NUDERMRXPAK 60- dimethicone, calcipotriene
NuCare Pharmaceuticals,Inc.

FOR TOPICAL DERMATOLOGIC USE ONLY.

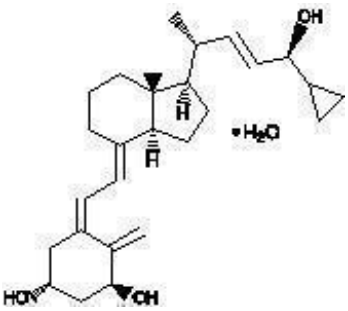
Rx only

Not for Ophthalmic, Oral or Intravaginal Use.

DESCRIPTION

Calcipotriene Cream, 0.005% contains calcipotriene monohydrate, a synthetic vitamin D_3 derivative, for topical dermatological use.

Chemically, calcipotriene monohydrate is (5Z,7E,22E,24S)-24-cyclopropyl-9,10-secochola-5,7,10(19),22-tetraene-1α,3β,24-triol monohydrate, with the empirical formula $C_{27}H_{40}O_3 \cdot H_2O$, a molecular weight of 430.6, and the following structural formula:



Calcipotriene monohydrate is a white or off-white crystalline substance. Calcipotriene Cream contains calcipotriene monohydrate equivalent to 50 µg/g anhydrous calcipotriene in a cream base of cetearyl alcohol, ceteth-20, diazolidinyl urea, dichlorobenzyl alcohol, dibasic sodium phosphate, edetate disodium, dl-alpha tocopherol, glycerin, mineral oil, petrolatum, and water.

CLINICAL PHARMACOLOGY

In humans, the natural supply of vitamin D depends mainly on exposure to the ultraviolet rays of the sun for conversion of 7-dehydrocholesterol to vitamin D_3 (cholecalciferol) in the skin. Calcipotriene is a synthetic analog of vitamin D_3.

Clinical studies with radiolabelled calcipotriene ointment indicate that approximately 6% (± 3%, SD) of the applied dose of calcipotriene is absorbed systemically when the ointment is applied topically to psoriasis plaques, or 5% (± 2.6%, SD) when applied to normal skin, and much of the absorbed active is converted to inactive metabolites within 24 hours of application. Systemic absorption of the cream has not been studied.

Vitamin D and its metabolites are transported in the blood, bound to specific plasma proteins. The active form of the vitamin, 1,25-dihydroxy vitamin D_3 (calcitriol), is known to be recycled via the liver and excreted in the bile. Calcipotriene metabolism following systemic uptake is rapid, and occurs via a similar pathway to the natural hormone.

CLINICAL STUDIES

Adequate and well-controlled trials of patients treated with Calcipotriene Cream have demonstrated improvement usually beginning after 2 weeks of therapy. This improvement continued with

approximately 50% of patients showing at least marked improvement in the signs and symptoms of psoriasis after 8 weeks of therapy, but only approximately 4% showed complete clearing.

INDICATIONS AND USAGE

Calcipotriene Cream, 0.005%, is indicated for the treatment of plaque psoriasis. The safety and effectiveness of topical calcipotriene in dermatoses other than psoriasis have not been established.

CONTRAINDICATIONS

Calcipotriene Cream is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation. It should not be used by patients with demonstrated hypercalcemia or evidence of vitamin D toxicity. Calcipotriene Cream should not be used on the face.

WARNINGS

Contact dermatitis, including allergic contact dermatitis, has been observed with the use of Calcipotriene Cream.

PRECAUTIONS

General

Use of Calcipotriene Cream may cause transient irritation of both lesions and surrounding uninvolved skin. If irritation develops, Calcipotriene Cream should be discontinued.

For external use only. Keep out of the reach of children. Always wash hands thoroughly after use.

Reversible elevation of serum calcium has occurred with use of topical calcipotriene. If elevation in serum calcium outside the normal range should occur, discontinue treatment until normal calcium levels are restored.

Information for Patients

Patients using Calcipotriene Cream should receive the following information and instructions:

1. This medication is to be used only as directed by the physician. It is for external use only. Avoid contact with the face or eyes. As with any topical medication, patients should wash their hands after application.
2. This medication should not be used for any disorder other than that for which it was prescribed.
3. Patients should report to their physician any signs of adverse reactions.
4. Patients that apply Calcipotriene Cream to exposed portions of the body should avoid excessive exposure to either natural or artificial sunlight (including tanning booths, sun lamps, etc.).

Carcinogenesis, Mutagenesis, Impairment of Fertility

When calcipotriene was applied topically to mice for up to 24 months at dosages of 3, 10 and 30 µg/kg/day (corresponding to 9, 30 and 90 µg/m ^{2}/day), no significant changes in tumor incidence were observed when compared to control. In a study in which albino hairless mice were exposed to both UVR and topically applied calcipotriene, a reduction in the time required for UVR to induce the formation of skin tumors was observed (statistically significant in males only), suggesting that calcipotriene may enhance the effect of UVR to induce skin tumors. Patients that apply Calcipotriene Cream to exposed portions of the body should avoid excessive exposure to either natural or artificial sunlight (including tanning booths, sun lamps, etc.). Physicians may wish to limit or avoid use of phototherapy in patients that use Calcipotriene Cream.

Calcipotriene did not elicit any mutagenic effects in an Ames mutagenicity assay, a mouse lymphoma TK

locus assay, a human lymphocyte chromosome aberration assay, or in a micronucleus assay conducted in mice.

Studies in rats at doses up to 54 µg/kg/day (324 µg/m ^{2}/day) of calcipotriene indicated no impairment of fertility or general reproductive performance.

Pregnancy

Teratogenic Effects

Studies of teratogenicity were done by the oral route where bioavailability is expected to be approximately 40-60% of the administered dose. Increased rabbit maternal and fetal toxicity was noted at 12 µg/kg/day (132 µg/m ^{2}/day). Rabbits administered 36 µg/kg/day (396 µg/m ^{2}/day) resulted in fetuses with a significant increase in the incidences of pubic bones, forelimb phalanges, and incomplete bone ossification. In a rat study, oral doses of 54 µg/kg/day (318 µg/m ^{2}/day) resulted in a significantly higher incidence of skeletal abnormalities consisting primarily of enlarged fontanelles and extra ribs. The enlarged fontanelles are most likely due to calcipotriene's effect upon calcium metabolism. The maternal and fetal calculated no-effect exposures in the rat (43.2 µg/m ^{2}/day) and rabbit (17.6 µg/m ^{2}/day) studies are approximately equal to the expected human systemic exposure level (18.5 µg/m ^{2}/day) from dermal application. There are no adequate and well-controlled studies in pregnant women. Therefore, Calcipotriene Cream should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

There is evidence that maternal 1,25-dihydroxy vitamin D $_3$ (calcitriol) may enter the fetal circulation, but it is not known whether it is excreted in human milk. The systemic disposition of calcipotriene is expected to be similar to that of the naturally occurring vitamin. Because many drugs are excreted in human milk, caution should be exercised when Calcipotriene Cream is administered to a nursing woman.

Pediatric Use

Safety and effectiveness of Calcipotriene Cream in pediatric patients have not been established. Because of a higher ratio of skin surface area to body mass, pediatric patients are at greater risk than adults of systemic adverse effects when they are treated with topical medication.

Geriatric Use

Of the total number of patients in clinical studies of calcipotriene cream, approximately 15% were 65 or older, while approximately 3% were 75 and over. There were no significant differences in adverse events for subjects over 65 years compared to those under 65 years of age. However, the greater sensitivity of older individuals cannot be ruled out.

ADVERSE REACTIONS

Clinical Trials Experience

In controlled clinical trials, the most frequent adverse experiences reported for Calcipotriene Cream, 0.005% were cases of skin irritation, which occurred in approximately 10-15% of patients. Rash, pruritus, dermatitis and worsening of psoriasis were reported in 1 to 10% of patients.

Postmarketing Experience

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The following adverse reactions associated with the use of Calcipotriene Cream have been identified

post-approval: contact dermatitis including allergic contact dermatitis.

OVERDOSAGE

Topically applied calcipotriene can be absorbed in sufficient amounts to produce systemic effects. Elevated serum calcium has been observed with excessive use of topical calcipotriene. If elevation in serum calcium should occur, discontinue treatment until normal calcium levels are restored. (See PRECAUTIONS.)

DOSAGE AND ADMINISTRATION

Apply a thin layer of Calcipotriene Cream to the affected skin twice daily and rub in gently and completely. The safety and efficacy of Calcipotriene Cream have been demonstrated in patients treated for eight weeks.

HOW SUPPLIED

Calcipotriene Cream, 0.005% is available in:

60 gram aluminum tubes (NDC 66993-877-61)

STORAGE

Store at controlled room temperature 15°C - 25°C (59°F - 77°F). Do not freeze.

Manufactured for: **Prasco Laboratories**, Mason, OH 45040 USA

Manufactured by: LEO Laboratories Ltd., Dublin 12, Ireland

To report SUSPECTED ADVERSE REACTIONS, contact LEO Pharma Inc. at 1-877-494-4536 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Revised 06/2017

Dimethicone, 118ml (68599-0203-4)

ACTIVE INGREDIENT

Dimethicone 5.0%

Purpose

Skin Protectant

KEEP OUT OF REACH OF CHILDREN

If swallowed, get medical help or contact a Poison Control Center right away.

USES

For the treatment and/or prevention of diaper rash.

Temporarily protects and helps relieve chapped or cracked skin.

WARNINGS

For external use only

DO NOT USE

- deep or puncture wounds
- animal bites
- serious burns

WHEN USING THIS PRODUCT

do not get into eyes

STOP USE AND ASK A DOCTOR IF

condition worsens

symptoms last more than 7 days or clear up and occur again within a few days

DIRECTIONS

- Cleanse skin with THERATM Moisturizing Body Cleanser or THERATM Foaming Body Cleanser
- Apply cream liberally until entire area is covered
- Apply as needed

OTHER INFORMATION

-Protect from freezing. Avoid excessive heat.

INACTIVE INGREDIENTS

Aleurites Moluccana Seed Oil, Aloe Barbadensis (Aloe Vera) Lead Juice, SAFFLEXTM (Consisting of: Calcium Pantothenate (Vitamin B5), Maltodextrin, Niacinamide (Vitamin B3), Pyridoxine HCl (Vitamin B6), Silica, Sodium Ascorbyl Phosphate (Vitamin C), Sodium Starch Octenylsuccinate, Tocopheryl Acetate (Vitamin E)), Bisabolol, Butylene Glycol, Caprylyl Glycol, Carthamus Tinctorius (Safflower) Oleosomes, Carthamus Tintorius (Safflower) Seed Oil, Cetyl Alcohol, Chlorphenesin, Dimethicone Crosspolymer, Disodium EDTA, Glycerin, Glyceryl Stearate, Lavender Ylang Fragrance, PEG-100 Stearate, Pentaery Tetra-di-t-Butyl Hydroxyhydrocinnamate, Phenoxyethanol, Purified Water, Sodium Hyaluronate, Stearic Acid, Triethanolamine, Zingiber (Ginger) Root Extract.

DIMETHICONE THERA BODY SHIELD

CALCIPOTRIENE CREAM 60G

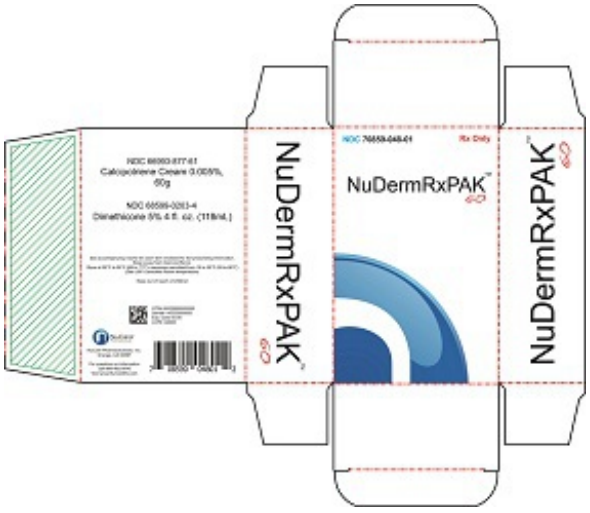
NDC 66993-877-61

Calcipotriene Cream 0.005%

Net Wt. 60 g

Rx only

NuDermRxPAK 60



NUDERMRXPAK 60

dimethicone, calcipotriene kit

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:70859-048

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:70859-048-01	1 in 1 KIT	05/24/2019	

Quantity of Parts		
Part #	Package Quantity	Total Product Quantity
Part 1	1 TUBE	60 g
Part 2	1 TUBE	118 mL

Part 1 of 2

CALCIPOTRIENE

calcipotriene cream

Product Information	
Item Code (Source)	NDC:66993-877
Route of Administration	TOPICAL

Active Ingredient/Active Moiety		
Ingredient Name	Basis of Strength	Strength
CALCIPOTRIENE (UNII: 143NQ3779B) (CALCIPOTRIENE - UNII:143NQ3779B)	CALCIPOTRIENE	50 ug in 1 g

Inactive Ingredients	
Ingredient Name	Strength
EDETATE DISODIUM (UNII: 7FLD91C86K)	
.ALPHA.-TOCOPHEROL, DL- (UNII: 7QWA1RIO01)	
DIAZOLIDINYL UREA (UNII: H5RIZ3MPW4)	
SODIUM PHOSPHATE, DIBASIC (UNII: GR686LBA74)	
CETETH-20 (UNII: I835H2IHHX)	
DICHLOROBENZYL ALCOHOL (UNII: 1NKX3648J9)	
WATER (UNII: 059QF0KO0R)	
CETOSTEARYL ALCOHOL (UNII: 2DMT128M1S)	
MINERAL OIL (UNII: T5L8T28FGP)	
GLYCERIN (UNII: PDC6A3C0OX)	
PETROLATUM (UNII: 4T6H12BN9U)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:66993-877-61	60 g in 1 TUBE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA020554	10/01/1996	

Part 2 of 2

THERA DIMETHICONE BODY SHIELD

dimethicone cream

Product Information

Item Code (Source)	NDC:68599-0203
Route of Administration	TOPICAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
DIMETHICONE (UNII: 92RU3N3Y1O) (DIMETHICONE - UNII:92RU3N3Y1O)	DIMETHICONE	50 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
CAPRYLYL GLYCOL (UNII: 00YIU5438U)	
WATER (UNII: 059QF0KO0R)	
GLYCERYL MONOSTEARATE (UNII: 230OU9XXE4)	
SAFFLOWER OIL (UNII: 65UEH262IS)	
PHENOXYETHANOL (UNII: HIE492ZZ3T)	
HYALURONATE SODIUM (UNII: YSE9PPT4TH)	
PYRIDOXINE HYDROCHLORIDE (UNII: 68Y4CF58BV)	
CETYL ALCOHOL (UNII: 936JST6JCN)	
ALOE VERA LEAF (UNII: ZY81Z83H0X)	
NIACINAMIDE (UNII: 25X51I8RD4)	
BUTYLENE GLYCOL (UNII: 3XUS85K0RA)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	
CHLORPHENESIN (UNII: I670DAL4SZ)	
STEARIC ACID (UNII: 4ELV7Z65AP)	
GINGER (UNII: C5529G5JPQ)	
CALCIUM PANTOTHENATE (UNII: 568ET80C3D)	
LEVOMENOL (UNII: 24WE03BX2T)	
PEG-100 STEARATE (UNII: YD01N1999R)	
.ALPHA.-TOCOPHEROL ACETATE, DL- (UNII: WR1WPI7EW8)	
GLYCERIN (UNII: PDC6A3C0OX)	
MALTODEXTRIN (UNII: 7CVR7L4A2D)	
SODIUM ASCORBYL PHOSPHATE (UNII: 836SJG51DR)	
TROLAMINE (UNII: 9O3K93S3TK)	
KUKUI NUT OIL (UNII: TP11QR7B8R)	

SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:68599-0203-4	118 mL in 1 TUBE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
OTC monograph final	part347	07/29/2016	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA020554	10/01/1996	

Labeler - NuCare Pharmaceuticals,Inc. (010632300)

Establishment

Name	Address	ID/FEI	Business Operations
NuCare Pharmaceuticals,Inc.		010632300	manufacture(70859-048)

Revised: 5/2019 NuCare Pharmaceuticals,Inc.