NAME OF THE MEDICINAL PRODUCT

DERMACOMBIN CREAM
DERMACOMBIN OINTMENT

QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mg/g triamcinolone acetonide, 100,000 units/g nystatin, 2.5 mg/g neomycin (as sulphate), 0.25 mg/g gramicidin

Excipients:
Cream: purified water, petrolatum white, cetomacrogol emulsifying wax, paraffin liquid, sodium phosphate dibasic, propylene glycol, citric acid, ethyl alcohol 95%, perfume, methyl paraben, propyl paraben.
Ointment: Paraffin liquid, polyethylene oxidized wax**.**

INDICATIONS AND CLINICAL USE

For the relief of corticosteroid-responsive inflammatory or pruritic dermatoses caused, threatened or complicated by infection due to bacteria and/or candida.

Dermacombin Cream and Dermacombin Ointment contain antibiotic ingredients, gramicidin and neomycin. To reduce the development of drug-resistant bacteria and maintain the effectiveness of gramicidin and neomycin, Dermacombin Cream and Dermacombin Ointment should only be used for the authorized indication and clinical use.

DOSAGE AND ADMINISTRATION

Posology

Apply a small quantity two or three times daily. Do not apply more than prescribed by physician. For external use only.

CONTRAINDICATIONS

Dermacombin Cream and Dermacombin Ointment are contraindicated as follow:
In Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see "**QUALITATIVE AND QUANTITATIVE COMPOSITION"**.

- In Tuberculous and most viral lesions of the skin (including herpes simplex, vaccinia and varicella) and fungal skin lesions except candidiasis.
- In primary skin infections.
- For ophthalmic use.
- For application to the external auditory canal of patients with perforated eardrums or patients with otitis media.

- As Occlusive therapy in patients with atopic dermatitis.

WARNINGS AND PRECAUTIONS

General

Patients should be advised to inform subsequent physicians of the prior use of corticosteroids. Dermacombin Cream and Dermacombin Ointment should not be used under occlusive dressings (**see ADVERSE REACTIONS**).

Cardiovascular

Topical corticosteroids should be used with caution in patients with stasis dermatitis and other skin diseases associated with impaired circulation. If a symptomatic response is not noted within 7 days, the patient should be re-evaluated. Prolonged use of topical antibiotics should be avoided.

Endocrine and Metabolism

Although adrenal suppression and other systemic adverse effects are rare with topical corticosteroid preparations, their possible occurrence must be kept in mind, particularly when these preparations are used over large areas or for an extended period of time. Prolonged use may lead to steroid withdrawal when the medication is discontinued.

Because of the potential hazard of nephrotoxicity and ototoxicity, avoid prolonged use or the use of large amounts in the treatment of skin infections following burns, tropic ulceration and other conditions when absorption of neomycin is possible.

Gramicidin absorption following topical administration is unlikely; however, hemolysis may occur should the drug enter the blood. If gramicidin is allowed in close proximity to the sub- arachnoid space, a chemical arachnoiditis may occur (**see ADVERSE REACTIONS**).

Ophthalmologic

Topical corticosteroids should be used with caution on lesions close to the eye. Posterior subcapsular cataracts have been observed following systemic corticosteroid therapy (**see ADVERSE REACTIONS**).

Sensitivity

Hypensitivity of nystatin is extremely uncommon. Sensitivity reactions following the topical use of gramicidin or triamcinolone acetonide are rarely encountered. Burning, itching, irritation, dryness, erythema, folliculitis, hypertrichosis, acnelform eruptions, tinnitus, deafness and hypopigmentation have been reported with topical corticosteroids.

An increase in the incidence of patients allergic to neomycin has been reported in literature.

Neomycin itself may cause an allergic otitis extena. Systemic neomycin toxicity has occurred rarely following topical administration; tinnitus and deafness have been reported (**see ADVERSE REACTIONS**).

Susceptibility/Resistance

Development of Drug Resistant Bacteria: Prescribing Dermacombin Cream and Dermacombin Ointment in the absence of the authorized indications is unlikely to provide benefit to the patient and risks the development of resistant organisms.

Potential for Microbial Overgrowth: As with any antibiotic preparation, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi other than candida. Constant observation of the patient is essential. Should superinfection due to non-susceptible organisms occur, Dermacombin Cream and Dermacombin Ointment should be discontinued and appropriate therapy instituted.

Skin

When steroid preparations are used for long periods in intertriginous areas or under occlusive dressings, striae may occur. Damage to collagen, which constitutes a middle layer of the tympanic membrane, may occur. Delayed healing and systemic effects, including adrenal suppression and subcapsular cataracts, may occur if absorbed in appreciable amounts.

If local irritation or sensitization develops, Dermacombin Cream and Dermacombin Ointment should be discontinued and appropriate therapy instituted. Prolonged use of corticosteroids may produce atrophy of the skin and subcutaneous tissues, particularly on flexor surfaces and on the face. If this is noted, discontinue the use of the product.

The use of occlusive dressings is not recommended with products containing anti-infective agents (**see ADVERSE REACTIONS**).

Special Populations

Pregnant Women: The safety of Topical Corticosteroid preparations during pregnancy and lactation has not been established. The potential benefit of the use of topical corticosteroids during pregnancy should be weighed against possible hazards to the fetus.

Nursing Women: It is not known whether Topical Corticosteroids are excreted in human milk. Topical Corticosteroids should not be used during breast feeding unless the potential benefit justifies the potential risk to the nursing infant.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

The following adverse skin reactions have been reported with the use of topical corticosteroids: dryness, itching, burning, local irritation, skin atrophy, striae, atrophy of subcutaneous tissue, folliculitis, acneiform eruptions, hypertrichosis,

change in skin pigmentation and telangiectasia. Adrenal suppression has also been reported following topical corticosteroid therapy. Posterior subcapsular cataracts have been observed following systemic corticosteroid therapy. Hypersensitivity reactions to neomycin, gramicidin, and nystatin have been reported. Systemic neomycin toxicity has occurred rarely following topical administration; tinnitus and deafness have also been reported. Overgrowth of non-susceptible organisms has occurred.

Reporting of suspected adverse reactions
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form:
http://sideeffects.health.gov.il

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Percutaneous absorption of corticosteroids can occur, especially if used over a large area for prolonged periods of time. If large amounts of corticosteroids are absorbed, toxic effects may include mild reversible suppression of adrenal function, ecchymoses of the skin, peptic ulceration, hypertension, aggravation of infections, hirsutism, acne, edema and muscle weakness due to protein depletion. Prolonged use of large amounts of Dermacombin Cream and Ointment would likely increase the absorption of neomycin which in turn would enhance the potential for nephrotoxicitiy and ototoxicity as well as ulceration.

No specific antidote is available, treatment should be primarily symptomatic and administration of the cream or ointment discontinued.

ACTION AND CLINICAL PHARMACOLOGY

Dermacombin Cream and Dermacombin Ointment (Triamcinolone Acetonide, Nystatin, Neomycin Sulfate and Gramicidin) provide relief from the itching and burning associated with secondarily infected inflammatory conditions by virtue of:

- the anti-inflammatory antipruritic and vasoconstrictive properties of triamcinolone acetonide;
- the broad spectrum anti-bacterial activity of neomycin and gramicidin;
- the anti-candidal activity of nystatin.

PHARMACEUTICAL INFORMATION

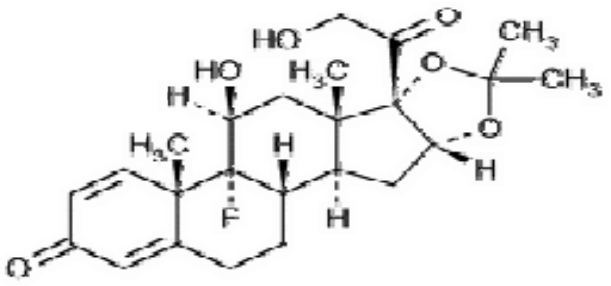
Drug Substances

Proper name: Triamcinolone Acetonide

Chemical name: Pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16,17-[(1- methylethylidene)bis(oxy)]-, (11 β ,16)-. α
9-Fluoro-11 β ,16 ,17,21-tetrahydroxypregna-1,4-diene-3,20-dione cyclic 16,17-acetal with acetone

Molecular formula and molecular mass: C24H31FO6
434.50

Structural formula:



Physicochemical properties:

Description: White to cream-colored, crystalline powder, having not more than a slight odor.

Solubility: Sparingly soluble in dehydrated alcohol, in chloroform, and in methanol; practically insoluble in water.

Proper name: Neomycin Sulfate Physicochemical properties:
Description: White to slightly yellow powder, or cryodesiccated solid. Is odorless or practically so and is hygroscopic. Its solutions are dextrorotatory.

Solubility: Freely soluble in water; very slightly soluble in alcohol; insoluble in acetone, in chloroform, and in ether.

Proper name: Gramicidin Physicochemical properties:
Description: White or practically white, odorless, crystalline powder. Solubility: Soluble in alcohol; insoluble in water.
Melting Temperatures: Not lower the 229 °C, determined after drying.

Proper name: Nystatin Physicochemical properties:
Description: Yellow to light tan powder, having an odor suggestive of cereals. Is hygroscopic, and is affected by long exposure to light, heat, and air.

Solubility: Freely soluble in dimethylformamide and in dimethyl sulfoxide; sparingly to slightly soluble in methanol, in *n*-propyl alcohol, and in *n*- butyl alcohol; practically insoluble in water and in alcohol; insoluble in chloroform and in ether.

pH: Between 6.0 and 8.0, in a 3% aqueous suspension

STORAGE AND STABILITY

Store at a cool place, at temperature below 25 °C.

SHELF LIFE

The expiry date of the products is printed on the package materials.

Shelf-life after first opening: 6 months

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dermacombin Cream is a light yellow, homogenous, water washable cream.
Dermacombin Ointment is a yellow, homogenous oily ointment.

List of excipients
Dermacombin Cream: purified water, petrolatum white, cetomacrogol emulsifying wax, paraffin liquid, sodium phosphate dibasic, propylene glycol, citric acid, ethyl alcohol 95%, perfume, methyl paraben, propyl paraben.
Dermacombin Ointment: paraffin liquid, polyethylene oxidized wax.

Dermacombin Cream is available in 5g and 15 g aluminium tubes.
Dermacombin Ointment is available in 5 g and 15 g aluminium tubes.

MARKETING AUTHORISATION HOLDER AND MANUFACTURER

TARO PHARMACEUTICAL INDUSTRIES LTD.
14 Hakitor ST. Haifa Bay 2624761

MARKETING AUTHORISATION NUMBERS

Dermacombin cream 133.54.23775
Dermacombin ointment 015.28.24536

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