyperglycaemia, Cushingoid state and benign intracranial hypertension. Cessation of treatment with appropriate symptomatic and supportive treatment is indicated.

ADVERSE DRUG REACTIONS:
Possible side effects can include: Dry and/or peeling skin, Itchy or irritated skin, Perioral dermatitis, Edema, Erythema
Seek immediate medical attention if you suffer an allergic reaction. Possible symptoms to watch out for may include: Skin Rashes, Hives, Swelling, Difficulty breathing, Trouble swallowing.

STORAGE:
Keep this medication in the container it came in, tightly closed, and out of reach of children. Store it in cool & dark place. ***DO NOT FREEZE.***

Strains of fungi having a natural resistance to clotrimazole are rare. Only a single isolate of Candida guilliermondi has been reported to have primary resistance to clotrimazole.
No single-step or multiple-step resistance to clotrimazole has developed during successive passages of Candida albicans and Trichophyton mentagrophytes. No appreciable change in sensitivity was detected after successive passage of isolates of C. albicans, C. krusei, or C. pseudotropicalis in liquid or solid media containing clotrimazole. Also, resistance could not be developed in chemically induced mutant strains of polyene-resistant isolates of C. albicans. Slight, reversible resistance was noted in three isolates of C. albicans tested by one investigator. There is a single report that records the clinical emergence of C. albicans strain with considerable resistance to flucytosine and miconazole, and with cross-resistance to clotrimazole, the strain remained sensitive to nystatin and amphotericin B.

In studies of the mechanism of action, the minimum fungicidal concentration of clotrimazole caused leakage of intracellular phosphorus compounds into the ambient medium with concomitant breakdown of cellular nucleic acids and accelerated potassium efflux. Both these events began rapidly and extensively after addition of the drug.

Following topical and vaginal administration, however, clotrimazole appears to be minimally absorbed.

Six hours after the application of radioactive clotrimazole 1% cream and 1% solution onto intact and acutely inflamed skin, the concentration of clotrimazole varied from 100 mcg/cm3 in the stratum corneum to 0.5 to 1 mcg/cm3 in the stratum reticulare, and 0.1 mcg/cm3 in the subcutis. No measurable amount of radioactivity (≤ 0.001 mcg/mL) was found in the serum within 48 hours after application under occlusive dressing of 0.5 mL of the solution or 0.8 g of the cream. Only 0.5% or less of the applied radioactivity was excreted in the urine.

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