Marine LIFESCIENCES

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT:

Norbaclear (Clotrimazole USP + Betamethasone Dipropionate USP +Neomycin USP Cream)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Cream contains:

1. Clotrimazole USP.....1%W/W
2. Betamethasone Dipropionate USP
   Eq. To Betamethasone… 0.05%W/W
3. Neomycin Sulphate USP
   Eq.to Neomycin Base 0.5%W/W
   Chlorocresol……0.1%w/w
   (Preservative)
   Cream Base.....q.s

3. PHARMACEUTICAL FORM:

Cream, 1%/0.05%/0.5% (base).
Smooth, uniform, white to off-white cream.

4. CLINICAL PARTICULARS:

Therapeutic Indication:

Short-term topical treatment of tinea infections due to Trichophyton rubrum; T.mentagrophytes; Epidermophyton floccusum and Microsporum canis; candidiasis due to Candida albicans.
Treating certain fungal skin infections, including ringworm, athlete's foot, and jock itch. It also relieves redness, swelling, and itching associated with infection.
Clotrimazole/Betamethasone cream is an antifungal and corticosteroid combination. It works by weakening the cell membrane of certain fungi. It also acts as an anti-inflammatory and anti-itching agent.
Clotrimazole and Betamethasone Dipropionate cream is a combination of an azole antifungal and corticosteroid and is indicated for the topical treatment of symptomatic inflammatory tinea pedis, tinea cruris,and tinea corporis due to Epidermophyton floccosum, Trichophyton mentagrophytes, and Trichophyton rubrum in patients 17 years and older.
Neomycin Sulphate is indicated for the treatment of corticosteroid-responsive dermatoses with secondary infection. It has not been demonstrated that this steroid-antibiotic combination provides greater benefit than the steroid component alone after 7 days of treatment.

Posology and method of administration:

Mode Of Action:

Apply to affected area 2-3 times a day with gentle rub.To be use under medical supervision.

Posology

Adults and children over the age of 12 years. Topical administration twice daily for two weeks (tinea cruris,tinea corporis and candidiasis) or for four weeks (tinea pedis).

Paediatric population

Norbaclear cream is not recommended for children under the age of twelve years.

Method of administration

Topical administration only.

Treatment of tinea corporis or tinea cruris:

Apply a thin film of Clotrimazole and Betamethasone Dipropionate cream into the affected skin areas twice aday for one week.
Do not use more than 45 grams per week. Do not use with occlusive dressings.

If a patient shows no clinical improvement after 1 week of treatment with Clotrimazole and Betamethasone Dipropionate cream, the diagnosis should be reviewed.
Do not use longer than 2 weeks.

Treatment of tinea pedis:

Gently massage a sufficient amount of Clotrimazole and Betamethasone Dipropionate cream into the affectedskin areas twice a day for two weeks.
Do not use more than 45 grams per week. Do not use with occlusive dressings.

If a patient shows no clinical improvement after 2 weeks of treatment with Clotrimazole and Betamethasone Dipropionate cream, the diagnosis should be reviewed.
Do not use longer than 4 weeks.

Clotrimazole and Betamethasone Dipropionate cream is for topical use only. It is not for oral, ophthalmic, or intravaginal use.
Avoid contact with eyes. Wash hands after each application.

Contraindications:

Clotrimazole, Betamethasone Dipropionate and Neomycin cream is contraindicated in patients who are sensitive to Clotrimazole, Betamethasone Dipropionate, other corticosteroids or imidazole, or to any ingredient in these preparations.

Special warnings and precautions for use:

Local and systemic toxicity is common especially following long continued use on large areas of damaged skin and in flexures. If used on the face, courses should be limited to 5 days.

NORBACLEAR CREAM SHOULD NOT BE USED WITH OCCLUSIVE DRESSING.

Topical corticosteroids may be hazardous in psoriasis for a number of reasons including rebound relapses following the development of tolerance, risk of generalised pustular psoriasis and local and systemic toxicitydue to impaired barrier function of the skin.

Any of the side effects that are reported following systemic use of corticosteroids, including adrenal suppression, manifestation of Cushing's syndrome, hyperglycemia, and glycosuria may also occur with topical steroids, especially in infants and children.

Norbaclear Cream is not intended for ophthalmic use.

Visual disturbance may be reported with systemic and topical (including, intranasal, inhaled and intraocular) corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes of visual disturbances which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy(CSCR) which have been reported after use of systemic and topical corticosteroids.

Paediatric population

- Long term continuous therapy should be avoided in all children irrespective of age.
- Norbaclear cream should not be used with adhesive dressing.
- The safety and effectiveness of Norbaclear cream has not been established in children below the age of 12.
- If used on children, courses should be limited to 5 days.

Hypothalamic-pituitary adrenal axis suppression, Cushing's syndrome and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestation of adrenal suppression in childreninclude linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestation of intracranial hypertension include bulging fontanelles, headaches, andbilateral papilloedema.

Interaction with other medicinal products and other forms of interaction:

There are no known interactions

Fertility, pregnancy and lactation:

Pregnancy

Advise pregnant women that Clotrimazole and Betamethasone Dipropionate cream may increase the risk of having a low birth weight infant and to use Clotrimazole and Betamethasone Dipropionate cream on the smallest area of skin and for the shortest duration possible.

Lactation

Advise a woman to use Clotrimazole and Betamethasone Dipropionate cream on the smallest area of skin andfor the shortest duration possible while breastfeeding. Advise breastfeeding women not to apply Clotrimazoleand

Betamethasone Dipropionate cream directly to the nipple and areola to avoid direct infant exposure

Effects on ability to drive and use machines:

Norbaclear cream has no influence on the ability to drive and use machines.

Undesirable effects

Adverse reactions reported for Norbaclear include: burning and stinging, maculopapular rash, oedema, paraesthesia and secondary infection.

Reported reactions to Clotrimazole include erythema, stinging, blistering, peeling, oedema, pruritus, urticaria and general irritation of the skin.

Reactions to Betamethasone Dipropionate include: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hyper pigmentation, hypo pigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae miliaria, capillary fragility(ecchymoses), blurred vision and sensitisation.

In children receiving topical corticosteroids, Hypothalamic-pituitary adrenal (HPA) axis suppression (HPA) axis suppression, Cushing's syndrome and intracranial hypertension have been reported.

5. Pharmacological properties:

Pharmacodynamic properties:

A) Norbaclear Cream contains the Dipropionate ester of Betamethasone, a glucocorticoid exhibiting the general properties of corticosteroids, and Clotrimazole which is an imidazole antifungal agent.
Topical corticosteroids are effective in the treatment of a range of dermatomes because of their anti-inflammatory anti-pruritic and vasoconstrictive actions.
Clotrimazole is a broad-spectrum antifungal agent with activity against Trichomones, Staphylococci and Bacteroides.
Neomycin Sulphate is a topical corticosteroids share anti-inflammatory, anti-pruritic and vasoconstrictiveactions

B) Clotrimazole and Betamethasone Dipropionate
Clotrimazole and Betamethasone Dipropionate Cream, USP has been shown to be at least as effective as clotrimazole alone in a different cream vehicle. No comparative studies have been conducted with Clotrimazole and Betamethasone Dipropionate Lotion and Clotrimazole alone. Use of corticosteroids in the treatment of a fungal infection may lead to suppression of host inflammation leading to worsening or decreased cure rate.

Clotrimazole
Skin penetration and systemic absorption of Clotrimazole following topical application of Clotrimazole and Betamethasone Dipropionate Cream or Lotion have not been studied. The following information was obtained using 1% Clotrimazole cream and solution formulations. Six hours after the application of radioactive clotrimazole 1% cream and 1% solution onto intact and acutely inflamed skin, the concentrationof clotrimazole varied from 100 mcg/cm3 in the stratum corneum, to 0.5 to 1 mcg/cm3 in the reticular dermis,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.
Neomycin Sulphate: Topical corticosteroids share anti-inflammatory, anti-pruritic and vasoconstrictive actions

Microbiology
Mechanism of Action

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.

Activity In Vivo

Clotrimazole has been shown to be active against most strains of the following dermatophytes, both *in vitro* and in clinical infections.
Activity In Vitro

In vitro, clotrimazole has been shown to have activity against many dermatophytes, but the clinical significance of this information is unknown.

Drug Resistance: Strains of dermatophytes having a natural resistance to clotrimazole have not been reported. Resistance to azoles including clotrimazole has been reported in some Candida species. No single-step or multiple-step resistance to clotrimazole has developed during successive passages of Trichophyton mentagrophytes.

Betamethasone Dipropionate

Betamethasone Dipropionate, a corticosteroid, has been shown to have topical (dermatologic) and systemic pharmacologic and metabolic effects characteristic of this class of drugs.

Neomycin Sulphate:

The mechanism of anti-inflammatory activity of the topical corticosteroids is unclear. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinicalefficacies of the topical corticosteroids. There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.

Pharmacokinetic properties:

a) Norbaclear is intended for treatment of skin conditions and is applied topically. Thus there are minimal pharmacokinetic aspects related to bioavailability at the site of action.

Clotrimazole penetrates the epidermis after topical administration but there is little, if any, systemicabsorption.

The extent of percutaneous absorption of topical corticosteroids is determined by many factors including vehicle, integrity of skin and use of occlusion.

Systemically absorbed topical corticosteroids are bound to plasma proteins metabolised in the liver andexcreted by the kidneys. Some corticosteroids and their metabolites are also excreted in the bile.

b) Skin penetration and systemic absorption of **clotrimazole and betamethasone** dipropionate followingtopical application of clotrimazole and betamethasone dipropionate cream has not been studied.
The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including thevehicle, 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.

Preclinical safety data:

Not available.

6 Pharmaceutical particulars

List of excipients;

1 Perfume Fragrance B 2225 IHS
2 Titanium Dioxide BP (MICRONISED)
3 Cetamacrogal 1000 (CETODET 500) IHS
4 Cetosteryl Alcohol BP
5 Light Liquid Paraffine BP
6 Propylene Glycol USP
7 White Soft Paraffin BP
8 Para Meta Cresol BP
9 Methyl Paraben BP
10 Propyl Paraben BP
11 Di.Sodium Hydrogen Orthophosphate (ANHY) BP
12 Di. Sodium EDTA BP
13 Sodium Hydrogen Orthophospahte BP

Incompatibilities: Not applicable.

Shelf life: 36 Months

Nature and contents of container: Lami tube of 30gm.

Special precautions for disposal and other handling:

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F).Keep out of reach of children.

ATTENTION PHARMACIST: Dispense with enclosed Patient Information Leaflet.

ATTENTION PATIENT: See Patient Information Leaflet before using this product.

FOR TOPICAL USE ONLY. NOT FOR OPHTHALMIC, ORAL OR INTRAVAGINAL USE. NOT RECOMMENDED
FOR PATIENTS UNDER THE AGE OF 17 YEARS AND NOT RECOMMENDED FOR DIAPER DERMATITIS.

7 Applicant/manufacturer:

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