CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-142

FINAL PRINTED LABELING

OLUX™ Foam, 0.05%

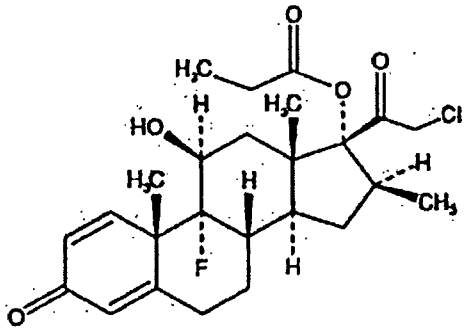
(clobetasol propionate)

Rx Only
For Dermatologic Use Only
Not for Ophthalmic Use

DESCRIPTION

OLUX Foam contains clobetasol propionate, USP, a synthetic corticosteroid, for topical dermatologic use. Clobetasol, an analog of prednisolone, has a high degree of glucocorticoid activity and a slight degree of mineralocorticoid activity.

Clobetasol propionate is (11β,16β)-21-chloro-9-fluoro-11-hydroxy-16-methyl-17 (1-oxopropoxy)-pregna-1,4-diene-3,20-dione, with the empirical formula $C_{25}H_{32}ClFO_5$, a molecular weight of 466.98 (CAS Registry Number 25122-46-7).
The following is the chemical structure:



Clobetasol propionate

Clobetasol propionate is a white or almost white, odorless, crystalline powder and is insoluble in water.

Each gram of OLUX Foam contains 0.5 mg clobetasol propionate, USP, in a thermolabile foam, which consists of ethanol (60%), purified water, propylene glycol, cetyl alcohol, stearyl alcohol, polysorbate 60, citric acid, and potassium citrate. OLUX Foam is dispensed from an aluminum can pressurized with a hydrocarbon propellant (propane/butane).

CLINICAL PHARMACOLOGY

Like other topical corticosteroids, clobetasol propionate foam has anti-inflammatory, antipruritic, and vasoconstrictive properties. The precise mechanism of the anti-inflammatory activity of topical steroids in the treatment of steroid-responsive dermatoses, in general, is uncertain. 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.

Pharmacokinetics:

Topical corticosteroids can be absorbed from intact healthy skin. The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Occlusion, inflammation and/or other disease processes in the skin may also increase percutaneous absorption.

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Due to the fact that circulating levels are well below the level of detection, the use of pharmacodynamic endpoints for assessing the systemic exposure of topical corticosteroids is necessary. 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.

CLINICAL STUDIES

The safety and efficacy of OLUX Foam has been demonstrated in an adequate and well-controlled clinical trial conducted in 188 patients with moderate to severe scalp psoriasis. Patients were treated twice daily for 2 weeks with OLUX Foam, vehicle foam, a commercially available clobetasol propionate solution (Temovate® Scalp Application), or Vehicle solution. After 2 weeks of treatment, study results of the 188 patients demonstrated that the efficacy of OLUX Foam in treating scalp psoriasis was superior to that of vehicle (foam and solution), and was comparable to that of Temovate Scalp Application (see Table below).

	OLUX Foam n (%)	Vehicle Foam n (%)
Subjects with Scalp Psoriasis Parameter Clear at Endpoint		
Scaling	42 (68)	3 (10)
Erythema	27 (44)	2 (6)
Plaque Thickness	41 (66)	3 (10)
Treatment Successes*	39 (63)	1 (3)
Total number of patients	62	31

*Defined as an Investigator's Global Assessment of "completely clear" or " almost clear," and a plaque thickness score of 0, an erythema score of 0 or 1, and a scaling score of 0 or 1 at Endpoint, scored on a severity scale of 0-4.

INDICATIONS AND USAGE

OLUX Foam is a super-potent topical corticosteroid indicated for short-term topical treatment of the inflammatory and pruritic manifestations of moderate to severe corticosteroid-responsive dermatoses of the scalp.

In a controlled pharmacokinetic study 3 of 13 patients experienced reversible suppression of the adrenal following 14 days of OLUX Foam therapy. Treatment beyond 2 consecutive weeks is not recommended, and the total dosage should not exceed 50 g per week because of the potential for the drug to suppress the

hypothalamic-pituitary-adrenal (HPA) axis. Use in children under 12 years of age is not recommended.

CONTRAINDICATIONS

OLUX Foam 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 super potent topical corticosteroid that has been shown to suppress the adrenal at 7.0 g of OLUX Foam per day. Lesser amounts of OLUX Foam were not studied. Systemic absorption of topical corticosteroids has caused reversible adrenal 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 augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings.

Therefore, patients applying a topical steroid to a large surface area or to areas under occlusion should be evaluated periodically for evidence of adrenal suppression. If adrenal 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 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.

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, OLUX Foam 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 OLUX Foam should be discontinued until the infection has been adequately controlled.

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 treated scalp area should not be bandaged or otherwise covered or wrapped so as to be occlusive unless directed by the physician.
4. Patients should report to their physician any signs of local adverse reactions.

Laboratory Tests: The following tests may be helpful in evaluating patients for adrenal suppression:

ACTH stimulation test
A.M. plasma cortisol test
Urinary free cortisol test

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential of clobetasol propionate.

Clobetasol propionate was non-mutagenic in three different test systems: the Ames test, the *Saccharomyces cerevisiae* gene conversion assay, and the *E. coli* B WP2 fluctuation test.

Studies in the rat following subcutaneous administration of clobetasol propionate at dosage levels up to 0.05 mg/kg per day revealed that the females exhibited an increase in the number of resorbed embryos and a decrease in the number of living fetuses at the highest dose.

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.

Clobetasol propionate has not been tested for teratogenicity by the topical route; however, it 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.

Teratogenicity studies in mice using the subcutaneous route resulted in fetotoxicity at the highest dose tested (1 mg/kg) and teratogenicity at all dose levels tested down to 0.03 mg/kg. These doses are approximately 1.4 and 0.04 times, respectively, the human topical dose of OLUX based on body surface area comparisons. Abnormalities seen included cleft palate and skeletal abnormalities.

In rabbits, clobetasol propionate was teratogenic at doses of 0.003 and 0.01 mg/kg. These doses are approximately 0.02 and 0.05 times, respectively, the human topical dose of OLUX based on body surface area comparisons. Abnormalities seen included cleft palate, cranioschisis, and other skeletal abnormalities.

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

Drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

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 breast milk. Because many drugs are excreted in human milk, caution should be exercised when OLUX Foam is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of OLUX Foam in pediatric patients have not been established; therefore, use in children under 12 years of age is not recommended. Because of a higher ratio of skin surface area to body mass, pediatric patients are at a greater risk than adults of adrenal suppression and Cushing's syndrome when they are treated with topical corticosteroids. They are therefore 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.

Adrenal 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.

Geriatric Use: Clinical studies of OLUX Foam did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, 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 a controlled trial (188 patients) with OLUX Foam, the only reported adverse reactions were one case each of dry skin, eczema, and skin hypertrophy. In larger controlled trials with other clobetasol propionate formulations, the most frequently reported adverse reactions have included burning, stinging, irritation, pruritus, erythema, folliculitis,

cracking and fissuring of the skin, numbness of the fingers, skin atrophy, and telangiectasia (all less than 2%).

The following additional local adverse reactions have been reported with topical corticosteroids, but they may occur more frequently with the use of occlusive dressings and higher potency corticosteroids such as OLUX Foam. These reactions are listed in an approximate decreasing order of occurrence: irritation, dryness, folliculitis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, skin atrophy, striae, and miliaria.

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

OVERDOSAGE

Topically applied OLUX Foam can be absorbed in sufficient amounts to produce systemic effects. (See **PRECAUTIONS**.)

DOSAGE AND ADMINISTRATION

Note: For proper dispensing of foam, hold the can upside down and depress the actuator.

OLUX Foam should be applied to the affected scalp area twice daily, once in the morning and once at night. Invert the can and dispense a small amount of OLUX Foam (up to a maximum of a golf-ball-size dollop) into the cap of the can, onto a saucer or other cool surface, or directly on the lesion, taking care to avoid contact with the eyes. Dispensing directly onto hands is not recommended, as the foam will begin to melt immediately upon contact with warm skin. Move the hair away from the affected area of the scalp so that the foam can be applied to each affected area. Gently massage into affected scalp area until the foam disappears. Repeat until entire affected scalp area is treated.

OLUX Foam is a super-high-potency topical corticosteroid; therefore, treatment should be limited to 2 consecutive weeks and amounts greater than 50 g/week should not be used. Use in pediatric patients under 12 years of age is not recommended.

Unless directed by a physician, OLUX Foam should not be used with occlusive dressings.

HOW SUPPLIED

OLUX Foam is supplied in a 100-gram aluminum can; box of one (NDC 63032-031-00).

Store at controlled room temperature 68-77°F (20-25°C).

WARNING

FLAMMABLE. AVOID FIRE, FLAME OR SMOKING DURING AND IMMEDIATELY FOLLOWING APPLICATION. Keep out of reach of children. Contents under pressure.

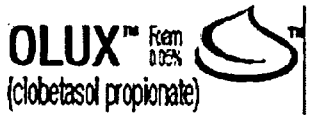
Do not puncture or incinerate container. Do not expose to heat or store at temperatures above 120°F (49°C).

Manufactured for:
Connetics Corporation
Palo Alto, CA 94303
USA

By:
CCL Pharmaceuticals
Runcorn WA7 1NU
United Kingdom

LB-0190/L00702 May 26, 2000

PATIENT INFORMATION



About OLUX™ Foam

Your doctor has prescribed OLUX Foam for the relief of dermatoses of the scalp, such as psoriasis. OLUX Foam works because its active ingredient is clobetasol propionate, 0.05%. Clobetasol propionate belongs to a group of medicines known as topical corticosteroids. These agents are used to reduce the inflammation, redness, swelling, itching, and tenderness associated with dermatologic conditions.

Other ingredients in OLUX Foam include ethanol, purified water, propylene glycol, cetyl alcohol, stearyl alcohol, polysorbate 60, citric acid, and potassium citrate. The foam is dispensed from an aluminum can that is pressurized by a hydrocarbon propellant (propane and butane).

If you answer YES to one or more of the following questions, tell your doctor (or pharmacist) before using this medicine, so you can get advice about what to do.

- Are you allergic to any of the ingredients contained in OLUX Foam?
- Are you pregnant? Planning on becoming pregnant while using OLUX Foam? Or are you breastfeeding?
- Do you think you have an infection on your scalp?

How to apply OLUX Foam

Turn the can upside down and dispense a small amount of OLUX Foam into the cap of the can, onto a clean saucer or other cool, clean surface, or directly onto the lesion, taking care to avoid contact with the eyes. Dispensing directly onto hands is not recommended, as the foam will begin to melt immediately upon contact with warm skin.

Move the hair away from the affected area of your scalp so that the foam can be applied to each affected area. Gently massage into the affected scalp area until the foam disappears. Repeat until entire affected scalp area is treated.

Apply twice daily, once in the morning and once at night. Use only enough to cover the affected areas.

Wash your hands after applying OLUX Foam and discard any unused dispensed medication.

Do not wash or rinse the treated areas immediately after applying OLUX Foam.

- Use this medication only for the condition for which it was prescribed. OLUX Foam should not be applied to the face, groin, or armpits.
- **OLUX Foam is for external use only.**

- **Keep the foam away from your eyes,** as it will sting. If the foam gets into your eyes, rinse well with cold water. If the stinging continues, contact your doctor immediately.

PATIENT INFORMATION

OLUX™ Foam 0.05% (clobetasol propionate)

WHAT YOU SHOULD KNOW ABOUT OLUX FOAM:

What to do if you miss an application

If you forget to apply OLUX Foam at the scheduled time, use it as soon as you remember, and then go back to your regular schedule. If you remember at or about the time of your next daily application, apply that dose and continue with your normal application schedule. If you miss several doses, tell your doctor.

About side effects

As with all medications, there may be some side effects. The most frequent side effects associated with the use of clobetasol propionate formulations include mild burning, stinging, or itching at the site of application. These side effects typically disappear shortly after application.

Let your doctor know if you notice any of the following:

- Any unusual effects that you do not understand.
- Affected areas that do not seem to be healing after 2 weeks of using the foam.

Important safety notes

- The treated areas should not be bandaged or covered unless directed by your doctor.
- Keep this and all medicines out of the reach of children.
- Treatment should be limited to 2 consecutive weeks.
- Treatment should be limited to no more than 50 g of medication per week.
- Use in patients under 12 years of age is not recommended.
- Keep the foam away from your eyes.

- Store the can at controlled room temperature, 68-77°F (20-25°C), and protect it from direct sunlight, as this is a pressurized container.

- **Keep away from and do not spray near fire, open flame, or direct heat—this product is flammable.** Do not smoke while using or holding the can. Keep the can away from all sources of ignition. Do not pierce or burn the can, and never throw the can in a fire, even if empty.

- When you have finished your treatment, dispose of the can safely. A completely empty can is recyclable.

- Do not use the foam after the expiration date shown on the bottom of the can.

- Do not give OLUX Foam to anyone else. Your doctor has prescribed this medicine for your use only.

This pamphlet has been designed to provide you with important information about OLUX Foam, but does not address every aspect of the foam. If, after reading this pamphlet, you have any questions or concerns, please speak with your doctor or pharmacist.

This information applies only to OLUX Foam.

via foam