TEMOVATE- clobetasol propionate cream
TEMOVATE- clobetasol propionate ointment
PharmaDerm a division of Fougera Pharmaceuticals Inc.

TEMOVATE® (clobetasol propionate cream) Cream, 0.05%
TEMOVATE® (clobetasol propionate ointment) Ointment, 0.05%

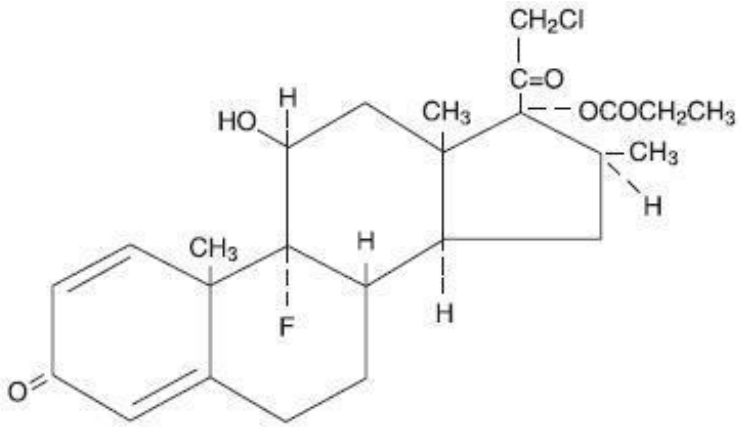
FOR TOPICAL DERMATOLOGIC USE ONLY—
NOT FOR OPHTHALMIC, ORAL, OR INTRAVAGINAL USE

Rx only

DESCRIPTION

TEMOVATE® (clobetasol propionate cream and ointment) Cream and Ointment, 0.05% contain 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.

Chemically, clobetasol propionate is (11ß,16ß)-21-chloro-9-fluoro-11-hydroxy-16-methyl-17-(1-oxopropoxy)-pregna-1,4-diene-3,20-dione, and it has the following structural formula:



Clobetasol propionate has the molecular formula $C_{25}H_{32}ClFO_5$ and a molecular weight of 467. It is a white to cream-colored crystalline powder insoluble in water.

TEMOVATE® Cream contains clobetasol propionate 0.5 mg/g in a cream base of propylene glycol, glyceryl monostearate, cetostearyl alcohol, glyceryl stearate, PEG 100 stearate, white wax, chlorocresol, sodium citrate, citric acid monohydrate, and purified water.

TEMOVATE® Ointment contains clobetasol propionate 0.5 mg/g in a base of propylene glycol, sorbitan sesquioleate, and white petrolatum.

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

Studies performed with TEMOVATE® Cream and Ointment indicate that they are in the super-high range of potency as compared with other topical corticosteroids.

INDICATIONS AND USAGE

TEMOVATE® Cream and Ointment are super-high potency corticos-teroid formulations indicated for the relief of the inflammatory and pru-ritic manifestations of corticosteroid-responsive dermatoses. Treatment beyond 2 consecutive weeks is not recommended, and the total dosage should not exceed 50 g/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

TEMOVATE® (clobetasol propionate cream and ointment) Cream and Ointment, 0.05% are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparations.

PRECAUTIONS

General: TEMOVATE® Cream and Ointment should not be used in the treatment of rosacea or perioral dermatitis, and should not be used on the face, groin, or axillae.

Systemic absorption of topical corticosteroids can produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal from treatment. Manifestations of Cushing 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 super-potent 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.

TEMOVATE® Cream and Ointment produced HPA axis suppression when used at doses as low as 2 g/day for 1 week in patients with eczema.

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 that require 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, TEMOVATE® Cream and Ointment 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.

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 TEMOVATE® Cream and Ointment 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. 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.

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/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 nonmutagenic in 3 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. Cortico-steroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. Some corticos-teroids 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 TEMOVATE® 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 TEMOVATE® 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. TEMOVATE® Cream and Ointment 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 cor-ticosteroid 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 TEMOVATE® Cream or Ointment is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of TEMOVATE® Cream and Ointment in pediatric patients have not been established. Use in pediatric patients 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 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.

HPA axis suppression, Cushing 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 TEMOVATE® Cream and Ointment, 0.05% 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 TEMOVATE® 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.

In controlled clinical trials, the most frequent adverse events reported for TEMOVATE® Ointment were burning sensation, irritation, and itching in 0.5% of treated patients. Less frequent adverse reactions were stinging, cracking, erythema, folliculitis, numbness of fingers, skin atrophy, and telangiectasia.

Cushing 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 TEMOVATE® Cream and Ointment can be absorbed in sufficient amounts to produce systemic effects (see PRECAUTIONS).

DOSAGE AND ADMINISTRATION

Apply a thin layer of TEMOVATE® Cream or Ointment to the affected skin areas twice daily and rub in gently and completely (see INDICATIONS AND USAGE).

TEMOVATE® Cream and Ointment are super-high potency topical corti-costeroids; therefore, **treatment should be limited to 2 consecutive weeks and amounts greater than 50 g/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.

TEMOVATE® Cream and Ointment should not be used with occlusive dressings.

HOW SUPPLIED

TEMOVATE® (clobetasol propionate cream) Cream, 0.05% is supplied in:
30-g tubes (NDC 10337-163-30), and
60-g tubes (NDC 10337-163-60).

TEMOVATE® (clobetasol propionate ointment) Ointment, 0.05% is supplied in:
15-g tubes (NDC 10337-162-15), and
30-g tubes (NDC 10337-162-30).

Store between 15° and 30°C (59° and 86°F). TEMOVATE® Cream should not be refrigerated.

PharmaDerm®

A division of Fougera Pharmaceuticals Inc.
Melville, NY 11747 USA
www.pharmaderm.com

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R01/18

PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 30 G CONTAINER

PharmaDerm®

NDC 10337-163-30

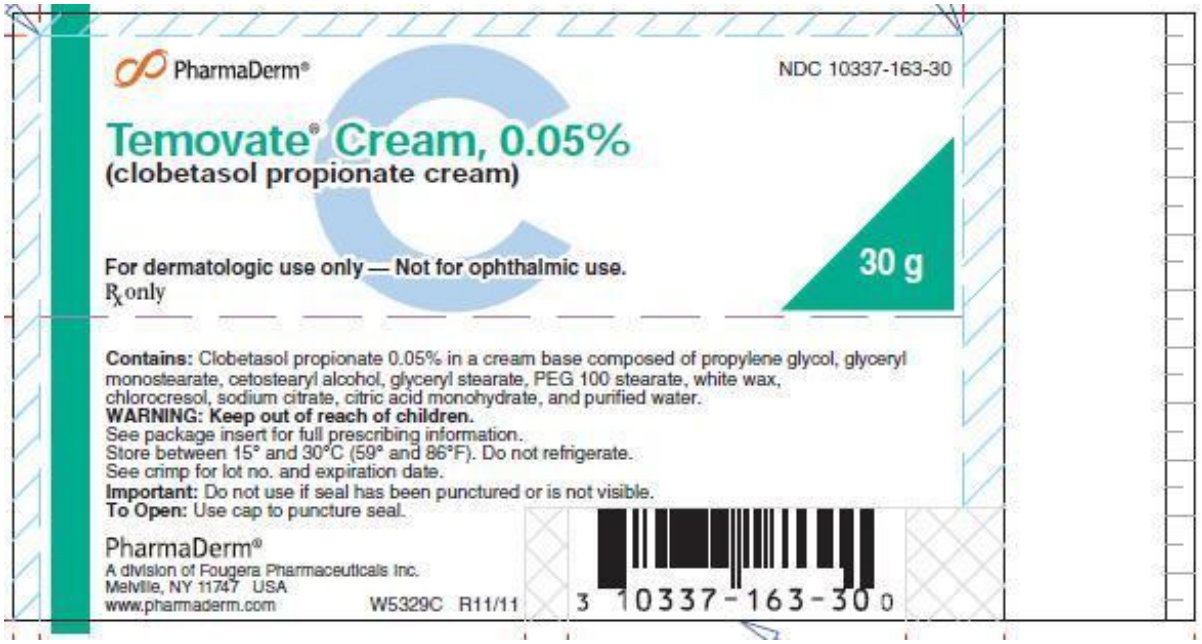
Temovate® Cream, 0.05%

(clobetasol propionate cream)

For dermatologic use only — Not for ophthalmic use.

Rx only

30 g



PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 30 G CARTON

PharmaDerm®

NDC 10337-163-30

Temovate® Cream, 0.05%

(clobetasol propionate cream)

For dermatologic use only —Not for ophthalmic use.

Rx only

30 g

PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 30 G CONTAINER

PharmaDerm®

NDC 10337-162-30

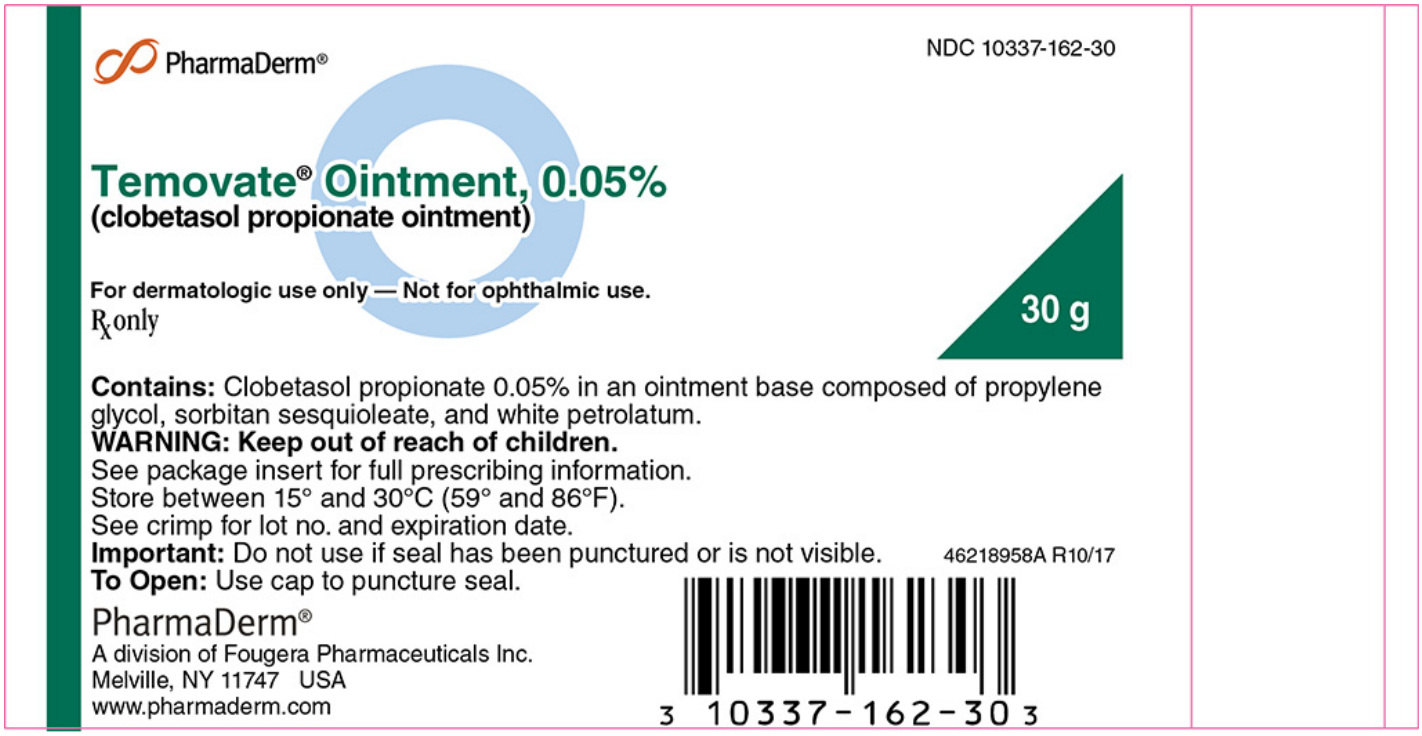
Temovate® Ointment, 0.05%

(clobetasol propionate ointment)

For dermatologic use only — Not for ophthalmic use.

Rx only

30 g



PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 30 G CARTON

PharmaDerm®

NDC 10337-162-30

Temovate® Ointment, 0.05%

(clobetasol propionate ointment)

For dermatologic use only — Not for ophthalmic use.

Rx only

30 g

TEMOVATE

clobetasol propionate cream

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:10337-163
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: 2DMT128M1S)	
PEG-100 stearate (UNII: YD01N1999R)	
white wax (UNII: 7G1J5DA97F)	
chlorocresol (UNII: 36W53O7109)	
citric acid monohydrate (UNII: 2968PHW8QP)	
water (UNII: 059QF0KO0R)	
SODIUM CITRATE, UNSPECIFIED FORM (UNII: 1Q73Q2JULR)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:10337-163-30	1 in 1 CARTON	09/30/1996	
1		30 g in 1 TUBE; Type 0: Not a Combination Product		
2	NDC:10337-163-60	1 in 1 CARTON	09/30/1996	
2		60 g in 1 TUBE; Type 0: Not a Combination Product		

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

TEMOVATE

clobetasol propionate ointment

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:10337-162
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)	
sorbitan sesquioleate (UNII: 0W8RRI5W5A)	
petrolatum (UNII: 4T6H12BN9U)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:10337-162-15	1 in 1 CARTON	02/23/1996	
1		15 g in 1 TUBE; Type 0: Not a Combination Product		
2	NDC:10337-162-30	1 in 1 CARTON	02/23/1996	
2		30 g in 1 TUBE; Type 0: Not a Combination Product		

Marketing Information			
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA074407	02/23/1996	

Labeler - PharmaDerm a division of Fougera Pharmaceuticals Inc. (043838424)

Revised: 3/2019 PharmaDerm a division of Fougera Pharmaceuticals Inc.