

CLOBETASOL PROPIONATE- clobetasol propionate cream
Northstar RxLLC

CLOBETASOL PROPIONATE CREAM USP, 0.05%

(Potency expressed as clobetasol propionate)

FOR DERMATOLOGIC USE ONLY.

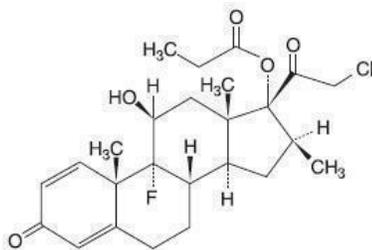
NOT FOR OPHTHALMIC, ORAL OR INTRAVAGINAL USE.

Rx only

DESCRIPTION:

Clobetasol propionate cream, USP contains the active compound clobetasol propionate, 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 a white to cream-colored crystalline powder insoluble in water. Chemically, it is 21-chloro-9-fluoro-11 β ,17-dihydroxy-16 β -methylpregna-1,4-diene-3,20-dione 17-propionate, and it has the following structural formula:



Molecular Formula: $C_{25}H_{32}ClFO_5$

Molecular Weight: 466.98

Each gram of the 0.05% cream contains clobetasol propionate 0.5 mg in a cream base of propylene glycol, glyceryl monostearate, cetostearyl alcohol, glyceryl stearate/PEG 100 stearate, white wax, chlorocresol, sodium citrate anhydrous, citric acid anhydrous, and purified water.

CLINICAL PHARMACOLOGY:

Like other topical corticosteroids, clobetasol propionate 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 A2 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 A2.

Pharmacokinetics: The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Occlusive dressings with hydrocortisone for up to 24 hours has not been demonstrated to increase penetration; however, occlusion of hydrocortisone for 96 hours markedly enhances penetration. Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin may increase percutaneous absorption. Greater absorption was observed for the clobetasol propionate gel formulation as compared to the cream formulation in *in vitro* human skin penetration studies. Studies

performed with clobetasol propionate gel, cream and ointment indicate that they are in the super-high range of potency as compared with other topical corticosteroids.

INDICATIONS AND USAGE:

Clobetasol propionate cream is a super-high potency corticosteroid formulation indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid responsive dermatoses. 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 pediatric patients under 12 years of age is not recommended. As with other highly active corticosteroids, therapy should be discontinued when control has been achieved. If no improvement is seen within 2 weeks, reassessment of the diagnosis may be necessary.

CONTRAINDICATIONS:

Clobetasol propionate cream is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

PRECAUTIONS:

General: Clobetasol propionate is a highly potent topical corticosteroid that has been shown to suppress the HPA axis at doses as low as 2 g per day.

Systemic absorption of topical corticosteroids can produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal from treatment. Manifestations of Cushing's syndrome, hyperglycemia, and glucosuria can also be produced in some patients by systemic absorption of topical corticosteroids while on therapy.

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. This may be done by using the ACTH stimulation, A.M. plasma cortisol, and urinary free cortisol tests. Patients receiving superpotent corticosteroids should not be treated for more than 2 weeks at a time and only small areas should be treated at any one time due to the increased risk of HPA 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 corticosteroid. 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, clobetasol propionate should be discontinued and appropriate therapy instituted. Allergic contact dermatitis with corticosteroids is usually diagnosed by observing *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. If concomitant skin infections are present or develop, an appropriate antifungal or antibacterial agent should be used. If a favorable response does not occur promptly, use of clobetasol propionate should be discontinued until the infection has been adequately controlled.

Clobetasol propionate cream should not be used in the treatment of rosacea or perioral dermatitis and it should not be used on the face, groin, or axillae.

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. 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 skin area should not be bandaged, otherwise covered or wrapped, so as to be occlusive unless directed by the physician.
4. Patients should report any signs of local adverse reactions to the physician.
5. Patients should inform their physicians that they are using clobetasol propionate if surgery is contemplated.

Laboratory Tests: The following tests may be helpful in evaluating patients for HPA axis suppression: ACTH stimulation test, A.M. plasma cortisol test, Urinary free cortisol test.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential of clobetasol propionate. Studies in the rat following subcutaneous administration at dosage levels up to 50 mcg/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. 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.

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 when applied topically; however, it is absorbed percutaneously, and when administered subcutaneously it was a significant teratogen in both the rabbit and 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 clobetasol propionate gel, cream and ointment. Abnormalities seen included cleft palate and skeletal abnormalities. In rabbits, clobetasol propionate was teratogenic at doses of 3 and 10 mcg/kg. These doses are approximately 0.02 and 0.05 times, respectively, the human topical dose of clobetasol propionate gel, cream and ointment. 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. Clobetasol propionate cream 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 clobetasol propionate cream is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of clobetasol propionate cream in pediatric patients have not been established. 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 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 or after withdrawal of treatment. Adverse effects including striae have been reported with inappropriate use of topical corticosteroids in infants and children (see PRECAUTIONS).

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.

Geriatric Use: Clinical studies of clobetasol propionate drug products in US clinical trials 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.

ADVERSE REACTIONS:

In controlled clinical trials, the most frequent adverse reactions reported for clobetasol propionate cream were burning and stinging sensation in 1% of treated patients. Less frequent adverse reactions were itching, skin atrophy, and cracking and fissuring of the skin.

Cushing's syndrome has been reported in infants and adults as a result of prolonged use of topical clobetasol propionate formulations. The following additional local adverse reactions have been reported with topical corticosteroids, and they may occur more frequently with the use of occlusive dressings and higher potency corticosteroids. These reactions are listed in an approximately decreasing order of occurrence: dryness, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, irritation, striae, and miliaria.

OVERDOSAGE:

Topically applied clobetasol propionate cream can be absorbed in sufficient amounts to produce systemic effects (see **PRECAUTIONS**).

DOSAGE AND ADMINISTRATION:

Apply a thin layer of clobetasol propionate cream, USP to the affected skin areas twice daily and rub in gently and completely. (SEE **INDICATIONS AND USAGE**.)

Clobetasol propionate cream is a super-high potency topical corticosteroid; therefore, **treatment should be limited to 2 consecutive weeks, and amounts greater than 50 g per week should not be used.**

As with other highly active corticosteroids, therapy should be discontinued when control has been achieved. If no improvement is seen within 2 weeks, reassessment of diagnosis may be necessary.

Clobetasol propionate cream should not be used with occlusive dressings.

HOW SUPPLIED:

Clobetasol Propionate Cream USP, 0.05% is supplied in tamper-evident tubes as follows:

15 g (NDC 16714-730-01)	30 g (NDC16714-730-02)
45 g (NDC 16714-730-03)	60 g (NDC16714-730-04)

Store at controlled room temperature 15° to 30°C (59° to 86°F). DO NOT REFRIGERATE.

Manufactured for: Northstar Rx LLC., Memphis, TN 38141

Manufactured By: E.FOUGERA & CO.

A division of Fougera Pharmaceuticals Inc.

Melville, New York 11747.

46208621A I07-2017

PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 15 G CONTAINER

NDC 16714-730-01

CLOBETASOL

PROPIONATE Cream USP, 0.05%

Northstar Rx LLC.

Rx Only

FOR DERMATOLOGIC USE ONLY.

NOT FOR OPHTHALMIC USE.

NET WT 15 grams

The image shows the principal display panel for a 15g container of Clobetasol Propionate Cream, USP 0.05%. The label features a blue header with 'NDC 16714-730-01' on the left and 'Rx only' on the right. The product name 'Clobetasol Propionate Cream, USP' is prominently displayed in large black font, with '0.05%' in a larger blue font below it. Underneath, it states 'FOR DERMATOLOGIC USE ONLY. NOT FOR OPHTHALMIC USE.' A blue banner at the bottom left contains the 'NORTHSTAR' logo, and the bottom right corner indicates '15 g'. The main body of the label contains detailed text: 'Each gram contains: Clobetasol propionate, USP 0.5 mg in a cream base of propylene glycol, glyceryl monostearate, cetostearyl alcohol, glyceryl stearate/PEG 100 stearate, white wax, chlorocresol, sodium citrate anhydrous, citric acid anhydrous, and purified water.' It also includes 'Usual dosage: See package insert for full prescribing information.', storage instructions ('Store at controlled room temperature 15° to 30°C (59° to 86°F). Do not refrigerate.'), and a warning to 'KEEP OUT OF THE REACH OF CHILDREN.' The manufacturer information is listed as 'Manufactured for: Northstar Rx LLC., Memphis, TN 38141 ©2005 NorthStar Healthcare Holdings UC Manufactured By: E. FOUGERA & CO. A division of Fougera Pharmaceuticals Inc. Melville, New York 11747. 46208613A I07-2017'. On the right side, there are three horizontal bars and the number '18'. Below the text, there is a barcode with 'N 3' to its left and '1' to its right, and the NDC number '16714-730-01' printed below the bars.

NDC 16714-730-01 **Rx only**

Clobetasol Propionate Cream, USP
0.05%

FOR DERMATOLOGIC USE ONLY. NOT FOR OPHTHALMIC USE.

NORTHSTAR **15 g**

Each gram contains: Clobetasol propionate, USP 0.5 mg in a cream base of propylene glycol, glyceryl monostearate, cetostearyl alcohol, glyceryl stearate/PEG 100 stearate, white wax, chlorocresol, sodium citrate anhydrous, citric acid anhydrous, and purified water.

Usual dosage: See package insert for full prescribing information.

Store at controlled room temperature 15° to 30°C (59° to 86°F). Do not refrigerate.

KEEP OUT OF THE REACH OF CHILDREN.

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A division of Fougera Pharmaceuticals Inc.
Melville, New York 11747. 46208613A I07-2017

Important: The opening of this product is covered by a metal tamper-resistant seal. If this seal has been punctured or is not visible, do not use and return product to place of purchase.

To open: To puncture the seal, reverse the cap and place the puncture-top onto the tube. Push down firmly until seal is open.

To close: Screw the cap back onto the tube.

See crimp of tube for Lot Number and Expiration Date.

N 3  1
16714-730-01

18

PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 15 G CARTON

NDC 16714-730-01

Rx only

CLOBETASOL PROPIONATE

Cream USP, 0.05%

Northstar Rx LLC.

FOR DERMATOLOGIC USE ONLY.

NOT FOR OPHTHALMIC USE.

NET WT 15 grams

NDC 16714-730-01 **Rx only**

Clobetazol Propionate Cream, USP 0.05%

FOR DERMATOLOGIC USE ONLY. NOT FOR OPHTHALMIC USE.

NORTHSTAR™ 15 g

46208617A
107-2017
#18

Rx only

Clobetazol Propionate Cream, USP 0.05% 15 g

NORTHSTAR™

NDC 16714-730-01

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Manufactured By: E. FOUGERA & CO.
A division of Fougera Pharmaceuticals Inc., Melville, New York 11747.

NDC 16714-730-01 **Rx only**

Clobetazol Propionate Cream, USP 0.05%

FOR DERMATOLOGIC USE ONLY. NOT FOR OPHTHALMIC USE.

NORTHSTAR™ 15 g

Each gram contains: Clobetazol propionate, USP 0.5 mg in a cream base of propylene glycol, glyceryl monostearate, cetostearyl alcohol, glyceryl stearate/PEG 100 stearate, white wax, chlorocresol, sodium citrate anhydrous, citric acid anhydrous, and purified water.
Usual dosage: See package insert for full prescribing information.
Store at controlled room temperature 15° to 30°C (59° to 86°F). Do not refrigerate.
KEEP OUT OF THE REACH OF CHILDREN.
Important: The opening of this product is covered by a metal tamper-resistant seal. If this seal has been punctured or is not visible, do not use and return product to place of purchase.
To open: To puncture the seal, reverse the cap and place the puncture-top onto the tube. Push down firmly until seal is open.
To close: Screw the cap back onto the tube.
See carton and crimp of tube for Lot Number and Expiration Date.

CLOBETASOL PROPIONATE

clobetasol propionate cream

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:16714-730
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CLOBETASOL PROPIONATE (UNII: 779619577M) (CLOBETASOL - UNII:ADN79D536H)	CLOBETASOL PROPIONATE	0.5 mg in 1 g

Inactive Ingredients

Ingredient Name	Strength
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
GLYCERYL MONOSTEARATE (UNII: 230OU9XXE4)	
CETOSTEARYL ALCOHOL (UNII: 2DMT128MIS)	

PEG-100 STEARATE (UNII: YD01N1999R)	
WHITE WAX (UNII: 7G1J5DA97F)	
CHLORO CRESOL (UNII: 36W53O7109)	
ANHYDROUS TRISODIUM CITRATE (UNII: RS7A450LGA)	
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:16714-730-01	15 g in 1 TUBE; Type 0: Not a Combination Product	11/06/2017	
2	NDC:16714-730-02	30 g in 1 TUBE; Type 0: Not a Combination Product	11/06/2017	
3	NDC:16714-730-03	45 g in 1 TUBE; Type 0: Not a Combination Product	11/06/2017	
4	NDC:16714-730-04	60 g in 1 TUBE; Type 0: Not a Combination Product	11/06/2017	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA074392	09/30/1996	

Labeler - Northstar RxLLC (830546433)

Revised: 11/2017

Northstar RxLLC