

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

TACLONEX® (calcipotriene and betamethasone dipropionate) Topical Suspension, 0.005%/0.064%

TACLONEX® (calcipotriene and betamethasone dipropionate) Topical Suspension, 0.005%/0.064% with Applicator

Initial U.S. Approval: 2006

RECENT MAJOR CHANGES

Indications and Usage (1)	08/2014
Dosage and Administration (2)	08/2014

INDICATIONS AND USAGE

Taclonex® Topical Suspension is a vitamin D analog and a corticosteroid combination product indicated for the topical treatment of:

- Plaque psoriasis of the scalp and body in patients 18 years and older
- Plaque psoriasis of the scalp in patients age 12 to 17 years (1)

DOSAGE AND ADMINISTRATION

- Shake bottle before use (2).
- Apply Taclonex® Topical Suspension to affected areas once daily for up to 8 weeks. Discontinue therapy when control is achieved. (2)
- Adult patients should not use more than 100 g per week. (2)
- Patients age 12 to 17 years should not use more than 60 g per week. (2)
- Do not use with occlusive dressings unless directed by a physician. (2)
- Avoid use on the face, groin, or axillae, or if skin atrophy is present at the treatment site. (2)

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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)
- Taclonex® Topical Suspension can cause reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency during and after withdrawal of treatment. Risk factors include the use of high-potency topical corticosteroid, use over a large surface area or to areas under occlusion, prolonged use, altered skin barrier, liver failure, and use in pediatric patients. Modify use should HPA axis suppression develop. (5.2, 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.

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

Revised: 06/2016

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Taclonex[®] Topical Suspension is indicated for the topical treatment of:

- Plaque psoriasis of the scalp and body in patients 18 years and older
- Plaque psoriasis of the scalp in patients 12 to 17 years

2 DOSAGE AND ADMINISTRATION

Bottle: Instruct patients to shake bottle prior to using Taclonex[®] Topical Suspension and to wash their hands after applying the product.

Applicator: Instruct patients to wash their hands if they get Taclonex[®] Topical Suspension on their fingers.

Apply Taclonex[®] Topical Suspension to affected areas once daily for up to 8 weeks. Therapy should be discontinued when control is achieved.

Patients 18 years and older should not use more than 100 g per week and patients 12 to 17 years should not use more than 60 g per week.

Taclonex[®] Topical Suspension should not be used with occlusive dressings unless directed by a physician. Taclonex[®] Topical Suspension is not for oral, ophthalmic, or intravaginal use. Avoid use on the face, groin, or axillae, or if skin atrophy is present at the treatment site.

3 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). Taclonex[®] Topical Suspension is a viscous, nearly odorless, almost clear, colorless to slightly off-white suspension.

Applicator: After priming, each full actuation delivers a consistent amount of Taclonex[®] Topical Suspension.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Hypercalcemia and Hypercalciuria

Hypercalcemia and hypercalciuria have been observed with use of Taclonex[®] Topical Suspension. If hypercalcemia or hypercalciuria develop, discontinue treatment until parameters of calcium metabolism have normalized. The incidence of hypercalcemia and hypercalciuria following Taclonex[®] Topical Suspension treatment of more than 8 weeks has not been evaluated. [See *Clinical Pharmacology* (12.2)]

5.2 Effects on Endocrine System

Taclonex[®] Topical Suspension can cause reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for clinical glucocorticosteroid insufficiency. This may occur during treatment or upon withdrawal of treatment. Factors that predispose a patient to HPA axis suppression include the use of high-potency steroids, large treatment surface areas, prolonged use, use of occlusive dressings, altered skin barrier, liver failure, and young age. Evaluation for HPA axis suppression may be done by using the adrenocorticotrophic hormone (ACTH) stimulation test.

In a trial evaluating the effects of Taclonex[®] Topical Suspension and Taclonex[®] Ointment on the HPA axis, 32 adult subjects were treated with both Taclonex[®] Topical Suspension on the scalp and Taclonex[®] 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[®] 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)]

In a trial evaluating the effects of Taclonex[®] Topical Suspension on the HPA axis, 31 subjects aged 12 to 17 years were treated with Taclonex[®] Topical Suspension on the scalp. Adrenal suppression was identified in 1 of 30 evaluable subjects (3.3%) after 4 weeks of treatment. [See Clinical Pharmacology (12.2)]

If HPA axis suppression is documented, gradually withdraw the drug, reduce the frequency of application, or substitute with a less potent corticosteroid.

Cushing's syndrome and hyperglycemia may also occur due to the systemic effects of the topical corticosteroid. These complications are rare and generally occur after prolonged exposure to excessively large doses, especially of high-potency topical corticosteroids.

Pediatric patients may be more susceptible to systemic toxicity due to their larger skin surface to body mass ratios. [See Use in Specific Populations (8.4) and Clinical Pharmacology (12.2)]

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

5.3 Allergic Contact Dermatitis with Topical Corticosteroids

Allergic contact dermatitis to a topical corticosteroid is usually diagnosed by observing a failure to heal rather than a clinical exacerbation. Such an observation should be corroborated with appropriate diagnostic patch testing.

5.4 Allergic Contact Dermatitis with Topical Calcipotriene

Allergic contact dermatitis has been observed with use of topical calcipotriene. Such an observation should be corroborated with appropriate diagnostic patch testing.

5.5 Eye Irritation

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

5.6 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 Conducted in Subjects 18 years and older with Scalp Psoriasis

The rates of adverse reactions given below were derived from randomized, multicenter, prospective vehicle- and/or active controlled clinical trials in adult 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 $\geq 1\%$ 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

Number and Percentage with Adverse Reactions in Scalp Psoriasis Trials (Events Reported by $\geq 1\%$ of Subjects and for Which a Relationship is Possible)				
	Taclonex[®] Topical Suspension	Betamethasone dipropionate in vehicle	Calcipotriene in vehicle	Vehicle
	N=1,953	N=1,214	N=979	N=173
Event	# of subjects (%)			
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[®] Topical Suspension were pruritus (3.6%), psoriasis (2.4%), erythema (2.1%), skin irritation (1.4%), and folliculitis (1.2%).

Clinical Trials Conducted in Subjects 18 years and older with Psoriasis on the Body

In randomized, multicenter, prospective vehicle- and/or active controlled clinical trials in adult 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[®] Topical Suspension and the median weekly dose was 22.6 g.

There were no adverse reactions that occurred in ≥1% of subjects treated with Taclonex[®] 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.

Clinical Trials Conducted in Subjects 12 to 17 years with Scalp Psoriasis

In two uncontrolled prospective clinical trials, a total of 109 subjects aged 12-17 years with plaque psoriasis of the scalp were treated with Taclonex[®] Topical Suspension once daily for up to 8 weeks. The median weekly dose was 40 g. Adverse reactions included acne, acneiform dermatitis and application site pruritus (0.9% each).

6.2 Postmarketing Experience

Because adverse 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.

Postmarketing reports for local adverse reactions to topical corticosteroids may also include: atrophy, striae, telangiectasias, itching, dryness, hypopigmentation, perioral dermatitis, secondary infection, and miliaria.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects: Pregnancy Category C

Animal reproduction studies have not been conducted with Taclonex[®] Topical Suspension. Taclonex[®] 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[®] 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/m²/day); a dosage of 36 mcg/kg/day (432 mcg/m²/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/m²/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/m²/day) and rabbit (48 mcg/m²/day) derived from oral studies are lower than the maximum topical dose of calcipotriene in man (460 mcg/m²/day).

Corticosteroids have been shown to be 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/m²/day) and 2.5 mcg/kg/day (30 mcg/m²/day), respectively. Those dose levels are lower than the maximum topical dose in man (about 5,950 mcg/m²/day). The abnormalities observed included umbilical hernia, exencephaly and cleft palate.

8.3 Nursing Mothers

Systemically administered corticosteroids appear in human milk and can 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[®] Topical Suspension is administered to a nursing woman.

The patient should be instructed not to use Taclonex[®] Topical Suspension on the breast when nursing.

8.4 Pediatric Use

Safety and effectiveness of the use of Taclonex[®] Topical Suspension in pediatric patients under the age of 12 years have not been established.

The safety and effectiveness of Taclonex[®] Topical Suspension for the treatment of plaque psoriasis of the scalp have been established in the age group 12 to 17 years. Two prospective, uncontrolled trials (N=109) were conducted in pediatric subjects age 12 to 17 years with scalp psoriasis, including assessment of HPA axis suppression in 30 subjects. [See *Warnings and Precautions (5.2)*, *Adverse Reactions (6.1)* and *Clinical Pharmacology (12.2)*].

Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of systemic toxicity when treated with topical drugs. They are, therefore, also at greater risk of HPA axis suppression and adrenal insufficiency upon the use of topical corticosteroids. [See *Warnings and Precautions (5.2)*]

Rare systemic toxicities such as Cushing's syndrome, linear growth retardation, delayed weight gain, and intracranial hypertension have been reported in pediatric patients, especially those with prolonged exposure to large doses of high potency topical corticosteroids.

Local adverse reactions including striae have also been reported with use of topical corticosteroids in pediatric patients.

8.5 Geriatric Use

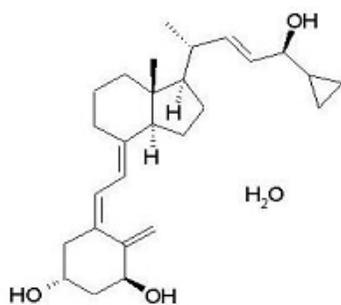
Clinical studies of Taclonex[®] Topical Suspension in plaque psoriasis on non-scalp areas included 124 subjects who were 65 years of age or over, and 36 were 75 years of age or over. Clinical studies of Taclonex[®] Topical Suspension in scalp psoriasis included 334 subjects who were 65 years or over and 84 subjects who were 75 years or over.

No overall differences in safety or effectiveness of Taclonex[®] Topical Suspension were observed between these subjects and younger subjects, and other reported clinical experience has not identified any differences in response between elderly and younger patients. However, greater sensitivity of some older individuals cannot be ruled out.

11 DESCRIPTION

Taclonex[®] Topical Suspension contains calcipotriene hydrate and betamethasone dipropionate. It is intended for topical use only. Calcipotriene hydrate is a synthetic vitamin D₃ analog.

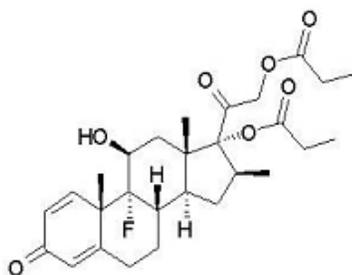
Chemically, calcipotriene hydrate is 9,10-secochola-5,7,10(19),22-tetraene-1,3,24-triol,24-cyclo-propyl-,monohydrate, (1 α ,3 β ,5Z,7E,22E,24S) with the empirical formula C₂₇H₄₀O₃·H₂O, a molecular weight of 430.6, and the following structural formula:



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 β ,16 β), with the empirical formula C₂₈H₃₇FO₇, 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® 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, polyoxypropylene stearyl ether, all-rac-alpha-tocopherol, butylhydroxytoluene, and mineral oil. Taclonex® Topical Suspension is an odorless clear to slightly off white suspension.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Taclonex® Topical Suspension combines the pharmacological effects of calcipotriene hydrate as a synthetic vitamin D₃ analog and betamethasone dipropionate as a synthetic corticosteroid. However, while their pharmacologic and clinical effects are known, the exact mechanisms of their actions in plaque psoriasis are unknown.

12.2 Pharmacodynamics

Hypothalamic-Pituitary-Adrenal (HPA) Axis Suppression:

HPA axis suppression was evaluated in three trials (Trial A, B, and C) following the application of Taclonex® 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® Topical Suspension on the scalp in combination with Taclonex® Ointment on the body for 4 to 8 weeks. Adrenal suppression as indicated by a 30-minute post-stimulation cortisol level ≤ 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® 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 ≤ 18 mcg/dL was observed in 3 out of 43 subjects (7.0%) after 4 weeks of treatment and in none of the 36 subjects who continued treatment for 8 weeks.

In Trial C, HPA axis suppression was evaluated in subjects 12 to 17 years (N=30) with plaque psoriasis of the scalp involving at least 20% of the scalp area. Treatment consisted of once daily application of Taclonex® Topical Suspension to the affected area on the scalp for up to 8 weeks. Adrenal suppression as indicated by a 30-minute post-stimulation cortisol level ≤ 18 mcg/dL was observed in 1 of 30 evaluable subjects (3.3%) after 4 weeks of treatment and in no subjects who continued treatment for 8 weeks.

Effects on Calcium Metabolism

In Trial A described above, the effects of once daily application of Taclonex® Topical Suspension on the scalp in combination with Taclonex® Ointment on the body for 4 to 8 weeks on calcium metabolism were also examined. Following once daily application of Taclonex® Topical Suspension on the scalp in combination with Taclonex® 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® 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).

In addition, calcium metabolism was evaluated in a total of 109 subjects aged 12 to 17 years with plaque psoriasis of the scalp involving at least 10% of the scalp area undergoing once daily application of Taclonex® Topical Suspension to the scalp for up to 8 weeks. No cases of hypercalcemia and no clinically relevant changes in urinary calcium were reported.

12.3 Pharmacokinetics

Absorption

Taclonex® Topical Suspension:

The systemic effect of Taclonex® 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® Topical Suspension on the scalp in combination with Taclonex® 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[®] 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 α,β -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 6 β -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/m²/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.

A 104-week oral carcinogenicity study was conducted with calcipotriene in male and female rats at doses of 1, 5 and 15 mcg/kg/day (corresponding to dosages of approximately 6, 30, and 90 mcg/m²/day). Beginning week 71, the dosage for high-dose animals of both genders was reduced to 10 mcg/kg/day (corresponding to a dosage of approximately 60 mcg/m²/day). A treatment-related increase in benign C-cell adenomas was observed in the thyroid of females that received 15 mcg/kg/day. A treatment-related increase in benign pheochromocytomas was observed in the adrenal glands of males that received 15 mcg/kg/day. No other statistically significant differences in tumor incidence were observed when compared to control. The relevance of these findings to patients is unknown.

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/m²/day and 39 mcg/m²/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 120, 260, and 1200 mcg/m²/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/m²/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/m²/day), and in female rats at oral doses of up to 1000 mcg/kg/day (6000 mcg/m²/day), of betamethasone dipropionate indicated no impairment of fertility.

14 CLINICAL STUDIES

Clinical Trials Conducted in Subjects 18 Years and Older with Scalp Psoriasis

Two multicenter, randomized, double-blind trials were conducted in adult subjects with scalp psoriasis. In Trial One, 1,407 subjects were randomized to 1 of 4 treatment groups: Taclonex[®] 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[®] 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 2 contains the response rates in each of these 2 trials.

Table 2

Percentage of Patients with Clear or Almost Clear Disease According to the Investigator’s Global Assessment of Disease Severity in Trials on the Scalp				
	Taclonex[®] Topical Suspension	Betamethasone Dipropionate in vehicle	Calcipotriene in vehicle	Vehicle
Trial One	(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%
Trial Two	(N = 512)	(N = 517)	(N = 251)	-
Week 2	47.1%	36.4%	12.7%	-
Week 8	67.2%	59.6%	41.0%	-

Clinical Trials Conducted in Subjects 12 to 17 years with Scalp Psoriasis

Two prospective, uncontrolled trials (N=109) were conducted in subjects 12 to 17 years with scalp psoriasis. In trial one 78 subjects with at least moderate scalp psoriasis at baseline and at least 10% scalp involvement were evaluated for safety. Seventy four percent (74%) of subjects had disease of moderate severity at baseline. In trial two, 31 subjects with at least moderate scalp psoriasis at baseline and at least 20% scalp involvement were evaluated for safety (including 30 subjects evaluated for HPA axis suppression). Sixty eight percent (68%) of subjects had disease of moderate severity at baseline. Subjects were treated once daily for up to 8 weeks with Taclonex[®] Topical Suspension. Calcium metabolism was evaluated in all subjects (N=109).

Psoriasis on the Body in Subjects 18 Years and Older

One multicenter, randomized, double-blind trial was conducted in subjects with plaque psoriasis on non-scalp areas, excluding face, axillae, and groin. In this trial, 1152 subjects were randomized to 1 of 4 treatment groups: Taclonex[®] 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 plaque psoriasis. 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 3 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[®] 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[®] 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)

60 g cartridge with applicator (NDC 50222-499-60)

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.

Bottle: Keep the bottle in the outer carton when not in use. Unused product should be discarded six months after the bottle has been opened.

Applicator: Unused product should be discarded six months after the cartridge has been opened.

16.3 Handling

Bottle: Shake before use.

Applicator: Follow the enclosed "Instructions for 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:

- Instruct adult patients (18 years and older) not to use more than 100 g per week.
- Instruct pediatric patients (12 to 17 years) not to use more than 60 g per week.
- Discontinue therapy when control is achieved unless directed otherwise by the physician.
- Do not apply Taclonex[®] 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.
- If applied to the scalp, do not wash hair or take a bath or shower right after application.
- Avoid use of Taclonex[®] Topical Suspension on the face, underarms, groin or eyes. If this medicine gets on face or in eyes, wash area right away.
- Do not occlude the treatment area with a bandage or other covering unless directed by the physician.
- Note that local reactions and skin atrophy are more likely to occur with occlusive use, prolonged use or use of higher potency corticosteroids.
- *Bottle:* Instruct patients to shake bottle prior to using Taclonex[®] Topical Suspension and to wash hands after application.
- *Applicator:* Instruct patients to wash hands if Taclonex[®] Topical Suspension gets on the fingers. Instruct patients not to use other products containing calcipotriene or a corticosteroid with Taclonex[®] Topical Suspension without first talking to the physician.
- Instruct patients who use Taclonex[®] Topical Suspension to avoid excessive exposure to either natural or artificial sunlight (including tanning booths, sun lamps, etc.).

PATIENT INFORMATION
Taclonex[®] (TAK-lo-NEKS)
(calcipotriene and betamethasone dipropionate)
Topical Suspension, 0.005%/0.064%

Taclonex[®] (TAK-lo-NEKS)
(calcipotriene and betamethasone dipropionate)
Topical Suspension, 0.005%/0.064% with Applicator

Important: Taclonex[®] Topical Suspension is for use on skin only (topical). Do not get Taclonex[®] Topical Suspension near or in your mouth, eyes, or vagina.

There are other medicines that contain the same medicine that is in Taclonex[®] Topical Suspension and are used to treat plaque psoriasis. Do not use other products containing calcipotriene or a corticosteroid medicine with Taclonex[®] Topical Suspension without talking to your doctor first.

What is Taclonex[®] Topical Suspension?

Taclonex[®] Topical Suspension is a prescription medicine used on the skin only (topical use) to treat:

- plaque psoriasis of the scalp and body in adults 18 years of age and older
- plaque psoriasis of the scalp in children from 12 to 17 years of age

It is not known if Taclonex[®] Topical Suspension is safe and effective in children under 12 years of age.

What should I tell my doctor before using Taclonex[®] Topical Suspension?

Before you use Taclonex[®] Topical Suspension, tell your doctor about all of your medical conditions, including if you:

- have a calcium metabolism disorder
- 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[®] Topical Suspension will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Taclonex[®] Topical Suspension passes into your breast milk. You should not use Taclonex[®] Topical suspension on your breast if you breastfeed.

Tell your doctor about all the medicines you take, including prescription and over-the counter medicines, vitamins, and herbal supplements.

How should I use Taclonex[®] Topical Suspension?

See the “Instructions for Use” for detailed information about the right way to use Taclonex[®] Topical Suspension Bottle or Taclonex[®] Topical Suspension with Applicator.

- Use Taclonex[®] Topical Suspension exactly as your doctor tells you to use it.
- Your doctor should tell you how much Taclonex[®] Topical Suspension to use and where to use it.
- Your doctor will decide which type of Taclonex[®] Topical Suspension to prescribe to you. Taclonex[®] Topical Suspension comes in:
 - a carton containing a 60 g bottle or a carton containing 120 g (2 bottles of 60 g)
 - an applicator, 60 g
- If you are 18 years of age or older, you should not use more than 100 grams of Taclonex[®] Topical Suspension in **1 week**.
- If you are 12 to 17 years of age, you should not use more than 60 grams of Taclonex[®] Topical Suspension in **1 week**.
- Do not use Taclonex[®] Topical Suspension longer than prescribed. Using too much Taclonex[®] Topical Suspension, or using it too often, or for too long can increase your risk for having serious side effects.
- Apply Taclonex[®] Topical Suspension to affected areas on the skin 1 time a day for up to 8 weeks. You should stop treatment when your plaque psoriasis is under control, unless your doctor gives you other instructions.
- Do not apply Taclonex[®] 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[®] Topical Suspension on your face or in your eyes, wash the area with water right away.
- Avoid using Taclonex[®] Topical Suspension on your face, groin, or armpits (axilla), or if you have thinning of your skin (atrophy) at the treatment site.
- Do not wash your hair, take a bath, or shower right after applying Taclonex[®] Topical Suspension as the medicine will not work as well to treat your psoriasis.

- **Do not bandage or cover the treated skin area, unless instructed by your doctor.**

What should I avoid while using Taclonex[®] Topical Suspension?

Avoid spending a long time in sunlight. Avoid tanning booths and sun lamps.

What are the possible side effects of Taclonex[®] Topical Suspension?

Taclonex[®] 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[®] 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[®] Topical Suspension in your eyes**

The most common side effects of Taclonex[®] 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[®] 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[®] Topical Suspension?

- Store Taclonex[®] Topical Suspension at room temperature between 68°F to 77°F (20°C to 25°C).
- Do not refrigerate **Taclonex[®] Topical Suspension**.
- Bottle: Keep the bottle in the outer carton when not in use.
- Bottle and Applicator: Discard unused Taclonex[®] Topical Suspension 6 months after it has been opened.

Keep Taclonex[®] Topical Suspension and all medicines out of the reach of children.

General information about Taclonex[®] Topical Suspension.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use Taclonex[®] Topical Suspension for a condition for which it was not prescribed. Do not give Taclonex[®] 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[®] Topical Suspension. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about Taclonex[®] Topical Suspension that is written for health professionals.

What are the ingredients in Taclonex[®] Topical Suspension?

Active ingredients: calcipotriene hydrate and betamethasone dipropionate.

Inactive ingredients: hydrogenated castor oil, polyoxypropylene stearyl ether, all-rac-alpha-tocopherol, butylhydroxytoluene and mineral oil.

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

Distributed by: LEO Pharma Inc., 1 Sylvan Way, Parsippany, NJ 07054, USA

For more information, go to www.taclonex.com or call 1-877-494-4536.

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

Revised 06/2016

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

Important: Taclonex[®] Topical Suspension is for use on skin only (topical). Do not get Taclonex[®] Topical Suspension near or in your mouth, eyes, or vagina.

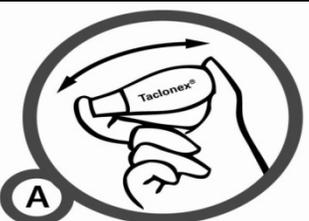
Read this Instructions for Use before you start using Taclonex[®] Topical Suspension and each time you get a refill. There may be new information. This information does not take the place of talking with your doctor about your medical condition or treatment.

How to apply Taclonex[®] Topical Suspension to your body:

Follow your doctor's instructions of how much Taclonex[®] Topical Suspension to use and where to use it. Apply Taclonex[®] Topical Suspension directly to areas affected by plaque psoriasis and gently rub in. Wash your hands after applying Taclonex[®] Topical Suspension, unless you are treating areas on your hands.

How to apply Taclonex[®] Topical Suspension to your scalp:

You do not need to wash your hair before you apply Taclonex[®] Topical Suspension.

 A circular illustration showing a hand holding a Taclonex bottle and shaking it. A curved arrow indicates the motion. A small circle with the letter 'A' is in the bottom left corner.	<p>Step 1: Shake the bottle before use. Remove the cap from the bottle. (See Figure A).</p>
 A circular illustration showing a top-down view of a person's head with their hair parted down the middle. A small circle with the letter 'B' is in the bottom left corner.	<p>Step 2: Locate the area to treat using your fingers and part your hair. (See Figure B).</p>
 A circular illustration showing a hand holding the Taclonex bottle and squeezing a drop of liquid onto the tip of a finger. A small circle with the letter 'C' is in the bottom left corner.	<p>Step 3: Squeeze a drop of Taclonex[®] Topical Suspension to your fingertip. (See Figure C).</p>
 A circular illustration showing a person's head with their hair parted. A hand is shown applying the drop of suspension to the scalp and rubbing it in. A small circle with the letter 'D' is in the bottom left corner.	<p>Step 4: Use your fingers to apply the drop of Taclonex[®] Topical Suspension directly to scalp affected by plaque psoriasis. Gently rub in. (See Figure D).</p>
<p>Step 5: After applying Taclonex[®] Topical Suspension, put the cap back on the bottle.</p> <p>Step 6: Wash your hands after applying Taclonex[®] Topical Suspension. Do not wash your hair right after you apply Taclonex[®] Topical Suspension to your scalp.</p>	

How should I store Taclonex Topical Suspension?

- Store the Taclonex[®] Topical[®] Suspension at room temperature between 68°F to 77°F (20°C to 25°C).
- Do not refrigerate Taclonex[®] Topical Suspension.
- Keep bottle in the outer carton when not in use.
- Discard unused Taclonex[®] Topical Suspension 6 months after it has been opened

Keep Taclonex[®] Topical Suspension and all medicines out of the reach of children.

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

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

Distributed by:
LEO Pharma Inc.
1 Sylvan Way
Parsippany, NJ 07054, USA

Revised 06/2016

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

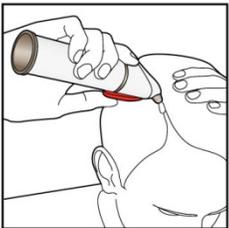
Important: Taclonex® Topical Suspension is for use on skin only (topical). Do not get Taclonex® Topical Suspension near or in your mouth, eyes, or vagina.

Read this Instructions for Use before you start using Taclonex® Topical Suspension with Applicator 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.

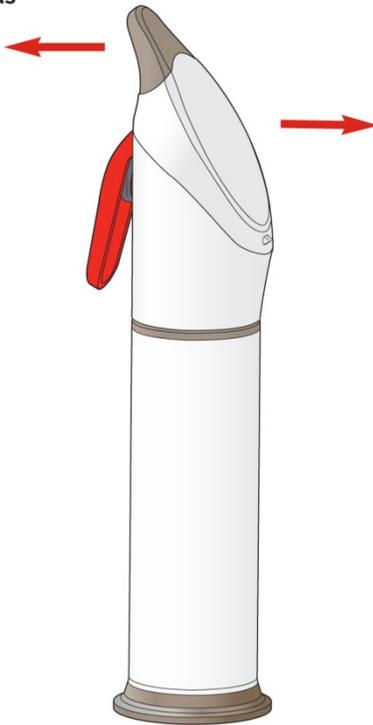
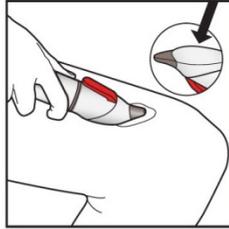
Do not share the Taclonex® Topical Suspension or the Applicator with other people.

Assembled Taclonex® Topical Suspension with Applicator

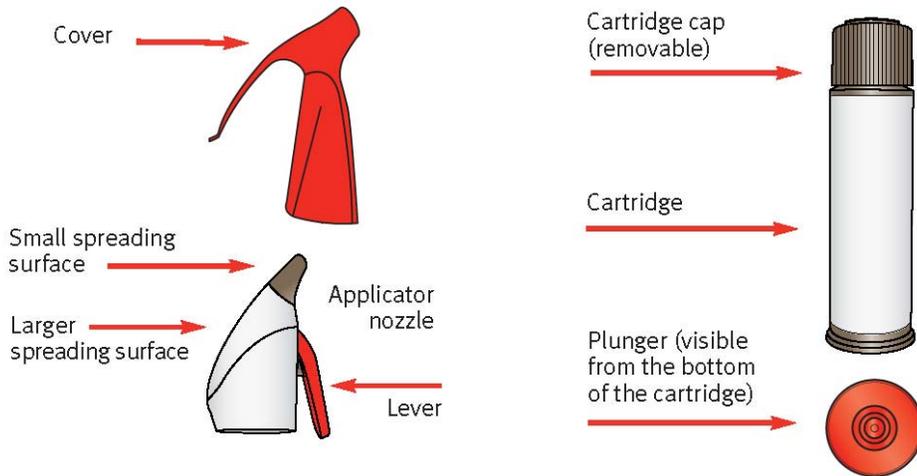
**Spreading surface
for small treatment areas**



**Spreading surface
for large treatment areas**



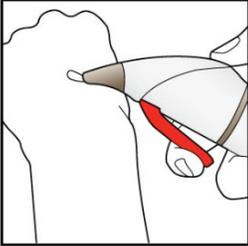
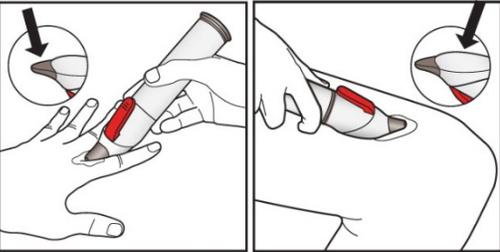
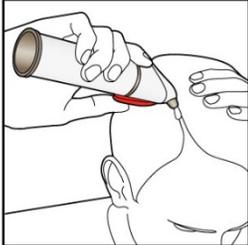
Parts of Your Taclonex® Topical Suspension with Applicator.



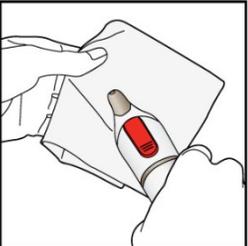
Preparing your Taclonex® Topical Suspension with Applicator:

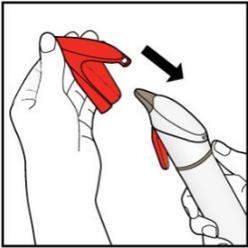
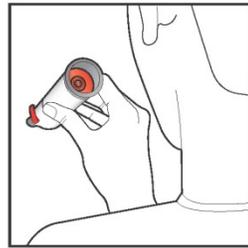
	<p>Step 1: Check the expiration date on the cartridge label.</p> <p>Do not use if expired. The expiration date on the cartridge refers to the last day of that month.</p> <p>Write the date that you assembled the applicator on the cartridge label. Do not use the applicator more than 6 months after this date.</p>
	<p>Step 2: Remove the cartridge cap.</p> <p>Hold the cartridge upright on a flat surface and twist the cap counter-clockwise to remove. Avoid tipping the cartridge as this may result in spilling the product.</p> <p>Throw away (discard) the cartridge cap after removing.</p>
	<p>Step 3: Attach the applicator head tightly.</p> <p>Keep the cartridge upright and align the applicator head.</p> <p>Screw the applicator head clockwise until the applicator head feels tightly sealed. Avoid touching the applicator nozzle. You will hear clicking sounds until it is tightly sealed.</p> <p>Note: Do not take apart (disassemble) the applicator. If you try to take the applicator apart, you may break the applicator.</p>
	<p>Step 4: Prime the applicator before first use.</p> <p>Hold the applicator while squeezing the lever with one hand. Gently push up on the center of the plunger with your thumb of your other hand, until you see the medicine come out at the nozzle tip.</p> <p>Note: If you travel in an airplane with your assembled Taclonex® Topical Suspension with Applicator, you may need to pump the lever a few times to re-prime before applying.</p>

Applying Taclonex[®] Topical Suspension with Applicator to the affected area:

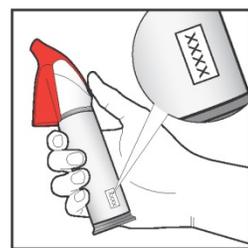
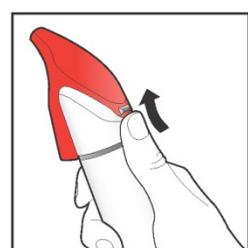
	<p>Step 5: Apply to the affected area.</p> <p>Place the applicator nozzle close to the affected area and press the lever one or more times to dispense the Taclonex[®] Topical Suspension.</p> <p>Release the lever fully between each pump to get a full dispense.</p> <p>One full pump delivers a consistent amount of Taclonex[®] Topical Suspension.</p>
	<p>Step 6: Use the spreading surfaces of the applicator head.</p> <p>Use the spreading surfaces to gently massage Taclonex[®] Topical Suspension into the affected skin.</p> <p>Be careful not to press the lever when spreading.</p>
	<p>Step 7: Use applicator nozzle to apply to scalp and hairline.</p> <p>Locate the area to treat using your fingers and part your hair.</p> <p>Use the applicator nozzle directly on the scalp or hairline.</p> <p>Press lever to dispense medicine and use the applicator nozzle to massage in Taclonex[®] Topical Suspension.</p>
<p>Step 8: After applying, check that the affected areas are fully treated with Taclonex[®] Topical Suspension.</p> <p>If needed, ask someone to help you apply Taclonex[®] Topical Suspension to areas you cannot reach or see.</p> <p>Wash your hands after use if you or someone helping you gets Taclonex[®] Topical Suspension on the fingers, unless you are treating areas on your hands. Do not wash your hair right after you apply Taclonex[®] Topical Suspension to your scalp.</p>	

After using Taclonex[®] Topical Suspension with Applicator:

	<p>Step 9: Clean your Taclonex[®] Topical Suspension with Applicator after each use.</p> <p>Following use, wipe the applicator head with one side of a clean, dry tissue for 3 seconds. After wiping, fold the tissue and use the other dry side of the tissue to wipe the applicator head again for an additional 3 seconds. Make sure that no product remains on the applicator head. Avoid pumping the applicator while cleaning.</p> <p>Note: Do not wash the applicator with water, detergents, or other products. Do not use moist or wet materials to wipe the applicator.</p>
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	<p>Step 10: Cover the applicator.</p> <p>Put the cover on after each use to keep the applicator head clean.</p> <p>Make sure you hear the cover click in place to prevent dispensing the product during storage and transportation.</p>
	<p>Step 11: Estimate the amount of remaining Taclonex® Topical Suspension.</p> <p>To estimate the amount of remaining Taclonex® Topical Suspension, look in the bottom of the cartridge to see the plunger position.</p>

Before using Taclonex® Topical Suspension with Applicator again:

	<p>Step 12: Check expiration date on the cartridge label before each use.</p> <p>Do not use if expired or 6 months after opening the cartridge.</p>
	<p>Step 13: Remove cover by lifting the tab at rear.</p>

How should I store Taclonex® Topical Suspension with Applicator?

- Store the Taclonex® Topical Suspension at room temperature between 68°F to 77°F (20°C to 25°C).
- Do not refrigerate Taclonex® Topical Suspension.
- Use Taclonex® Topical Suspension within 6 months after it has been opened.

Keep Taclonex® Topical Suspension with Applicator and all medicines out of the reach of children.

How should I throw away (dispose of) the Taclonex® Topical Suspension with Applicator?

- The Applicator should be thrown away (disposed of) when it is empty or has passed the expiration date.
- Ask your pharmacist for instructions on how to throw away (dispose of) the Taclonex® Topical Suspension with Applicator.

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

Manufactured by:

Distributed by:

LEO Laboratories Ltd.
285 Cashel Road
Dublin 12, Ireland

LEO Pharma Inc.
1 Sylvan Way
Parsippany, NJ 07054, USA

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