CALCIPOTRIENE- calcipotriene cream
Sandoz Inc.

Calcipotriene Cream USP, 0.005%

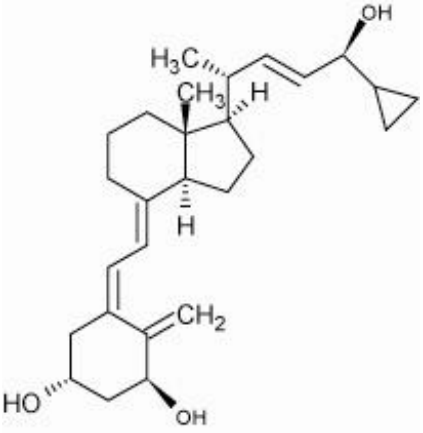
FOR TOPICAL DERMATOLOGIC USE ONLY.
Not for Ophthalmic, Oral or Intravaginal Use.

Rx Only

DESCRIPTION

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

Chemically, calcipotriene is (5Z,7E,22E,24S)-24-cyclopropyl-9,10-secochola-5,7,10(19),22-tetraene-1α,3β,24-triol, with the empirical formula $C_{27}H_{40}0_3$, a molecular weight of 412.3, and the following structural formula:



Calcipotriene is a white or off-white crystalline substance. Calcipotriene Cream, 0.005% contains calcipotriene equivalent to 50 mcg/g anhydrous calcipotriene in a cream base of ceteth-20, cetostearyl alcohol, diazolidinyl urea, dibasic sodium phosphate heptahydrate, 2,4-dichlorobenzyl alcohol, edetate disodium, glycerin, mineral oil, phosphoric acid, white petrolatum, sodium hydroxide and purified 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, 0.005% 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, 0.005% 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, 0.005% should not be used on the face.

WARNINGS

Contact dermatitis, including allergic contact dermatitis, has been observed with the use of calcipotriene cream, 0.005%.

PRECAUTIONS

General

Use of calcipotriene cream, 0.005% may cause transient irritation of both lesions and surrounding uninvolved skin. If irritation develops, calcipotriene cream, 0.005% 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, 0.005% 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, 0.005% 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 mcg/kg/day (corresponding to 9, 30 and 90 mcg/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, 0.005% 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, 0.005%.

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 mcg/kg/day (324 mcg/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 to 60% of the administered dose. Increased rabbit maternal and fetal toxicity was noted at 12 mcg/kg/day (132 mcg/m^2/day). Rabbits administered 36 mcg/kg/day (396 mcg/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 mcg/kg/day (318 mcg/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 mcg/m^2/day) and rabbit (17.6 mcg/m^2/day) studies are approximately equal to the expected human systemic exposure level (18.5 mcg/m^2/day) from dermal application. There are no adequate and well-controlled studies in pregnant women. Therefore, calcipotriene cream, 0.005% 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, 0.005% is administered to a nursing woman.

Pediatric Use

Safety and effectiveness of calcipotriene cream, 0.005% 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 to 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, 0.005% 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 USP, 0.005% to the affected skin twice daily and rub in gently and completely. The safety and efficacy of calcipotriene cream, 0.005%

have been demonstrated in patients treated for eight weeks.

HOW SUPPLIED

Calcipotriene Cream USP, 0.005% is available in:

60 gram aluminum tubes: NDC 0781-7117-35

120 gram aluminum tubes: NDC 0781-7117-83

Storage and Handling

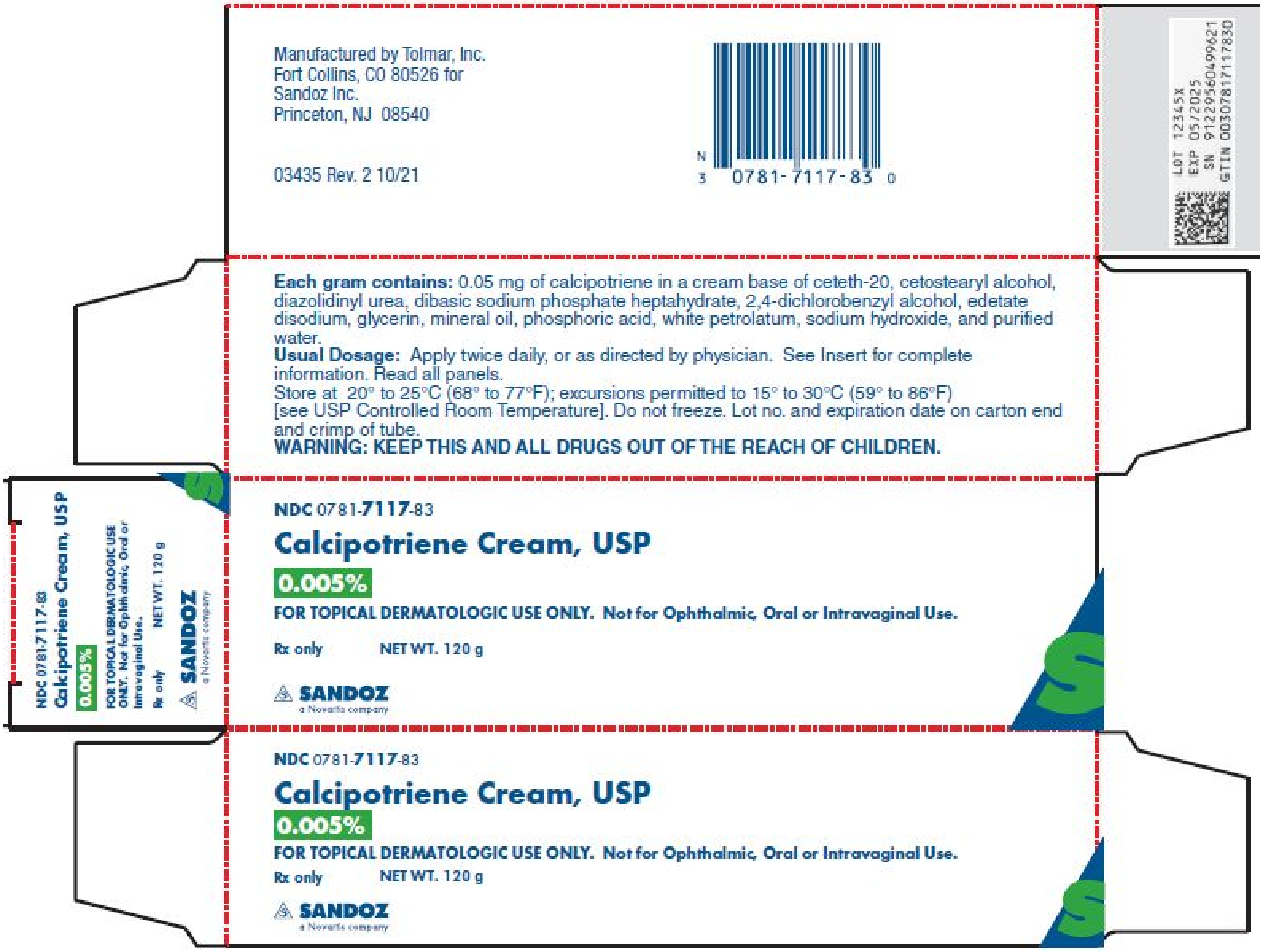
Store at 20º to 25ºC (68º to 77ºF); excursions permitted to 15º to 30ºC (59º to 86ºF) [see USP Controlled Room Temperature]. Do not freeze.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Manufactured by Tolmar, Inc.
Fort Collins, CO 80526 for
Sandoz Inc.
Princeton, NJ 08540

44473 Rev. 3 10/21

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL



CALCIPOTRIENE

calcipotriene cream

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0781-7117
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
CALCIPOTRIENE (UNII: 143NQ3779B) (CALCIPOTRIENE - UNII:143NQ3779B)	CALCIPOTRIENE	0.05 mg in 1 g

Inactive Ingredients	
Ingredient Name	**Strength**
CETETH-20 (UNII: I835H2IHHX)	
CETOSTEARYL ALCOHOL (UNII: 2DMT128M1S)	
DIAZOLIDINYL UREA (UNII: H5RIZ3MPW4)	

SODIUM PHOSPHATE, DIBASIC, HEPTAHYDRATE (UNII: 70WT22SF4B)	
DICHLOROBENZYL ALCOHOL (UNII: 1NKX3648J9)	
EDETATE DISODIUM (UNII: 7FLD91C86K)	
GLYCERIN (UNII: PDC6A3C0OX)	
MINERAL OIL (UNII: T5L8T28FGP)	
PHOSPHORIC ACID (UNII: E4GA8884NN)	
PETROLATUM (UNII: 4T6H12BN9U)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0781-7117-35	1 in 1 CARTON	07/27/2012	03/31/2024
1		60 g in 1 TUBE; Type 0: Not a Combination Product		
2	NDC:0781-7117-83	1 in 1 CARTON	07/27/2012	09/30/2024
2		120 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
ANDA	ANDA200935	07/27/2012	09/30/2024

Labeler - Sandoz Inc. (005387188)

Establishment

Name	Address	ID/FEI	Business Operations
TOLMAR, INC.		791156578	analysis(0781-7117) , label(0781-7117) , manufacture(0781-7117) , pack(0781-7117)

Establishment

Name	Address	ID/FEI	Business Operations
TOLMAR, INC.		079112310	analysis(0781-7117) , label(0781-7117) , manufacture(0781-7117) , pack(0781-7117)

Revised: 1/2024 Sandoz Inc.