Drugfield Pharmaceuticals Limited

SUMMARY OF PRODUCT CHARACTERISTICS

(SmPC)

BETROSIL® CREAM

(Tioconazole 1%$^{W}/_{W}$)

1. NAME OF THE MEDICINAL PRODUCT

BETROSIL® CREAM (Tioconazole 1%$^{W}/_{W}$)

2. QUALITATIVE AND QUANTITATIVECOMPOSITION

Each ml contains Tioconazole 1% $^{W}/_{W}$

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cream (semi-solid)

4. Clinical particulars

4.1 Therapeutic indications

Betrosil is indicated for topical treatment of skin infections due to susceptible dermatophyes

++or yeas such as Tinea corporis, Tinea capitis, and Tinea pedis .

Betrosil cream also show significant anti bacterial activity against Staphylococcus and Streptococcus spp. It may therefore be used in mycoses secondarily infected with such bacteria.

4.2 Posology and method of administration

Posology

Important Dosage and Administration Instructions

- Apply some cream to the lesions twice daily.
- Rub the cream with your finger into the skin until it has fully penetrated.
- The duration of therapy varies from 2 to 6 weeks depending on the localization and the severity of the lesion.
- Treatment should continue at least once a week after disappearance of all signs and symptoms.

Method of administration

Topical administration

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients in the excipients listed in section 6.1.
The following conditions should not be treated with betamethasone valerate:
• Untreated cutaneous infections

- Rosacea
- Acne vulgaris
- Pruritus without inflammation
- Perianal and genital pruritus
- Perioral dermatitis
- Primary cutaneous viral infections
- Primary infected skin lesions caused by infection with fungi or bacteria
- Primary or secondary infections due to yeasts
- Secondary infections due to Pseudomonas or Proteus species
- Otitis externa when the ear drum is perforated, because of the risk of ototoxicity.

Betamethasone valerate is contraindicated in dermatoses in infants under one year of age, including dermatitis.

4.4 Special warnings and precautions for use

Hypersensitivity: Betamethasone valerate-neomycin sulphate should be used with caution in patients with a history of local hypersensitivity to betamethasone, neomycin or to any of the excipients in the preparation. Local hypersensitivity reactions (see Adverse Reactions) may resemble symptoms of the condition under treatment. Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. Although this is less likely to occur with topically applied betamethasone valerate-neomycin sulphate. If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further. Reversible hypothalamic-pituitary-adrenal (HPA) axis suppression Manifestations of hypercortisolism (Cushing's syndrome) and

reversible hypothalamic-pituitary-adrenal (HPA) axis suppression can occur in some individuals as a result of increased systemic absorption of topical corticosteroids. If either of the above are observed, withdraw the drug gradually by reducing the frequency of application, or by substituting a less potent corticosteroid. Abrupt withdrawal of treatment may result in glucocorticosteroid insufficiency (see Adverse Reactions).Risk factors for increased corticosteroidal systemic effects are:•Potency and formulation of topical corticosteroid

•Duration of exposure •Application to a large surface area

•Use on occluded areas of skin e.g. on intertriginous areas or under occlusive dressings (nappies may act asan occlusive dressing)

•Increasing hydration of the stratum corneum

•Use on thin skin areas such as the face

•Use on broken skin or other conditions where the skin barrier may be impaired. Use in children in comparison with adults, children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic adverse effects. This is because children have an immature skin barrier and a greater surface area to body weight ratio compared with adults. In children under 12 years of age, long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal suppression can occur.

Infection : Extension of infection may occur due to the masking effect of the steroid. Any spread of infection requires withdrawal of topical corticosteroid therapy and administration of appropriate systemic antimicrobial therapy. Infection risk with occlusio n Bacterial infection is encouraged by the warm, moist conditions within skin folds or caused by occlusive dressings. When using occlusive dressings, the skin should be cleansed before a fresh dressing is applied.

Chronic leg ulcers : Topical corticosteroids are sometimes used to treat the dermatitis around chronic leg ulcers. However, this use may be associated with a higher occurrence of local hypersensitivity reactions and an increased risk of local infection

4.5 Interaction with other medicinal products and other forms of interaction

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. Following significant systemic absorption, neomycin sulphate can intensify and prolong the respiratory depressant effects of neuromuscular blocking agents. Possibility of cumulative toxicity should be considered when neomycin sulphate is applied topically in combination with systemic aminoglycoside therapy.

4.6 Pregnancy and Lactation

Pregnancy

There are limited data from the use of topical betamethasone valerate-neomycin sulphate in pregnant women. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development (see Non-clinical information). However, neomycin present in maternal blood can cross the placenta and may give rise to a theoretical risk of foetal toxicity (see Non-clinical information).Thus use of betamethasone valerate-neomycin sulphate is not recommended in pregnancy.

Lactation

Use of betamethasone valerate-neomycin sulphate is not recommended in lactation

Females and Males of Reproductive Potential

There are no data in humans to evaluate the effect of topical betamethasone valerate-neomycin sulphate on fertility.

4.7 Effects on ability to drive and use machines

There have been no studies to investigate the effect of betamethasone valerate on driving performance or the ability to operate machinery. A detrimental effect on such activities would not be anticipated from the adverse reaction profile of topical betamethasone valerate.

4.8 Undesirable effects

Immune System Disorders: Very rare

Local hypersensitivity

Endocrine Disorders: Very rare

Hypothalamic-pituitaryadrenal (HPA) axis: suppression(see also Skin and Subcutaneous Tissue Disorders),Cushingoid features (e.g. moon face, central obesity), delayed weight gain/growth retardation in children, osteoporosis, glaucoma, hyperglycaemia/glucosuria, cataract, hypertension, increased weight/obesity, decreased endogenous cortisol levels Skin and Subcutaneous

Tissue Disorders Common: Pruritus, local skin burning/pain of skinVery rare:Allergic contact dermatitis/dermatitis, erythema, rash, urticaria, pustular psoriasis (see Warnings and Precautions), skin thinning* / skin atrophy*, skin wrinkling*, skin dryness*, striae*, telangiectasias*, pigmentation changes*, hypertrichosis, exacerbation of underlying symptoms, alopecia*, trichorrhexis*General Disorders and Administration Site ConditionsVery rare: Application site irritation/pain*Skin features of hypothalamicpituitary-adrenal (HPA) axis suppression.

4.9 Overdose

Symptoms and Signs:

Topically applied betamethasone valerate-neomycin sulphate 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 (see Adverse Reactions).

Treatment

In the event of chronic overdose or misuse, topical corticosteroids should be withdrawn gradually by reducing the frequency of application, or by substituting a less potent corticosteroid, because of the risk of glucocorticosteroid insufficiency.Consideration should also be given to significant systemic absorption of neomycin sulphate (see Warnings and Precautions). If this is suspected, use of the product should be stopped and the patient's general status, hearing acuity, renal and neuromuscular functions should be monitored. Blood levels of neomycin sulphate should also be determined. Haemodialysis may reduce the serum level of neomycin sulphate.Further management should be as clinically indicated or as recommended by the National Poisons Centre, where available.

5. PHARMACOLOGICALPROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Benzomorphan derivatives}, ATC code: NO2ADO1

Mechanism of Action

Topical corticosteroids act as anti-inflammatory agents via multiple mechanisms to inhibit late phase allergic reactions including decreasing the density of mast cells, decreasing chemotaxis and activation of eosinophils, decreasing cytokine production by lymphocytes, monocytes, mast cells and eosinophils, and inhibiting the metabolism of arachidonic acid. Neomycin Sulphate is actively transported across the bacterial cell membrane, binds to a specific receptor protein on the 30 S subunit of bacterial ribosomes, and interferes with an initiation complex between mRNA (messenger RNA) and the 30 S subunit, inhibiting protein synthesis. DNA may be misread, thus producing nonfunctional proteins; polyribosomes are split apart and are unable to synthesize protein.

Pharmacodynamics

Topical corticosteroids have anti-inflammatory, antipruritic, and vasoconstrictive properties.

Tioconazole is a broad-spectrum imidazole antifungal agent that inhibits the growth of human pathogenic yeasts. Tioconazole exhibits fungicidal activity in vitro against Candida albicans, other species of the genus Candida, and against Torulopsis glabrata. Tioconazole prevents the growth and function of some fungal organisms by interfering with the production of substances needed

to preserve the cell membrane. This drug is effective only for infections caused by fungal organisms. It will not work for bacterial or viral infections.

5.2 Pharmacokinetic properties

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. Although not absorbed through intact skin, topical neomycin is readily absorbed from large denuded, burned, or granulating areas. Greater and more rapid absorption occurs with neomycin cream than with the ointment.

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.

5.3 Preclinical safety data

Subcutaneous administration of betamethasone valerate to mice or rats at doses ≥0.1 mg/kg/day or rabbits at doses ≥12 micrograms/kg/day during pregnancy produced foetal abnormalities including cleft palate and intrauterine growth retardation.

The effect on fertility of betamethasone valerate has not been evaluated in animals.

6. PHARMACEUTICALPARTICULARS

6.1 List of excipients

Liquid Paraffin (Heavy)
Ceto-stearyl Alcohol
Stearic Acid
Cetomacrogol 1000

Propylene Glycol

Benzyl Alcohol

Purified Water

6.2 Incompatibilities

None have been reported or are known

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30°C in tight container protected from light and moisture.

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

Betamethasone N Cream is presented in 20g printed aluminum tube with a screw cap packed in hardboard carton with leaflet enclosed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. APPLICANT/MANUFACTURER

Drugfield Pharmaceuticals Limited
Lynson Chemical Avenue Km38,
Lagos-Abeokuta Expressway
Sango-Otta, Ogun State, Nigeria
Tel: +2348033513989
Email:Info@drugfieldpharma.com