DISCLAIMER

All labeling reflected on this website is for informational and promotional purposes only. It is not intended to be used by healthcare professionals or patients for the purpose of prescribing or administering these products. Questions regarding the current content of product labeling should be directed to Akorn's Customer Service department at 800.932.5676.

Clobetasol Propionate Shampoo, 0.05%

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use CLOBETASOL PROPIONATE SHAMPOO safely and effectively. See full prescribing information for CLOBETASOL PROPIONATE SHAMPOO.

CLOBETASOL PROPIONATE shampoo, for topical use only
Initial U.S. Approval: 1985

INDICATIONS AND USAGE

Clobetasol propionate shampoo, 0.05% is a corticosteroid indicated for the treatment of moderate to severe scalp psoriasis in subjects 18 years of age and older. (1)

Limitations of Use: (1)
- Do not use on the face, axillae or groin. (1.2)
- Avoid any contact with the eyes and lips. (1.2)

DOSAGE AND ADMINISTRATION

- Not for oral, ophthalmic, or intravaginal use. (2)
- Clobetasol propionate shampoo, 0.05% should be applied onto dry (not wet) scalp once a day in a thin film to the affected areas only, and left in place for 15 minutes before lathering and rinsing. Clobetasol propionate shampoo, 0.05% contains a super-high potent topical corticosteroid; therefore treatment should be limited to 4 weeks. (2)
- As with other corticosteroids, therapy should be discontinued when control is achieved. (2)
- Total dosage should not exceed 50 g (50 mL or 1.75 fl. oz.) per week. (2)
- Clobetasol propionate shampoo should not be used with a shower cap or bathing cap. (2)

DOSAGE FORMS AND STRENGTHS

Shampoo, 0.05% (3)

CONTRAINDICATIONS

None (4)

WARNINGS AND PRECAUTIONS

Clobetasol propionate is a highly potent topical corticosteroid that has been shown to suppress the hypothalamic-pituitary-adrenal (HPA) axis at the lowest doses tested. (5.1) Cushing's syndrome, hyperglycemia and unmasking of latent diabetes mellitus can also result from systemic absorption of topical corticosteroids. (5.1)

Systemic absorption may require periodic evaluation for HPA axis suppression. Modify use if HPA axis suppression develops. (5.1)

Children may be more susceptible to systemic toxicity from use of topical corticosteroids. (5.1, 8.4)

If irritation develops in the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, use of clobetasol propionate shampoo should be discontinued until the infection has been adequately controlled. (5.3)

Local adverse reactions with topical corticosteroids may occur more frequently with the use of occlusive dressings and higher potency corticosteroids, including clobetasol propionate. These reactions include: folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, striae and miliaria. (5.4) (5)

ADVERSE REACTIONS

The most common adverse reactions are burning/stinging, pruritus, edema, folliculitis, acne, dry skin, irritant dermatitis, alopecia, urticaria, skin atrophy and telangiectasia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Hi-Tech Pharmacal Co., Inc. at 1-800-262-9010 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*. (6)

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

Revised: 03/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Indication

Clobetasol propionate shampoo, 0.05%, is a super-high potent topical corticosteroid formulation indicated for the treatment of moderate to severe forms of scalp psoriasis in subjects 18 years of age and older. Treatment should be limited to 4 consecutive weeks. The total dosage should not exceed 50 g (50 mL or 1.75 fl. oz.) per week.

Patients should be instructed to use clobetasol propionate shampoo, 0.05%, for the minimum time period necessary to achieve the desired results *[see Dosage and Administration (2)]*.

Use in patients younger than 18 years of age is not recommended due to numerically high rates of hypothalamic-pituitary-adrenal (HPA) axis suppression *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.4)]*.

1.2 Limitations of Use

Clobetasol propionate shampoo, 0.05%, should not be used on the face, groin or axillae. Avoid any contact of the drug product with the eyes and lips. In case of contact, rinse thoroughly with water all parts of the body that came in contact with the shampoo.

2 DOSAGE AND ADMINISTRATION

Clobetasol propionate shampoo, 0.05% is for topical use only, and not for ophthalmic, oral or intravaginal use.

Clobetasol propionate shampoo, 0.05%, should be applied onto dry (not wet) scalp once a day in a thin film to the affected areas only, and left in place for 15 minutes before lathering and rinsing.

The total dosage should not exceed 50 g (50 mL or 1.75 fl. oz.) per week.

Move the hair away from the scalp so that one of the affected areas is exposed. Position the bottle over the lesion. Apply a small amount of the shampoo directly onto the lesion, letting the product naturally flow from the bottle (gently squeeze the bottle), avoiding any contact of the product with the facial skin, eyes or lips. In case of contact, rinse thoroughly with water. Spread the product so that the entire lesion is covered with a thin uniform film. Massage gently into the lesion and repeat for additional lesion(s). Wash your hands after applying clobetasol propionate shampoo, 0.05%.

Leave the shampoo in place for 15 minutes, then add water, lather and rinse thoroughly all parts of the scalp and body that came in contact with the shampoo (e.g., hands, face, neck and shoulders). Avoid contact with eyes and lips. Minimize contact to non-affected areas of the body. Although no additional shampoo is necessary to cleanse your hair, you may use a non-medicated shampoo if desired.

Treatment should be limited to 4 consecutive weeks. As with other corticosteroids, therapy should be discontinued when control is achieved. If complete disease control is not achieved after 4 weeks of treatment with clobetasol propionate shampoo, 0.05%, treatment with a less potent topical steroid may be substituted. If no improvement is seen within 4 weeks, reassessment of the diagnosis may be necessary.

Clobetasol propionate shampoo, 0.05%, should not be used with occlusive dressings (shower cap or bathing cap) unless directed by a physician.

3 DOSAGE FORMS AND STRENGTHS

Shampoo, 0.05%, w/w. Each gram of clobetasol propionate shampoo, 0.05%, contains 0.5 mg of clobetasol propionate in a translucent, colorless to pale yellow viscous liquid.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Effects on the Endocrine System

Clobetasol propionate is a highly potent topical corticosteroid that has been shown to suppress the HPA axis at the lowest doses tested.

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.

The effect of clobetasol propionate shampoo, 0.05% on HPA axis suppression was evaluated in one trial in adolescents 12 to 17 years of age. In this trial, 5 of 12 evaluable subjects developed suppression of their HPA axis following 4 weeks of treatment with clobetasol propionate shampoo, 0.05% applied once daily for 15 minutes to a dry scalp before lathering and rinsing.

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 adrenocorticotropic hormone (ACTH) stimulation test may be helpful in evaluating patients for HPA axis suppression. If HPA axis suppression is documented, an attempt should be made to gradually withdraw the drug, to reduce the frequency of application, or to 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.

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 exposure.

Pediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios *[see Use in Specific Populations (8.4)]*.

5.2 Allergic Contact Dermatitis

If irritation develops, clobetasol propionate shampoo, 0.05%, should be discontinued and appropriate therapy instituted. Allergic contact dermatitis with corticosteroids is usually diagnosed by observing a failure to heal rather than noting a clinical exacerbation. Clinical diagnosis of allergic contact dermatitis can be confirmed with patch testing.

5.3 Concomitant Skin Infections

In the presence of dermatologic infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, use of clobetasol propionate shampoo, 0.05%, should be discontinued until the infection has been adequately controlled.

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. Clobetasol propionate is not recommended in patients with acne vulgaris, rosacea or perioral dermatitis.

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 directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In clinical trials with clobetasol propionate shampoo, 0.05%, the following adverse reactions have been reported: headache, burning/stinging, pruritus, edema, folliculitis, acne, dry skin, irritant dermatitis, alopecia, urticaria, skin atrophy and telangiectasia.

Table 1 summarizes selected adverse reactions that occurred in at least 1% of subjects in the Phase 2 and 3 studies for scalp psoriasis.

Table 1: Summary of Selected Adverse Reactions ≥1% by Body System

Body System	Clobetasol Propionate Shampoo, 0.05% N=558	Vehicle Shampoo, 0.05% N=127
Skin and Appendages	49 (8.8%)	28 (22.0%)
Discomfort Skin	26 (4.7%)	16 (12.6%)
Pruritus	3 (0.5%)	9 (7.1%)
Body As A Whole	33 (5.9%)	12 (9.4%)
Headache	10 (1.8%)	1 (0.8%)

Systemic absorption of topical corticosteroids has produced reversible HPA axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.

6.2 Postmarketing Experience

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The following adverse reactions have been identified during post-approval use of clobetasol propionate shampoo, 0.05%.

- *Endocrine disorders:* Cushing's syndrome, Adrenal suppression
- *Eye:* Eye pain, Vision blurred, Eye irritation
- *CNS:* Dizziness
- *GI:* Nausea
- *Skin:* Erythema, Skin exfoliation, Rash, Skin irritation, Hair color changes, Allergic contact dermatitis, Pain of skin, Skin tightness
- *Other:* Psoriasis (aggravation)

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic effects: Pregnancy Category C.

There are no adequate and well-controlled studies in pregnant women. Therefore, clobetasol propionate shampoo, 0.05% should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Some corticosteroids have been shown to be teratogenic after dermal application to laboratory animals.

Clobetasol propionate is absorbed percutaneously, and when administered subcutaneously it was a significant teratogen in both the rabbit and the mouse.

Clobetasol propionate has greater teratogenic potential than steroids that are less potent.

The effect of clobetasol propionate on pregnancy outcome and development of offspring was studied in the rat. Clobetasol propionate was administered subcutaneously to female rats twice daily (0, 12.5, 25, and 50 mcg/kg/day) from day 7 of presumed gestation through day 25 of lactation or day 24 presumed gestation for those rats that did not deliver a litter. The maternal no-observed-effect-level (NOEL) for clobetasol propionate was less than 12.5 mcg/kg/day due to reduced body weight gain and feed consumption during the gestation period. The reproductive NOEL in the dams was 25 mcg/kg/day (ratio of animal dose to proposed human dose of 0.07 on a mg/m^2/day basis) based on prolonged delivery at a higher dose level. The no-observed-adverse-effect-level (NOAEL) for viability and growth in the offspring was 12.5 mcg/kg/day (ratio of animal dose to proposed human dose of 0.03 on a mg/m^2/day basis) based on incidence of stillbirths, reductions in pup body weights on days 1 and 7 of lactation, increased pup mortality, increases in the incidence of umbilical hernia, and increases in the incidence of pups with cysts on the kidney at higher dose levels during the preweaning period. The weights of the epididymides and testes were significantly reduced at higher dosages. Despite these changes, there were no effects on the mating and fertility of the offspring.

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 topical administration of 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 clobetasol propionate shampoo, 0.05%, is administered to a nursing woman.

8.4 Pediatric Use

Use of clobetasol propionate shampoo, 0.05%, in patients under 18 years old is not recommended due to potential for HPA axis suppression *[see Warnings and Precautions (5.1)]*.

The effect of clobetasol propionate shampoo, 0.05%, on HPA axis suppression was evaluated in one trial in adolescents 12 to 17 years of age with moderate to severe scalp psoriasis with involvement of at least 25% of the scalp. In this trial, 5 of 12 evaluable subjects developed suppression of their HPA axis following 4 weeks of treatment with clobetasol propionate shampoo, 0.05%, applied once daily for 15 minutes to a dry scalp before lathering and rinsing. Only 1 of the 5 subjects who had suppression was tested for recovery of HPA axis, and this subject recovered after 2 weeks.

No studies have been performed in patients under the age of 12. Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of HPA axis suppression and Cushing's syndrome when they are treated with topical corticosteroids. They are therefore also at greater risk of adrenal insufficiency during and/or after withdrawal of treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children. Therefore, use is not recommended in patients under the age of 18.

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 an absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

8.5 Geriatric Use

Clinical studies of clobetasol propionate shampoo, 0.05%, did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently than younger subjects. In general, dose selection for an elderly patient should be made with caution, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

10 OVERDOSAGE

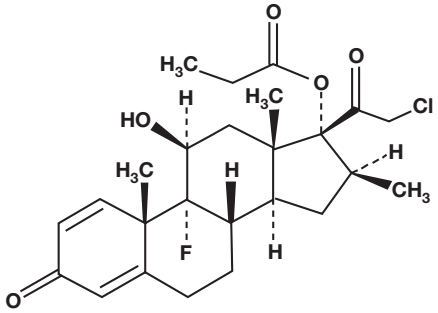
Topically applied, clobetasol propionate shampoo, 0.05%, can be absorbed in sufficient amounts to produce systemic effects *[see Warnings and Precautions (5.1)]*

11 DESCRIPTION

Clobetasol Propionate Shampoo, 0.05%, contains clobetasol propionate, a synthetic fluorinated corticosteroid, for topical use. The corticosteroids constitute a class of primarily synthetic steroids used topically as anti-inflammatory and antipruritic agents.

The chemical name of clobetasol propionate is 21-chloro-9-fluoro-11β, 17-dihydroxy-16β-methylpregna-1, 4-diene-3, 20-dione 17-propionate.

It has the following structural formula:



Clobetasol propionate

Clobetasol propionate has a molecular weight of 466.97 (CAS Registry Number 25122-46-7). The molecular formula is $C_{25}H_{32}ClFO_5$. Clobetasol propionate is a white to practically white crystalline, odorless powder insoluble in water.

Each gram of Clobetasol Propionate Shampoo, 0.05%, contains 0.5 mg of clobetasol propionate in a translucent, colorless to pale yellow viscous liquid shampoo base consisting of alcohol, citric acid, coco-betaine, polyquaternium-10, purified water, sodium citrate, and sodium laureth sulfate.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Like other topical corticosteroids, clobetasol propionate shampoo, 0.05%, has anti-inflammatory, antipruritic, and vasoconstrictive properties. The mechanism of the anti-inflammatory activity of the topical steroids, in general, is unclear. However, corticosteroids are thought to act by the induction of phospholipase A_2 inhibitory proteins, collectively called lipocortins. It is postulated that these proteins control the biosynthesis of potent mediators of inflammation such as prostaglandins and leukotrienes by inhibiting the release of their common precursor, arachidonic acid. Arachidonic acid is released from membrane phospholipids by phospholipase A_2.

12.2 Pharmacodynamics

Vasoconstrictor Assay

Clobetasol propionate shampoo, 0.05%, is in the super-high range of potency as demonstrated in vasoconstrictor studies in healthy subjects when compared with other topical corticosteroids. However, similar blanching scores do not necessarily imply therapeutic equivalence.

Hypothalamic-Pituitary-Adrenal (HPA) Axis Suppression

In studies evaluating the potential for hypothalamic-pituitary-adrenal (HPA) axis suppression, use of clobetasol propionate shampoo, 0.05%, resulted in demonstrable HPA axis suppression in 5 out of 12 (42%) adolescent subjects *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.4)]*.

12.3 Pharmacokinetics

The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle, the integrity of the epidermal barrier and occlusion.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and other disease processes in the skin may increase percutaneous absorption.

There are no human data regarding the distribution of corticosteroids to body organs following topical application. Nevertheless, once absorbed through the skin, topical corticosteroids are handled through metabolic pathways similar to systemically administered corticosteroids. They are metabolized, primarily in the liver, and are then excreted by the kidneys. In addition, some corticosteroids and their metabolites are also excreted in the bile.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Clobetasol propionate was not carcinogenic to rats when topically applied for 2 years at concentrations up to 0.005% which corresponded to doses up to 11 mcg/kg/day (ratio of animal dose to proposed human dose of 0.03 on a mg/m^2/day basis).

Clobetasol propionate at concentrations up to 0.001% did not increase the rate of formation of ultra violet light-induced skin tumors when topically applied to hairless mice 5 days per week for a period of 40 weeks.

Clobetasol propionate was negative in the *in vitro* mammalian chromosomal aberration test and in the *in vivo* mammalian erythrocyte micronucleus test.

The effect of subcutaneously administered clobetasol propionate on fertility and general reproductive toxicity was studied in rats at doses of 0, 12.5, 25, and 50 mcg/kg/day. Males were treated beginning 70 days before mating and females beginning 15 days before mating through day 7 of gestation. A dosage level of less than 12.5 mcg/kg/day clobetasol propionate was considered to be the no-observed-effect-level (NOEL) for paternal and maternal general toxicity based on decreased weight gain and for male reproductive toxicity based on increased weights of the seminal vesicles.The female reproductive NOEL was 12.5 mcg/kg/day (ratio of animal dose to proposed human dose of 0.03 on a mg/m^2/day basis) based on reduction in the numbers of estrous cycles during the pre-cohabitation period and an increase in the number of nonviable embryos at higher doses.

14 CLINICAL STUDIES

The safety and efficacy of clobetasol propionate shampoo, 0.05%, have been evaluated in two clinical trials involving 290 subjects with moderate to severe scalp psoriasis. In both trials, subjects were treated with either clobetasol propionate shampoo or the corresponding vehicle applied once daily for 15 minutes before lathering and rinsing for a period of 4 weeks. Efficacy results are presented in Table 2 below.

Table 2: Efficacy Results

	Clobetasol Propionate Shampoo, 0.05% N (%)		Shampoo Vehicle N (%)	
	Study A	**Study B**	**Study A**	**Study B**
Total Number of Subjects	95	99	47	49
Success Rate[1] at Endpoint[2]	40 (42.1%)	28 (28.3%)	1 (2.1%)	5 (10.2%)
Subjects with Scalp Psoriasis Parameter Clear (None) at Endpoint				
Erythema[3]	17 (17.9%)	12 (12.1%)	3 (6.4%)	1 (2.0%)
Scaling[3]	21 (22.1%)	15 (15.2%)	0 (0%)	2 (4.1%)
Plaque Thickening[3]	35 (36.8%)	34 (34.3%)	5 (10.6%)	5 (10.2%)

[1] Success rate defined as the proportion of subjects with a -0 (clear) or 1 (minimal) on a 0 to 5 point physician's Global Severity Scale for scalp psoriasis.

[2] At four (4) weeks or last observation recorded for a subject during the treatment period (baseline if no post-baseline data were available).

[3] Subjects with 0 (clear) on a 0 to 3 point scalp psoriasis parameter scale.

Clinical studies of clobetasol propionate shampoo, 0.05%, did not include sufficient numbers of non-Caucasian subjects to determine whether they respond differently than Caucasian subjects with regards to efficacy and safety.

16 HOW SUPPLIED/STORAGE AND HANDLING

Clobetasol Propionate Shampoo, 0.05%, is a translucent, colorless to pale yellow viscous liquid, supplied in 4 fl. oz. (118 mL) bottles.

NDC 50383-979-04

Storage: Keep tightly closed. Store at USP controlled room temperature 68° to 77°F (20° to 25°C), with excursions permitted between 59° and 86°F (15° to 30°C).

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information)

Information for Patients

Inform the patient using topical corticosteroids to adhere to following instructions:

- This medication is to be used as directed by the physician and should not be used longer than the prescribed time period.
- Clobetasol propionate shampoo, 0.05%, is for external use only. It should not be used on the face, underarms or groin areas. Avoid contact with the eyes and lips.
- This medication should not be used for any disorder other than that for which it was prescribed.
- The scalp area should not be covered while the medication is on the scalp (e.g., shower cap, bathing cap) so as to be occlusive unless directed by the physician.
- Patients should report any signs of local or systemic adverse reactions to their physician.
- As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 4 weeks, contact the physician.
- Patients should wash their hands after applying the medication.
- Patients should inform their physician(s) that they are using clobetasol propionate shampoo, 0.05%, if surgery is contemplated.
- Do not use other corticosteroid-containing products while using clobetasol propionate shampoo, 0.05%.
- Patients should not use more than 50 g (50 mL or 1.75 fl. oz.) per week of clobetasol propionate shampoo, 0.05%.

Manufactured by:
Hi-Tech Pharmacal Co., Inc.
Amityville, NY 11701

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