

**HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use TACLONEX® Topical Suspension safely and effectively. See full prescribing information for TACLONEX® Topical Suspension.

**TACLONEX® (calcipotriene and betamethasone dipropionate) Topical Suspension, 0.005%/0.064%**  
**Initial U.S. Approval: 2006**

**RECENT MAJOR CHANGES**

Indications and Usage (1) 10/2012

**INDICATIONS AND USAGE**

Taclonex® Topical Suspension is a vitamin D analog and corticosteroid combination product indicated for the topical treatment of plaque psoriasis of the scalp and body in patients 18 years and older (1)

**DOSAGE AND ADMINISTRATION**

- Apply Taclonex® Topical Suspension to affected areas once daily for up to 8 weeks. Treatment may be discontinued earlier, if cleared (2.1).
- Instruct patients not to exceed a maximum weekly dose of 100 g.
- Shake before use (2.1).
- Taclonex® Topical Suspension is not for oral, ophthalmic, or intravaginal use (2.2).

**DOSAGE FORMS AND STRENGTHS**

Topical Suspension, 0.005%/0.064%  
Each gram of Taclonex® Topical Suspension contains 52.18 mcg of calcipotriene hydrate (equivalent to 50 mcg of calcipotriene) and 0.643 mg of betamethasone dipropionate (equivalent to 0.5 mg of betamethasone) (3)

**CONTRAINDICATIONS**

None (4)

**WARNINGS AND PRECAUTIONS**

- Hypercalcemia and hypercalciuria have been reported. If either occurs, discontinue until parameters of calcium metabolism normalize (5.1)
- Topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome and unmask latent diabetes (5.2, 5.3)
- Rate of adrenal suppression increased with treatment duration (5.2)
- Systemic absorption may require evaluation for HPA axis suppression (5.2)
- Modify use if HPA axis suppression develops (5.2)
- Potent corticosteroids, use on large areas, prolonged use or occlusive use may increase systemic absorption (5.2)
- Local adverse reactions may include atrophy, striae, irritation, acneiform eruptions, hypopigmentation, and allergic contact dermatitis and may be more likely with occlusive use or more potent corticosteroids. Do not use on face, axillae, or groin. Do not use if atrophy is present at the treatment site. (5.4, 6.1)
- Children may be more susceptible to systemic toxicity when treated with topical corticosteroids (5.2, 5.3, 8.4)

**ADVERSE REACTIONS**

The most common adverse reactions (≥ 1%) are folliculitis and burning sensation of skin (6.1)

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](http://www.fda.gov/medwatch).

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 10/2013

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

Taclonex<sup>®</sup> Topical Suspension is indicated for the topical treatment of plaque psoriasis of the scalp and body in patients 18 years and older.

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 Usual Dosage and Administration

Apply Taclonex<sup>®</sup> Topical Suspension to affected areas once daily for up to 8 weeks. Treatment may be discontinued earlier, if cleared.

Instruct patients not to exceed a maximum weekly dose of 100 g.

#### 2.2 Important Administration Instructions

Instruct patients to shake bottle prior to using Taclonex<sup>®</sup> Topical Suspension and to wash their hands after applying the product. Taclonex<sup>®</sup> Topical Suspension is not for oral, ophthalmic, or intravaginal use.

### 3 DOSAGE FORMS AND STRENGTHS

Topical Suspension, 0.005%/0.064%

Each gram of Taclonex<sup>®</sup> Topical Suspension contains 52.18 mcg of calcipotriene hydrate (equivalent to 50 mcg of calcipotriene) and 0.643 mg of betamethasone dipropionate (equivalent to 0.5 mg of betamethasone). Taclonex<sup>®</sup> Topical Suspension is a viscous, nearly odorless, almost clear, colorless to slightly off-white suspension.

### 4 CONTRAINDICATIONS

None.

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Hypercalcemia and Hypercalciuria

Hypercalcemia and hypercalciuria have been observed with use of Taclonex<sup>®</sup> Topical Suspension. If hypercalcemia or hypercalciuria develop, discontinue treatment until parameters of calcium metabolism have normalized. The incidence of hypercalcemia and hypercalciuria following Taclonex<sup>®</sup> Topical Suspension treatment of more than 8 weeks has not been evaluated.

#### 5.2 Hypothalamic-Pituitary-Adrenal Axis Suppression

Systemic absorption of topical corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for clinical glucocorticosteroid insufficiency. This may occur during treatment or upon withdrawal of the topical corticosteroid.

In a trial of 32 subjects treated with both Taclonex<sup>®</sup> Topical Suspension on the scalp and Taclonex<sup>®</sup> Ointment on the body, adrenal suppression was identified in 5 of 32 subjects (16%) after 4 weeks of treatment and in 2 of 11 subjects (18%) who continued treatment for 8 weeks. In another trial of 43 subjects treated with Taclonex<sup>®</sup> Topical Suspension on body (including the scalp in 36 out of 43 subjects) adrenal suppression was identified in 3 out of 43 subjects (7%) after 4 weeks of treatment and in none of the 36 subjects who continued treatment for 8 weeks. [See *Clinical Pharmacology* (12.2)]

#### Evaluation of HPA Axis Suppression

Because of the potential for systemic absorption, use of topical corticosteroids may require that patients be periodically evaluated for HPA axis suppression. Factors that predispose a patient using a topical corticosteroid to HPA axis suppression include the use of more potent steroids, use over large surface areas, use over prolonged periods, use under occlusion, use on an altered skin barrier, and use in patients with liver failure.

An ACTH stimulation test may be helpful in evaluating patients for HPA axis suppression.

If HPA axis suppression is documented, attempt to withdraw the drug, reduce the frequency of application, or substitute a less potent steroid. Manifestations of adrenal insufficiency may require supplemental systemic corticosteroids. Recovery of HPA axis function is generally prompt and complete upon discontinuation of topical corticosteroids.

Pediatric patients may be more susceptible to systemic toxicity from use of topical corticosteroids. [See *Use in Specific Populations* (8.4)]

### 5.3 Cushing’s Syndrome, Hyperglycemia, and Diabetes Mellitus

Cushing’s syndrome, hyperglycemia, and unmasking of latent diabetes mellitus can also result from systemic absorption of topical corticosteroids.

Use of more than one corticosteroid-containing product at the same time may increase the total systemic corticosteroid exposure.

Pediatric patients may be more susceptible to systemic toxicity from use of topical corticosteroids. [See *Use in Specific Populations* (8.4)]

### 5.4 Local Adverse Reactions with Topical Corticosteroids

Local adverse reactions may be more likely to occur with occlusive use, prolonged use or use of higher potency corticosteroids. Reactions may include atrophy, striae, telangiectasias, burning, itching, irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, and miliaria. Some local adverse reactions may be irreversible. Do not use on face, axillae, or groin. Do not use if atrophy is present at the treatment site.

### 5.5 Allergic Contact Dermatitis with Topical Corticosteroids

Allergic contact dermatitis to any component of topical corticosteroids is usually diagnosed by a failure to heal rather than a clinical exacerbation. Clinical diagnosis of allergic contact dermatitis can be confirmed by patch testing.

### 5.6 Allergic Contact Dermatitis with Topical Calcipotriene

Allergic contact dermatitis has been observed with use of topical calcipotriene. Clinical diagnosis of allergic contact dermatitis can be confirmed by patch testing.

### 5.7 Concomitant Skin Infections

Treat concomitant skin infections with an appropriate antimicrobial agent. If the infection persists, discontinue Taclonex® Topical Suspension until the infection has been adequately treated.

### 5.8 Eye Irritation

Avoid eye exposures. Taclonex® Topical Suspension may cause eye irritation.

### 5.9 Risks of Ultraviolet Light Exposures

Patients who apply Taclonex® Topical Suspension to exposed skin 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 who use Taclonex® Topical Suspension.

## 6 ADVERSE REACTIONS

### 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directed compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

#### *Clinical Trials on the Scalp*

The rates of adverse reactions given below were derived from randomized, multicenter, prospective vehicle- and/or active controlled clinical trials in subjects with scalp psoriasis. Subjects applied study product once daily for 8 weeks, and the median weekly dose was 12.6 g.

Adverse reactions that occurred in ≥1% of subjects treated with Taclonex® Topical Suspension and at a rate higher than in subjects treated with vehicle are presented in Table 1:

Table 1

<b>Number and Percentage with Adverse Reactions in Scalp Psoriasis Trials (Events Reported by ≥1% of Subjects and for Which a Relationship is Possible)</b>				
	<b>Taclonex® Topical Suspension</b>	<b>Betamethasone dipropionate in vehicle</b>	<b>Calcipotriene in vehicle</b>	<b>Vehicle</b>
	<b>N=1,953</b>	<b>N=1,214</b>	<b>N=979</b>	<b>N=173</b>
<b>Event</b>	<b># of subjects (%)</b>			
Folliculitis	16 (1%)	12 (1%)	5 (1%)	0 (0%)
Burning sensation of skin	13 (1%)	10 (1%)	29 (3%)	0 (0%)

Other less common adverse reactions (<1% but >0.1%) were, in decreasing order of incidence: acne, exacerbation of psoriasis, eye irritation, and pustular rash.

In a 52-week trial, adverse reactions that were reported by >1% of subjects treated with Taclonex<sup>®</sup> Topical Suspension were pruritus (3.6%), psoriasis (2.4%), erythema (2.1%), skin irritation (1.4%), and folliculitis (1.2%).

#### *Clinical Trials on the Body*

In randomized, multicenter, prospective vehicle- and/or active controlled clinical trials in subjects with plaque psoriasis on non-scalp areas, subjects applied study product once daily for 8 weeks. A total of 824 subjects were treated with Taclonex<sup>®</sup> Topical Suspension and the median weekly dose was 22.6 g.

There were no adverse reactions that occurred in  $\geq 1\%$  of subjects treated with Taclonex<sup>®</sup> Topical Suspension and at a rate higher than in subjects treated with vehicle.

Other less common adverse reactions (<1% but >0.1%) were, in decreasing order of incidence: rash and folliculitis.

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

#### *Teratogenic Effects: Pregnancy Category C*

Animal reproduction studies have not been conducted with Taclonex<sup>®</sup> Topical Suspension. Taclonex<sup>®</sup> Topical Suspension contains calcipotriene that has been shown to be fetotoxic and betamethasone dipropionate that has been shown to be teratogenic in animals when given systemically. There are no adequate and well-controlled studies in pregnant women. Taclonex<sup>®</sup> Topical Suspension should be used during pregnancy only if the potential benefit to the patient justifies the potential risk to the fetus.

Teratogenicity studies with calcipotriene were performed by the oral route in rats and rabbits. In rabbits, increased maternal and fetal toxicity were noted at a dosage of 12 mcg/kg/day (144 mcg/m<sup>2</sup>/day); a dosage of 36 mcg/kg/day (432 mcg/m<sup>2</sup>/day) resulted in a significant increase in the incidence of incomplete ossification of the pubic bones and forelimb phalanges of fetuses. In a rat study, a dosage of 54 mcg/kg/day (324 mcg/m<sup>2</sup>/day) resulted in a significantly increased incidence of skeletal abnormalities (enlarged fontanelles and extra ribs). The enlarged fontanelles were most likely due to the effect of calcipotriene upon calcium metabolism. The estimated maternal and fetal no-adverse effect levels (NOAEL) in the rat (108 mcg/m<sup>2</sup>/day) and rabbit (48 mcg/m<sup>2</sup>/day) derived from oral studies are lower than the maximum topical dose of calcipotriene in man (460 mcg/m<sup>2</sup>/day).

Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels.

Betamethasone dipropionate has been shown to be teratogenic in mice and rabbits when given by the subcutaneous route at dosages of 156 mcg/kg/day (468 mcg/m<sup>2</sup>/day) and 2.5 mcg/kg/day (30 mcg/m<sup>2</sup>/day), respectively. Those dose levels are lower than the maximum topical dose in man (about 5,950 mcg/m<sup>2</sup>/day). The abnormalities observed included umbilical hernia, exencephaly and cleft palate.

Pregnant women were excluded from the clinical studies conducted with Taclonex<sup>®</sup> Topical Suspension.

### **8.3 Nursing Mothers**

Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects.

It is not known whether topically administered calcipotriene or corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk.

Because many drugs are excreted in human milk, caution should be exercised when Taclonex<sup>®</sup> Topical Suspension is administered to a nursing woman.

The patient should be instructed not to use Taclonex<sup>®</sup> Topical Suspension on the breast when nursing.

### **8.4 Pediatric Use**

Safety and effectiveness of the use of Taclonex<sup>®</sup> Topical Suspension in pediatric patients have not been studied. Because of a higher ratio of skin surface area to body mass, children under the age of 12 years are at particular risk of systemic adverse effects when they are treated with topical corticosteroids. [See *Warnings and Precautions* (5.2)]

HPA axis suppression, Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include low plasma cortisol levels and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

### **8.5 Geriatric Use**

Of the total number of subjects in the controlled clinical studies of Taclonex<sup>®</sup> Topical Suspension in psoriasis vulgaris on non-scalp areas, 124 were 65 years or older, while 36 were 75 years or older. Of the total number of subjects in the controlled clinical studies of Taclonex<sup>®</sup> Topical Suspension in scalp psoriasis, 334 were 65 years or older, while 84 were 75 years or older.

No overall differences in safety or effectiveness of Taclonex<sup>®</sup> Topical Suspension were observed between subjects in these age ranges versus younger subjects. All other reported clinical experience has not identified any differences in response between elderly and younger patients.

### 8.6 Unevaluated Uses

- Safety and efficacy in patients with known or suspected disorders of calcium metabolism have not been evaluated
- Safety and efficacy in patients with known erythrodermic, exfoliative, or pustular psoriasis have not been evaluated
- Safety and efficacy in patients with severe renal insufficiency or severe hepatic disorders have not been evaluated

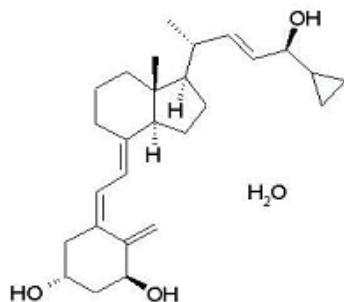
### 10 OVERDOSAGE

Taclonex<sup>®</sup> Topical Suspension can be absorbed in sufficient amounts to produce systemic effects [*See Warnings and Precautions (5.1)*].

### 11 DESCRIPTION

Taclonex<sup>®</sup> Topical Suspension contains calcipotriene hydrate and betamethasone dipropionate. It is intended for topical use only. Calcipotriene hydrate is a synthetic vitamin D<sub>3</sub> analog.

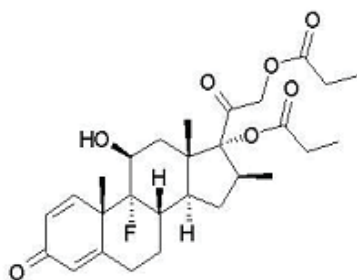
Chemically, calcipotriene hydrate is 9,10-secochola-5,7,10(19),22-tetraene-1,3,24-triol,24-cyclo-propyl-,monohydrate, (1 $\alpha$ ,3 $\beta$ ,5Z,7E,22E,24S) with the empirical formula C<sub>27</sub>H<sub>40</sub>O<sub>3</sub>·H<sub>2</sub>O, a molecular weight of 430.6, and the following structural formula:



Calcipotriene hydrate is a white to almost white, crystalline compound.

Betamethasone dipropionate is a synthetic corticosteroid.

Betamethasone dipropionate has the chemical name Pregna-1,4-diene-3,20-dione-9-fluoro-11-hydroxy-16-methyl-17,21-bis(1-oxopropoxy)-(11 $\beta$ ,16 $\beta$ ), with the empirical formula C<sub>28</sub>H<sub>37</sub>FO<sub>7</sub>, a molecular weight of 504.6, and the following structural formula:



Betamethasone dipropionate is a white to almost white, crystalline powder.

Each gram of Taclonex<sup>®</sup> Topical Suspension contains 52.18 mcg of calcipotriene hydrate (equivalent to 50 mcg of calcipotriene) and 0.643 mg of betamethasone dipropionate (equivalent to 0.5 mg of betamethasone) in a base of hydrogenated castor oil, PPG-15 stearyl ether and mineral oil. Taclonex<sup>®</sup> Topical Suspension is a viscous, nearly odorless, almost clear, colorless to slightly off-white suspension.

### 12 CLINICAL PHARMACOLOGY

## 12.1 Mechanism of Action

Taclonex<sup>®</sup> Topical Suspension combines the pharmacological effects of calcipotriene hydrate as a synthetic vitamin D<sub>3</sub> analog and betamethasone dipropionate as a synthetic corticosteroid. However, while their pharmacologic and clinical effects are known, the exact mechanisms of their actions in psoriasis vulgaris are unknown.

## 12.2 Pharmacodynamics

### *Hypothalamic-Pituitary-Adrenal (HPA) Axis Suppression:*

HPA axis suppression was evaluated in two trials (Trial A and B) following the application of Taclonex<sup>®</sup> Topical Suspension. In Trial A, HPA axis suppression was evaluated in adult subjects (N=32) with extensive psoriasis involving at least 30% of the scalp and, in total, 15-30% of the body surface area. Treatment consisted of once daily application of Taclonex<sup>®</sup> Topical Suspension on the scalp in combination with Taclonex<sup>®</sup> Ointment on the body for 4 to 8 weeks. Adrenal suppression as indicated by a 30-minute post-stimulation cortisol level  $\leq 18$  mcg/dL was observed in 5 of 32 subjects (15.6%) after 4 weeks of treatment and in 2 of 11 subjects (18.2%) who continued treatment for 8 weeks.

In Trial B, HPA axis suppression was evaluated in adult subjects (N=43) with extensive psoriasis involving 15-30% of the body surface area (including the scalp). Treatment consisted of once daily application of Taclonex<sup>®</sup> Topical Suspension to the body (including the scalp in 36 out of 43 subjects) for 4 to 8 weeks. Adrenal suppression as indicated by a 30-minute post-stimulation cortisol level  $\leq 18$  mcg/dL was observed in 3 out of 43 subjects (7%) after 4 weeks of treatment and in none of the 36 subjects who continued treatment for 8 weeks.

### *Effects on Calcium Metabolism*

In Trial A described above, the effects of once daily application of Taclonex<sup>®</sup> Topical Suspension on the scalp in combination with Taclonex<sup>®</sup> Ointment on the body for 4 to 8 weeks on calcium metabolism were also examined. Following once daily application of Taclonex<sup>®</sup> Topical Suspension on the scalp in combination with Taclonex<sup>®</sup> Ointment on the body, elevated urinary calcium levels outside the normal range were observed in two subjects (one at 4 weeks and one at 8 weeks).

In Trial B, the effects on calcium metabolism of once daily application of Taclonex<sup>®</sup> Topical Suspension to 15-30% of the body surface area (including the scalp) for 4 to 8 weeks were also examined. There was no change in mean serum or urinary calcium levels. Elevated urinary calcium levels outside the normal range were observed in two subjects (one at 4 weeks and one at 8 weeks).

## 12.3 Pharmacokinetics

### **Absorption**

#### *Taclonex<sup>®</sup> Topical Suspension:*

The systemic effect of Taclonex<sup>®</sup> Topical Suspension in psoriasis was investigated in Trials A and B described above. In Trial A, the serum levels of calcipotriene and betamethasone dipropionate and their major metabolites were measured after 4 and 8 weeks of once daily application of Taclonex<sup>®</sup> Topical Suspension on the scalp in combination with Taclonex<sup>®</sup> Ointment on the body. Calcipotriene and betamethasone dipropionate were below the lower limit of quantification in all serum samples of the 34 subjects evaluated.

However, one major metabolite of calcipotriene (MC1080) was quantifiable in 10 of 34 (29.4%) subjects at week 4 and in 5 of 12 (41.7%) subjects at week 8. The major metabolite of betamethasone dipropionate, betamethasone 17-propionate (B17P) was also quantifiable in 19 of 34 (55.9%) subjects at week 4 and 7 of 12 (58.3%) subjects at week 8. The serum concentrations for MC1080 ranged from 20-75 pg/mL. The clinical significance of this finding is unknown.

In Trial B, the plasma levels of calcipotriene and betamethasone dipropionate and their major metabolites were measured after 4 weeks of once daily application of Taclonex<sup>®</sup> Topical Suspension to 15-30% of the body surface area (scalp and non-scalp areas). Calcipotriene and its metabolite MC1080 were below the lower limit of quantification in all plasma samples. Betamethasone dipropionate was quantifiable in 1 sample each taken from 4 of 43 (9.3%) subjects. The metabolite of betamethasone dipropionate (B17P) was quantifiable in 16 of 43 (37.2%) subjects. The plasma concentrations of betamethasone dipropionate ranged from 30.9-63.5 pg/mL and that of its metabolite betamethasone 17-propionate ranged from 30.5-257 pg/mL. The clinical significance of this finding is unknown.

### **Metabolism**

#### *Calcipotriene:*

Calcipotriene metabolism following systemic uptake is rapid and occurs in the liver. The primary metabolites of calcipotriene are less potent than the parent compound.

Calcipotriene is metabolized to MC1046 (the  $\alpha,\beta$ -unsaturated ketone analog of calcipotriene), which is metabolized further to MC1080 (a saturated ketone analog). MC1080 is the major metabolite in plasma. MC1080 is slowly metabolized to calcitroic acid.

#### *Betamethasone dipropionate:*

Betamethasone dipropionate is metabolized to betamethasone 17-propionate and betamethasone, including the 6β-hydroxy derivatives of those compounds by hydrolysis. Betamethasone 17-propionate (B17P) is the primary metabolite.

### 13 NONCLINICAL TOXICOLOGY

#### 13.1 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<sup>2</sup>/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 ultra-violet radiation (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.

When betamethasone dipropionate was applied topically to CD-1 mice for up to 24 months at dosages approximating 1.3, 4.2, and 8.5 mcg/kg/day in females, and 1.3, 4.2, and 12.9 mcg/kg/day in males (corresponding to dosages of up to approximately 26 mcg/m<sup>2</sup>/day and 39 mcg/m<sup>2</sup>/day, in females and males, respectively), no significant changes in tumor incidence were observed when compared to control.

When betamethasone dipropionate was administered via oral gavage to male and female Sprague Dawley rats for up to 24 months at dosages of 20, 60, and 200 mcg/kg/day (corresponding to dosages of approximately 3, 10, and 30 mcg/m<sup>2</sup>/day), no significant changes in tumor incidence were observed when compared to control.

Calcipotriene did not elicit any genotoxic effects in the Ames mutagenicity assay, the mouse lymphoma TK locus assay, the human lymphocyte chromosome aberration test, or the mouse micronucleus test. Betamethasone dipropionate did not elicit any genotoxic effects in the Ames mutagenicity assay, the mouse lymphoma TK locus assay, or in the rat micronucleus test.

Studies in rats with oral doses of up to 54 mcg/kg/day (324 mcg/m<sup>2</sup>/day) of calcipotriene indicated no impairment of fertility or general reproductive performance. Studies in male rats at oral doses of up to 200 mcg/kg/day (1200 mcg/m<sup>2</sup>/day), and in female rats at oral doses of up to 1000 mcg/kg/day (6000 mcg/m<sup>2</sup>/day), of betamethasone dipropionate indicated no impairment of fertility.

### 14 CLINICAL STUDIES

#### *Clinical Trials on the Scalp*

Two multicenter, randomized, double-blind trials were conducted in subjects with scalp psoriasis. In Trial One, 1,407 subjects were randomized to 1 of 4 treatment groups: Taclonex<sup>®</sup> Topical Suspension, betamethasone dipropionate in the same vehicle, calcipotriene hydrate in the same vehicle, or the vehicle alone. Trial Two did not include a vehicle arm; 1,280 subjects were randomized to 1 of 3 treatment groups: Taclonex<sup>®</sup> Topical Suspension, betamethasone dipropionate in the same vehicle, or calcipotriene hydrate in the same vehicle. Both trials enrolled subjects with moderate to very severe scalp psoriasis. The majority of subjects had disease of moderate severity at baseline. Subjects were treated once daily for 8 weeks.

Efficacy was assessed as the proportion of subjects at Week 8 with absent or very mild disease according to the Investigator’s Global Assessment of Disease Severity. “Clear” was defined as no evidence of redness, thickness or scaling. “Almost clear” was defined as an overall clinical picture of lesions with the presence of minimal erythema. Table 3 contains the response rates in each of these 2 trials.

Table 2

<b>Percentage of Patients with Clear or Almost Clear Disease According to the Investigator’s Global Assessment of Disease Severity in Trials on the Scalp</b>				
	<b>Taclonex<sup>®</sup> Topical Suspension</b>	<b>Betamethasone Dipropionate in vehicle</b>	<b>Calcipotriene in vehicle</b>	<b>Vehicle</b>
<b>Trial One</b>	(N = 494)	(N = 531)	(N = 256)	(N = 126)
Week 2	55.5%	46.1%	18.4%	9.5%
Week 8	70.0%	63.1%	36.7%	19.8%
<b>Trial Two</b>	(N = 512)	(N = 517)	(N = 251)	-
Week 2	47.1%	36.4%	12.7%	-
Week 8	67.2%	59.6%	41.0%	-

#### *Clinical Trial on the Body*

One multicenter, randomized, double-blind trial was conducted in subjects with psoriasis vulgaris on non-scalp areas, excluding face, axillae, and groin. In this trial, 1152 subjects were randomized to 1 of 4 treatment groups: Taclonex<sup>®</sup> Topical Suspension, betamethasone dipropionate in the same vehicle, calcipotriene hydrate in the same vehicle, or the vehicle alone. The trial enrolled subjects with mild to moderate psoriasis vulgaris. Seventy-eight percent of subjects had disease of moderate severity at baseline. Subjects were treated once daily for 8 weeks.

Efficacy was assessed at Week 4 and Week 8 as the proportion of subjects who were “Clear” or “Almost clear” according to the Investigator’s Global Assessment of Disease Severity. Subjects with mild disease at baseline were required to be “Clear” to be considered a success. Table 2 contains the response rates in this trial.

Table 3

Percentage of Patients with Clear or Almost Clear Disease According to the Investigator’s Global Assessment of Disease Severity* in Trial on the Body				
	Taclonex <sup>®</sup> Topical Suspension (N = 482)	Betamethasone Dipropionate in vehicle (N = 479)	Calcipotriene in vehicle (N = 96)	Vehicle (N= 95)
Week 4	13.3%	12.5%	5.2%	2.1%
Week 8	29.0%	21.5%	14.6%	6.3%

\* Subjects with mild disease at baseline were required to be “Clear” to be considered a success.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

### 16.1 How Supplied

Taclonex<sup>®</sup> Topical Suspension is a viscous, nearly odorless, almost clear, colorless to slightly off-white suspension. It is available as: 60 g bottle (NDC 50222-501-06)

120 g (2 bottles of 60 g) (NDC 50222-501-66)

### 16.2 Storage

Store between 20°C-25°C (68°F-77°F); excursions permitted between 15°C-30°C (59°F-86°F). [See USP controlled room temperature.]

Do not refrigerate. Keep the bottle in the outer carton when not in use.

The product should be used within six months after it has been opened.

### 16.3 Handling

Shake before use.

Keep out of reach of children

## 17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information and Instructions for Use)

Inform patients of the following:

- This medication is to be used as directed by the physician.
- Do not use this medication for any disorder other than for which is has been prescribed
- This medication is for external use only.
- Avoid contact with the face or eyes. If this medicine gets on face or in eyes, wash area right away.
- Do not apply Taclonex<sup>®</sup> Topical Suspension to the scalp in the 12 hours before or after any chemical treatments to the hair. Since hair treatments may involve strong chemicals, talk with physician first.
- Wash hands after application.
- If applied to the scalp, do not wash hair or take a bath or shower right after application.
- Do not bandage or otherwise occlude the treated skin area unless directed by the physician.
- Instruct patients to report any signs of adverse reactions to their physician.
- Instruct patients not to use other products containing calcipotriene or a corticosteroid with Taclonex<sup>®</sup> Topical Suspension without first talking to the physician.
- Instruct patients who use Taclonex<sup>®</sup> Topical Suspension to avoid excessive exposure to either natural or artificial sunlight (including tanning booths, sun lamps, etc.).

**PATIENT INFORMATION**  
**Taclonex<sup>®</sup> (TAK-lo-NEKS)**  
**(calcipotriene and betamethasone dipropionate)**  
**Topical Suspension, 0.005%/0.064%**

Read the Patient Information that comes with Taclonex<sup>®</sup> Topical Suspension before you start using it and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or treatment.

**Important:** Taclonex<sup>®</sup> Topical Suspension is for use on skin only (topical). Do not get Taclonex<sup>®</sup> Topical Suspension near or in your mouth, eyes, or vagina.

Another product, Taclonex<sup>®</sup> Ointment contains the same medicine that is in Taclonex<sup>®</sup> Topical Suspension and is used to treat psoriasis vulgaris of the skin. If you use both medicines to treat your psoriasis vulgaris, be sure to follow your doctor's directions so that you do not use too much of one or both of these medicines.

**What is Taclonex<sup>®</sup> Topical Suspension?**

Taclonex<sup>®</sup> Topical Suspension is a prescription medicine that is for topical use only. Taclonex<sup>®</sup> Topical Suspension is used to treat psoriasis vulgaris in people 18 years of age and older.

It is not known if Taclonex<sup>®</sup> Topical Suspension is safe and effective in children under 18 years of age.

**What should I tell my doctor before using Taclonex<sup>®</sup> Topical Suspension?**

**Before you use Taclonex<sup>®</sup> Topical Suspension, tell your doctor if you:**

- have a skin infection on the area affected by psoriasis. Your skin infection should be treated before you start using Taclonex<sup>®</sup> Topical Suspension
- have a calcium metabolism disorder
- have one of the following types of psoriasis:
  - erythrodermic psoriasis
  - exfoliative psoriasis
  - pustular psoriasis
- have thinning-skin (atrophy) at the site to be treated.
- are getting light therapy (phototherapy treatments) for your psoriasis
- are pregnant or plan to become pregnant. It is not known if Taclonex<sup>®</sup> Topical Suspension will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Taclonex<sup>®</sup> Topical Suspension passes into your breast milk. You should not use Taclonex<sup>®</sup> Topical suspension on your breast if you breastfeed.

**Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins and herbal supplements.**

Especially tell your doctor if you use:

- other corticosteroid medicines
- other medicines for your psoriasis.

Know the medicine you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

**How should I use Taclonex<sup>®</sup> Topical Suspension?**

- Use Taclonex<sup>®</sup> Topical Suspension exactly as your doctor tells you to use it.

- Your doctor should tell you how much Taclonex<sup>®</sup> Topical Suspension to use and where to use it.
- Do not use more than the maximum recommended weekly amount of 100 grams of medicines containing calcipotriene (one of the active ingredients of Taclonex<sup>®</sup> Topical Suspension).
- Apply Taclonex<sup>®</sup> Topical Suspension to affected areas on the skin 1 time a day for up to 8 weeks. Treatment may be discontinued earlier if cleared.
- Shake the Taclonex<sup>®</sup> Topical Suspension bottle before you use it.
- Do not apply Taclonex<sup>®</sup> Topical Suspension to the scalp in the 12 hours before or after any chemical treatments to your hair. Since hair treatments may involve strong chemicals, talk with your doctor first.
- If you accidentally get Taclonex<sup>®</sup> Topical Suspension on your face or in your eyes wash the area with water right away.
- Wash your hands after using Taclonex<sup>®</sup> Topical Suspension.
- Do not wash your hair or take a bath or shower right after applying Taclonex<sup>®</sup> Topical Suspension as the medicine will not work as well to treat your psoriasis.
- Do not bandage or cover the treated skin area.

### **What should I avoid while using Taclonex<sup>®</sup> Topical Suspension?**

Avoid spending a long time in sunlight. Avoid tanning booths and sun lamps. Use sunscreen and wear a hat and clothes that cover treated areas if you have to be in the sunlight. Talk to your doctor if you get a sunburn.

### **What are the possible side effects of Taclonex<sup>®</sup> Topical Suspension?**

**Taclonex<sup>®</sup> Topical Suspension may cause serious side effects, including:**

- **too much calcium in your blood or urine**
- **adrenal gland problems**

Your doctor may do blood and urine tests to check your calcium levels and adrenal gland function while you are using Taclonex<sup>®</sup> Topical Suspension.

- **skin problems such as:**

- thinning of your skin
- burning
- inflammation
- itching
- irritation
- dryness
- changes in skin color
- redness
- infection
- raised bumps on your skin

- **eye irritation if you accidentally get Taclonex<sup>®</sup> Topical Suspension in your eyes.**

The most common side effects of Taclonex<sup>®</sup> Topical Suspension are inflamed hair pores (folliculitis) and skin burning.

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all of the possible side effects of Taclonex<sup>®</sup> Topical Suspension. For more information, ask your doctor or pharmacist.

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

### **How should I store Taclonex<sup>®</sup> Topical Suspension?**

- Store Taclonex<sup>®</sup> Topical Suspension between 68°F to 77°F (20°C to 25°C).

- Do not refrigerate Taclonex<sup>®</sup> Topical Suspension.
- Keep the bottle in the outer carton when not in use.

Use Taclonex<sup>®</sup> Topical Suspension within six months after it has been opened

**Keep Taclonex<sup>®</sup> Topical Suspension and all medicines out of the reach of children.**

**General information about Taclonex<sup>®</sup> Topical Suspension.**

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use Taclonex<sup>®</sup> Topical Suspension for a condition for which it was not prescribed. Do not give Taclonex<sup>®</sup> Topical Suspension to other people, even if they have the same symptoms you have. It may harm them.

This leaflet summarizes the most important information about Taclonex<sup>®</sup> Topical Suspension. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about Taclonex<sup>®</sup> Topical Suspension that is written for health professionals.

For more information, go to [www.taclonex.com](http://www.taclonex.com) or call 1-877-494-4536.

**What are the ingredients in Taclonex<sup>®</sup> Topical Suspension?**

Active ingredients: calcipotriene hydrate and betamethasone dipropionate.

Inactive ingredients: hydrogenated castor oil, PPG-15 stearyl ether and mineral oil.

**Instructions for Use  
Taclonex (TAK-lo-NEKS)  
(calcipotriene and betamethasone dipropionate)  
Topical Suspension, 0.005%/0.064%**

**Important:** For skin use only. Do not get Taclonex<sup>®</sup> Topical Suspension near or in your mouth, eyes or vagina.

Read these Instructions for Use before you start using Taclonex<sup>®</sup> Topical Suspension and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or treatment.

**How to apply Taclonex<sup>®</sup> Topical Suspension to your body:**

Follow your doctor's instructions of how much Taclonex<sup>®</sup> Topical Suspension to use and where to use it. Apply Taclonex<sup>®</sup> Topical Suspension directly to areas affected by psoriasis and gently rub in. Wash your hands after applying Taclonex<sup>®</sup> Topical Suspension.

**How to apply Taclonex<sup>®</sup> Topical Suspension to your scalp:**

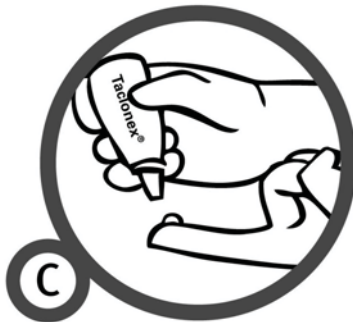
- You do not need to wash your hair before you apply Taclonex<sup>®</sup> Topical Suspension.



**Shake** bottle before use.  
Remove the cap.



It may help to part your  
hair before you use  
Taclonex<sup>®</sup> Topical  
Suspension.



Apply a drop of Taclonex<sup>®</sup>  
Topical Suspension to your  
fingertip.



Apply directly to scalp  
areas affected by psoriasis  
and gently rub in  
Taclonex<sup>®</sup> Topical  
Suspension.

- Do not wash your hair right after you apply Taclonex<sup>®</sup> Topical Suspension.
- Wash your hands after applying Taclonex<sup>®</sup> Topical Suspension.

This Patient Information and Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured by:  
LEO Laboratories Ltd. (LEO Pharma)  
285 Cashel Road  
Dublin 12, Ireland



Distributed by:  
LEO Pharma Inc.  
1 Sylvan Way, Parsippany, NJ 07054, USA  
1-877-494-4536  
U.S. Patent Nos. RE39,706 E, 6,753,013 and 6,787,529.  
024580-00

Scale	100%	Get-up	US	Item No.	028224	Rev. No.	YY	Sort by email
Subject	CRT 96 X 66 x 118 mm			Date	08/10/13	Date		
Sign.				Sign.		Sign.		

**ARTWORK**  
Please return to:  
LEO Pharma US  
Informal Market Access  
Industrieparken 55 - DK-2750 - Ballerup

Product Name: Taclonex® Topical Suspension - 120 g (2 x 60 g)  
Country: Ireland  
Supplier / Place of production: Ireland

Mock-up for registration purpose.

**1. PREP FROM** **MOCK-UP**

**1. Mock-up Approval Stamp (MAS)**

**Editorial Proof**

According to:  Instruction For Use, Mock-up Approval Stamp (MAS) SOP\_000647 and  SOP\_000962  
Sign: \_\_\_\_\_ Date: \_\_\_\_\_

According to:  Product name  Dosage form  Strength/Stripes  Pack size  Prompts  Item No./Reg. No.  Date: \_\_\_\_\_  
Sign: \_\_\_\_\_

Sealing label

Impriinting area

**Taclonex®**  
(calcipotriene and betamethasone dipropionate)  
Topical Suspension,  
0.005%/0.064%  
**Shake before use**  
Net Wt. 120 g (2 bottles of 60 g)

**Taclonex®**  
(calcipotriene and betamethasone dipropionate)  
Topical Suspension,  
0.005%/0.064%  
**Shake before use**

**Rx only**

NDC 50222-501-66

**For Topical Use Only**  
Net Wt. 120 g (2 bottles of 60 g)

Keep out of the reach of children.  
Usual dosage:  
See Prescribing Information.

Manufactured by:  
LEO Laboratories Ltd.  
285 Cashel Road  
Dublin 12, Ireland

Distributed by:  
LEO Pharma Inc.  
Sylvan Way  
Parlappany, NJ 07054, USA, 1-877-494-4536

U.S. Patent Nos. RE39,706 E, 6,753,013 and 6,787,529.

To report SUSPECTED ADVERSE REACTIONS,  
contact LEO Pharma Inc. at Phone 1-877-494-4536 or  
FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch)

Sealing label

**Taclonex®**  
(calcipotriene and betamethasone dipropionate)  
Topical Suspension,  
0.005%/0.064%  
**Shake before use**


**Rx only**

NDC 50222-501-66

**For Topical Use Only**  
Net Wt. 120 g (2 bottles of 60 g)

Each gram contains 50 mg of calcipotriene hydrate (equivalent to 50 mcg of calcipotriene) and 0.643 mg of betamethasone dipropionate (equivalent to 0.65 mg of betamethasone) in a base of hydrogenated castor oil, PPG-15 stearyl ether and mineral oil.


Store Taclonex® Topical Suspension between 68° - 77° F (20° - 25° C). Excursions permitted between 59° - 86° F (15° - 30° C). Keep the bottle in the outer carton when not in use.


  
3 50222-501-66 4

028224-YY

96 x 66 x 118

**LEO®**





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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

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/s/

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STANKA KUKICH  
11/07/2013