

CLOBETASOL PROPIONATE- clobetasol propionate gel
Padagis Israel Pharmaceuticals Ltd

Clobetasol Propionate Gel, 0.05%

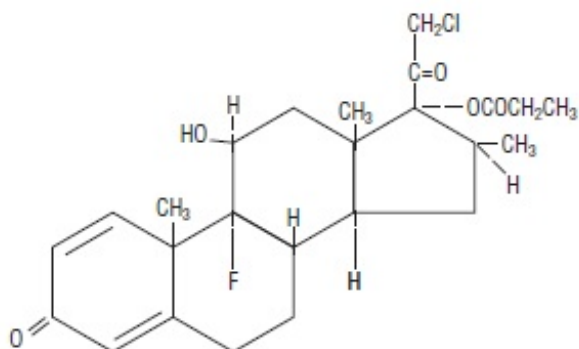
Rx Only

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

DESCRIPTION

Clobetasol Propionate Gel, 0.05% 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.

Chemically, clobetasol propionate is (11 β ,16 β)-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 empirical 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.

Clobetasol Propionate Gel, 0.05% contains clobetasol propionate 0.5 mg/g in a base of carbomer homopolymer type B, propylene glycol, purified water, and sodium hydroxide.

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. 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, 0.05% indicate that it is in the super-high range of potency as compared with other topical corticosteroids.

INDICATIONS AND USAGE

Clobetasol Propionate Gel, 0.05% 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/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.

CONTRAINDICATIONS

Clobetasol Propionate Gel, 0.05% 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/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 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 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 corticosteroid.

Recovery of HPA axis function is generally prompt and complete 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, Clobetasol Propionate Gel, 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 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 Gel, 0.05% should be discontinued until the infection has been adequately controlled.

Clobetasol Propionate Gel, 0.05% should not be used in the treatment of rosacea or perioral dermatitis, and 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 Gel, 0.05% 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/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 -

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. 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. 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 Gel, 0.05% 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 Gel, 0.05% is administered to a nursing woman.

Pediatric Use -

Safety and effectiveness of Clobetasol Propionate Gel, 0.05% in children and infants 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, children are at a greater risk than adults of HPA axis suppression when they are treated with topical corticosteroids. They are therefore also at greater risk of adrenal insufficiency after withdrawal of treatment and of

Cushing's syndrome while on 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, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Geriatric Use -

Clinical studies of clobetasol propionate gel, 0.05% 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 a controlled trial with clobetasol propionate gel, 0.05%, the only reported adverse reaction that was considered to be drug related was a report of burning sensation (1.8% of treated patients).

In larger controlled clinical 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 fingers, skin atrophy, and telangiectasia (all less than 2%).

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 are reported infrequently with topical corticosteroids, but may occur more frequently with super-high potency corticosteroids such as Clobetasol Propionate Gel, 0.05%. These reactions are listed in approximate decreasing order of occurrence: dryness, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, secondary infection, irritation, striae, and miliaria.

OVERDOSAGE

Topically applied Clobetasol Propionate Gel, 0.05% can be absorbed in sufficient amounts to produce systemic effects (see **PRECAUTIONS**).

DOSAGE AND ADMINISTRATION

Apply a thin layer of Clobetasol Propionate Gel, 0.05% to the affected skin areas twice daily and rub in gently and completely (see **INDICATIONS AND USAGE**).

Clobetasol Propionate Gel, 0.05% 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.

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 Gel, 0.05% should not be used with occlusive dressings.

HOW SUPPLIED

Clobetasol Propionate Gel, 0.05% is available as follows:

15 g tube (NDC 45802-**925**-14)

30 g tube (NDC 45802-**925**-94)

60 g tube (NDC 45802-**925**-96)

STORAGE

Store at 20-25°C (68-77°F) [see USP Controlled Room Temperature]. **Clobetasol Propionate Gel, 0.05% should not be refrigerated.**

Manufactured by Padagis®

Yeruham, Israel

www.padagis.com

Rev 03-23

2P100 RC PH6

PRINCIPAL DISPLAY PANEL - Carton

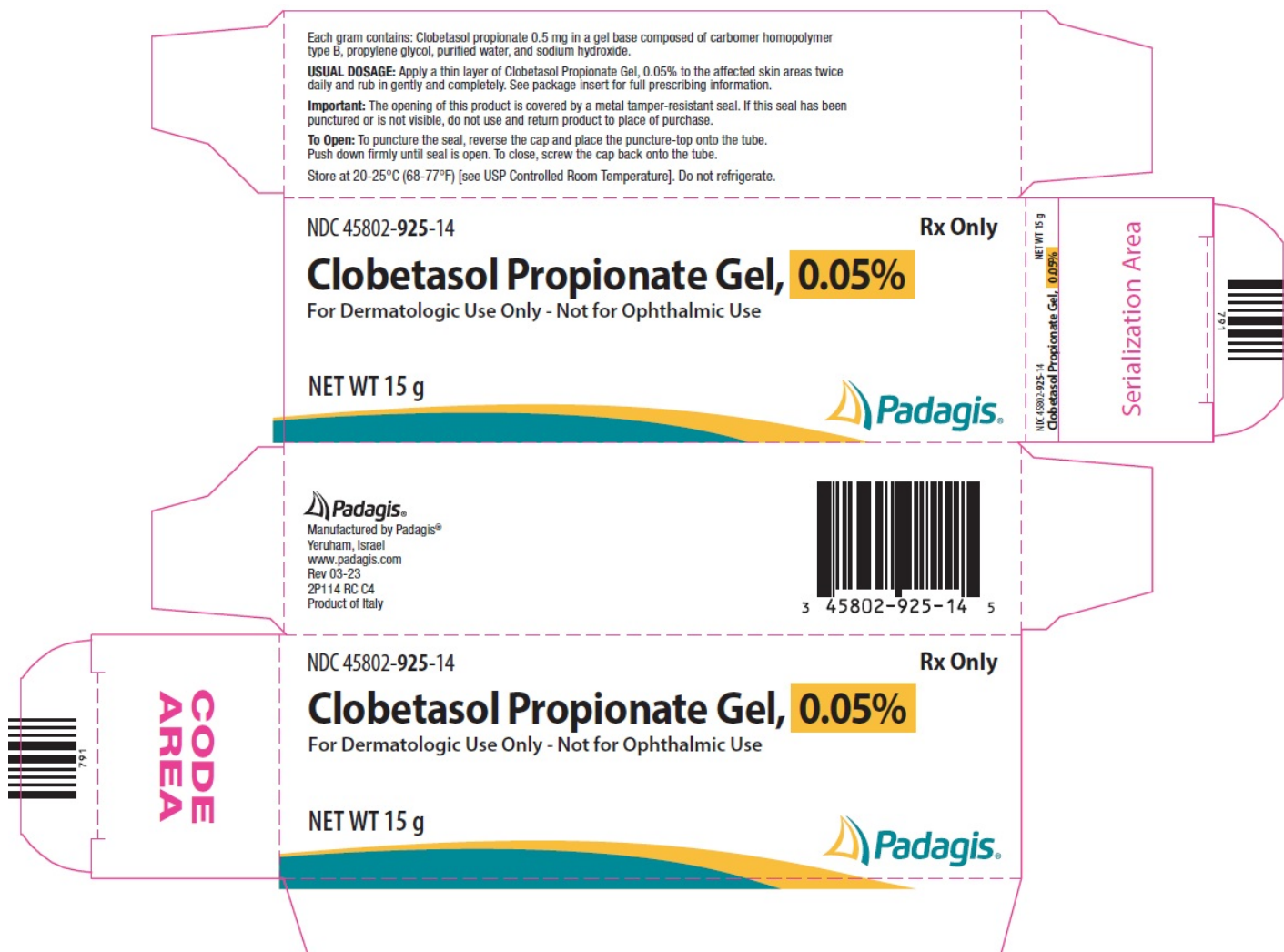
NDC 45082-925-14

Rx Only

Clobetasol Propionate Gel, 0.05%

For Dermatologic Use Only - Not for Ophthalmic Use

NET WT 15 g



The following image is a placeholder representing the product identifier that is either affixed or imprinted on the drug package label during the packaging operation.

S/N [insert product's serial number]
 Lot [insert product's lot number]
 Exp [insert product's expiration date]

CLOBETASOL PROPIONATE			
clobetasol propionate gel			
Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:45802-925
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
CARBOMER HOMOPOLYMER TYPE B (ALLYL PENTAERYTHRITOL CROSSLINKED) (UNII: HHT01Z NK31)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
WATER (UNII: 059QF0KO0R)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:45802-925-14	1 in 1 CARTON	07/30/2008	
1		15 g in 1 TUBE; Type 0: Not a Combination Product		
2	NDC:45802-925-94	1 in 1 CARTON	11/11/2008	
2		30 g in 1 TUBE; Type 0: Not a Combination Product		
3	NDC:45802-925-96	1 in 1 CARTON	07/31/2008	
3		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	ANDA075027	07/30/2008	

Labeler - Padagis Israel Pharmaceuticals Ltd (600093611)

Revised: 3/2023

Padagis Israel Pharmaceuticals Ltd