

# Final Sunscreen Regulations Expected This Fall

BY ELIZABETH MEHCATIE

The long-awaited regulation on sunscreen labeling is expected to be issued by the Food and Drug Administration this fall, more than 2 years after the agency proposed the regulation to address issues concerning testing and labeling requirements for ultraviolet A protection.

Rita Chappelle, a spokesperson for the

FDA, said in an interview that the agency anticipates a final ruling by September but is not providing any more specific information about what elements of the proposed rule would be included in the final rule.

The proposed rule, announced in the summer of 2007, includes a rating system that would use 1-4 stars on sunscreen product labels to indicate the degree of ultraviolet A (UVA) protection the prod-

uct provides and a prominent warning regarding skin cancer and other risks of sun exposure in the "Drug Facts" box. The proposed rule also caps the maximum sun protection factor (SPF) claim allowed at SPF 50+ and includes guidance on how to measure UVA protection.

Ms. Chappelle also said that changes are being made to the proposed rule based on comments that the FDA received in response to the proposal—even those that

came in after the 90-day comment period was closed in November 2007. The FDA received more than 3,000 comments in response to the proposal, which included a large amount of scientific data on topics such as UVA, UVB, and nanotechnology. The FDA had requested more information about the safety of sunscreen products that use nanotechnology because of the potential risk of nanoparticle ingredients penetrating the skin.

In an interview, Dr. Henry Lim, chairman of dermatology, at the Henry Ford Health System, Detroit, said that he did not know what the final rule would in-

**References:** 1. Clobex® Lotion Prescribing Information. September 2004. Galderma Laboratories, L.P. 2. Jarratt M, Breneman D, Gottlieb AB, et al. Clobetasol propionate shampoo 0.05%: a new option to treat patients with moderate to severe scalp psoriasis. *J Drugs Dermatol.* 2004;3:367-373. 3. Data on file. Galderma Laboratories.

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## CLOBEX® (clobetasol propionate) Shampoo, 0.05% Rx Only

**BRIEF SUMMARY**  
For External Use Only.  
Not for Ophthalmic Use

### INDICATIONS AND USAGE:

CLOBEX® (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 (see PRECAUTIONS). Treatment should be limited to 4 consecutive weeks because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis. The total dosage should not exceed 50 g (50 mL or 1.75 fl. oz.) per week.

Patients should be instructed to use CLOBEX® Shampoo, 0.05%, for the minimum time period necessary to achieve the desired results (see PRECAUTIONS).

Use in patients younger than 18 years of age is not recommended due to numerically high rates of HPA axis suppression (see PRECAUTIONS, Pediatric Use).

There were insufficient numbers of non-Caucasian patients to determine whether they responded differently than Caucasian patients with regards to efficacy and safety.

### CONTRAINDICATIONS:

Use of CLOBEX® (clobetasol propionate) Shampoo, 0.05%, is contraindicated in patients who are hypersensitive to clobetasol propionate, to other corticosteroids, or to any ingredient in this preparation.

### PRECAUTIONS:

**General:** 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 glucocorticosteroid insufficiency after withdrawal of treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on treatment.

Conditions which increase systemic absorption include the application of the more potent corticosteroids, use over large surface areas, prolonged use, and the addition of occlusive dressings or use on occluded areas. Therefore, patients applying a topical steroid to a large surface area or to areas under occlusion should be evaluated periodically for evidence of HPA axis suppression. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid. Recovery of HPA axis function is generally prompt and complete upon discontinuation of topical corticosteroids. Infrequently, signs and symptoms of glucocorticosteroid insufficiency may occur, requiring supplemental systemic corticosteroids. For information on systemic supplementation, see prescribing information for those products.

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

Pediatric patients may be more susceptible to systemic toxicity from equivalent doses due to their larger skin surface to body mass ratios. (See PRECAUTIONS - Pediatric Use).

If irritation develops, CLOBEX® Shampoo 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, as with most topical products not containing corticosteroids. Such an observation should be corroborated with appropriate diagnostic patch testing.

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 CLOBEX® Shampoo should be discontinued until the infection has been adequately controlled.

Although CLOBEX® Shampoo is intended for the topical treatment of moderate to severe scalp psoriasis, it should be noted that certain areas of the body, such as the face, groin, and axillae, are more prone to atrophic changes than other areas of the body following treatment with corticosteroids. CLOBEX® Shampoo 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.

**Information for patients:** Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the physician and should not be used longer than the prescribed time period. It is for external use only. Avoid contact with the eyes.
2. This medication should not be used for any disorder other than that for which it was prescribed.
3. 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.
4. Patients should report any signs of local or systemic adverse reactions to their physician.
5. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 4 weeks, contact the physician.
6. Patients should wash their hands after applying the medication.
7. Patients should inform their physician(s) that they are using CLOBEX® Shampoo if surgery is contemplated.
8. Patients should not use more than 50 g (50 mL or 1.75 fl. oz.) per week of CLOBEX® Shampoo.

**Laboratory tests:** The cortisyn stimulation test may be helpful in evaluating patients for HPA axis suppression.

**Carcinogenesis, mutagenesis, and impairment of fertility:** Long-term animal studies have not been performed to evaluate the carcinogenic potential of clobetasol propionate.

Clobetasol propionate did not produce any increase in chromosomal aberrations in Chinese hamster ovary cells *in vitro* in the presence or absence of metabolic activation. Clobetasol propionate was also negative in the micronucleus test in mice after oral administration.

Studies of the effect of CLOBEX® Shampoo on fertility have not been conducted.

**Pregnancy:** Teratogenic Effects: Pregnancy Category C: 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.

A teratogenicity study of clobetasol propionate in rats using the dermal route resulted in dose related maternal toxicity and fetal effects from 0.05 to 0.5 mg/kg/day. These doses are approximately 0.1 to 1.0 times, respectively, the maximum human topical dose of clobetasol propionate from CLOBEX® Shampoo. Abnormalities seen included low fetal weights, umbilical herniation, cleft palate, reduced skeletal ossification other skeletal abnormalities.

Clobetasol propionate administered to rats subcutaneously at a dose of 0.1 mg/kg from day 17 of gestation to day 21 postpartum was associated with prolongation of gestation, decreased number of offspring, increased perinatal mortality of offspring, delayed eye opening and delayed hair appearance in surviving offspring. Some increase in offspring perinatal mortality was also observed at a dose of 0.05 mg/kg. Doses of 0.05 and 0.1 mg/kg are approximately 0.1 and 0.2 fold the maximum human topical dose of clobetasol propionate from CLOBEX® Shampoo.

There are no adequate and well-controlled studies of the teratogenic potential of clobetasol propionate in pregnant women. CLOBEX® Shampoo should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**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 CLOBEX® Shampoo, 0.05%, is administered to a nursing woman.

**Pediatric use:** Use of CLOBEX® Shampoo, 0.05%, in patients under 18 years old is not recommended due to potential for HPA axis suppression (See PRECAUTIONS: General).

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

**Geriatric use:** Clinical studies of Clobetasol Propionate Shampoo, 0.05%, did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients. 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.

### ADVERSE REACTIONS:

In clinical trials with CLOBEX® Shampoo, the following adverse reactions have been reported: burning/stinging, pruritus, edema, folliculitis, acne, dry skin, irritant dermatitis, alopecia, urticaria, skin atrophy and telangiectasia.

The table below summarizes selected adverse events that occurred in at least 1% of subjects in the Phase 2 and 3 studies for scalp psoriasis.

Summary of Selected Adverse Events  $\geq 1\%$  by Body System

Body System	Clobetasol Propionate Shampoo N=558	Vehicle Shampoo 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%)

The following additional local adverse reactions have been reported infrequently with other topical corticosteroids, and they may occur more frequently with the use of occlusive dressings, especially with higher potency corticosteroids. These reactions are listed in an approximately decreasing order of occurrence: hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, skin atrophy, striae, and miliaria.

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

### OVERDOSAGE:

Topically applied, CLOBEX® Shampoo can be absorbed in sufficient amounts to produce systemic effects (See PRECAUTIONS).

US Patent Pending

Marketed by:  
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Manufactured by:  
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The new regulations will be beneficial to consumers, particularly with the added UVA information.



DR. LIM

clude, but that he and other dermatologists are looking forward to the release of the new regulations, which will be beneficial to consumers, particularly with the added information about UVA.

At a meeting that industry and American Academy of Dermatology representatives had with the FDA in December, Dr. Lim, chair of the Academy's council on science and research said that agency officials had questions about labeling issues, and asked industry representatives for information about the tests for UVA protection. ■

## Rosacea Research Grants Awarded

The National Rosacea Society awarded the following four research grants to advance the knowledge of rosacea:

► Dr. Robert W. Walters and Dr. Robert J. Lefkowitz of Duke University in Durham, N.C., received \$25,000 to investigate the role of beta-arrestin in cutaneous flushing.

► Dr. Curdin Conrad of the University of Texas M.D. Anderson Cancer Center in Houston, and Dr. Alexander Navarini of the University Hospital Zurich, received \$21,450 to investigate the role of plasmacytoid dendritic cell and interferon alpha in rosacea.

► Dr. Richard Gallo of the University of California, San Diego, and Dr. Kenshi Yamasaki of the Veterans Medical Research Foundation in San Diego, received \$25,000 to continue their research into how cathelicidins might contribute to the development of papulopustular rosacea. ► Dr. Joseph Rothnagel and Dr. Manuela Trabi of the University of Queensland, Australia, received \$18,000 to investigate the role of tissue kallikreins in the development of rosacea.

Researchers interested in applying for grants can visit [www.rosacea.org](http://www.rosacea.org). ■