

CLOBETASOL PROPIONATE- clobetasol propionate cream
Amneal Pharmaceuticals NY LLC

Clobetasol Propionate Cream, USP 0.05%

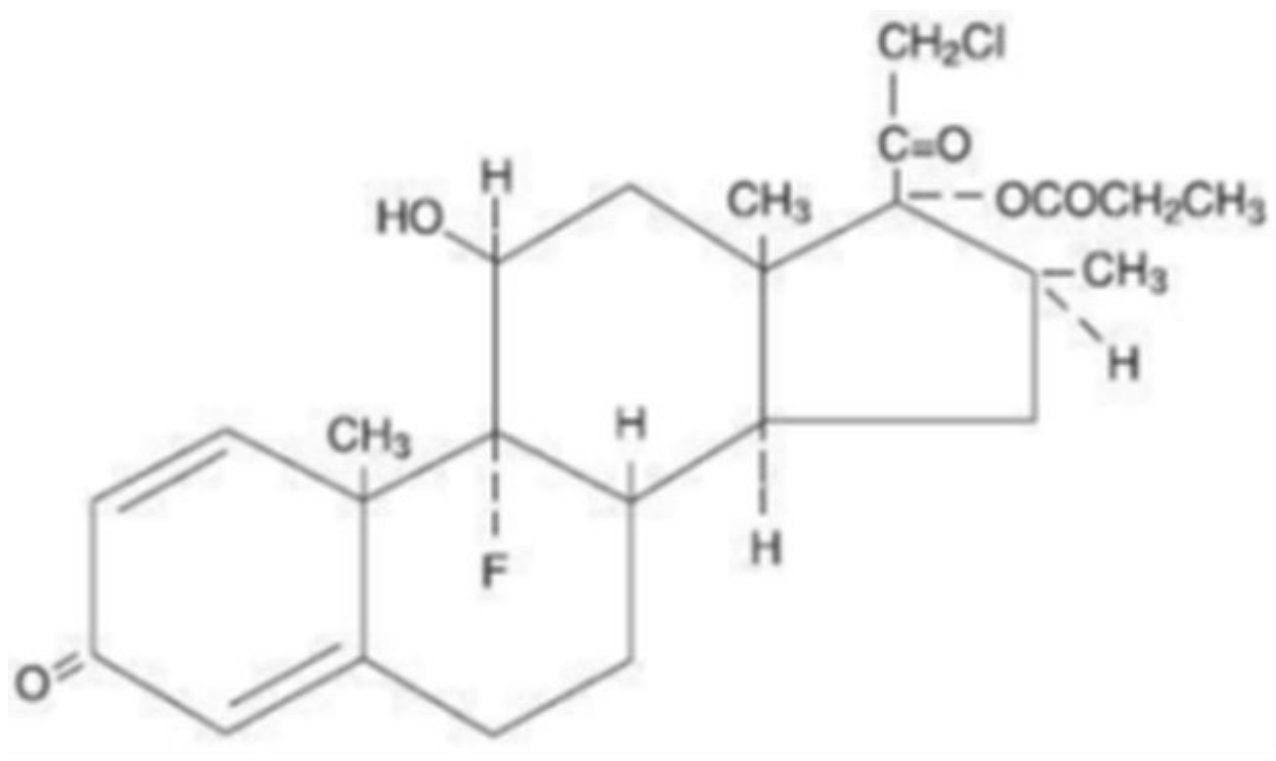
**FOR TOPICAL DERMATOLOGIC USE ONLY—
NOT FOR OPHTHALMIC, ORAL, OR INTRAVAGINAL USE**

Rx only

DESCRIPTION

Clobetasol propionate cream, USP 0.05% contains the active compound 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.

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



Clobetasol propionate, USP has the empirical formula $C_{25}H_{32}ClFO_5$ and a molecular weight of 466.97. It is a white to almost white crystalline powder insoluble in water.

Clobetasol propionate cream, USP, contains clobetasol propionate 0.5 mg/g in a cream base of anhydrous citric acid, cetyl alcohol, glycol stearate, lanolin oil, methylparaben, PEG-8 stearate, polysorbate 60, propylene glycol, propylparaben, purified water, sodium citrate, stearyl alcohol, and white petrolatum. Sodium hydroxide pellets may be used to adjust pH.

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 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 clobetasol propionate cream indicate that it is 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/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, 0.05% is contraindicated in those patients with a history of hypersensitivity to any of the components of the preparations.

PRECAUTIONS

General

Clobetasol propionate cream 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.

Clobetasol propionate cream 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, clobetasol propionate cream 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 cream 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. 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 cream.

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 cream. 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 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

A limited number of patients at or above 65 years of age have been treated with clobetasol propionate cream (n = 231) in US and non-US clinical trials. While the number of patients is too small to permit separate analysis of efficacy and safety, the adverse reactions reported in this population were similar to those reported by younger patients. Based on available data, no adjustment of dosage of clobetasol propionate cream in geriatric patients is warranted.

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 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.

To report SUSPECTED ADVERSE REACTIONS, contact Amneal Pharmaceuticals at 1-877-835-5472 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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 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/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.

Geriatric Use: In studies where geriatric patients (65 years of age or older, see **PRECAUTIONS**) have been treated with clobetasol propionate cream, safety did not differ from that in younger patients; therefore, no dosage adjustment is recommended.

HOW SUPPLIED

Clobetasol Propionate Cream, USP **0.05%** is available as a white to off-white cream. It is supplied as follows:

| | |
|------------|------------------|
| 15 g Tubes | NDC 69238-1532-5 |
| 30 g Tubes | NDC 69238-1532-3 |
| 45 g Tubes | NDC 69238-1532-4 |
| 60 g Tubes | NDC 69238-1532-6 |

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Clobetasol Propionate Cream, USP should not be refrigerated.

Distributed by:

Amneal Pharmaceuticals LLC

Bridgewater, NJ 08807

Rev. 02-2018-00

PRINCIPAL DISPLAY PANEL



NDC 69238-1532-5

Clobetasol Propionate Cream, USP 0.05%

For dermatologic use only - Not for ophthalmic use.

Rx only

15 g

Contains: Clobetasol propionate, 0.5 mg/g in a cream base composed of anhydrous citric acid, cetyl alcohol, glycol stearate, lanolin oil, methylparaben, PEG-8 stearate, polysorbate 60, propylene glycol, propylparaben, purified water, sodium citrate, stearyl alcohol, and white petrolatum. Sodium hydroxide pellets may be used to adjust pH.

WARNING: Keep out of reach of children.

USUAL DOSAGE: See package insert for full prescribing information.

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature]. Do not refrigerate. See crimp for lot no. and expiration date.

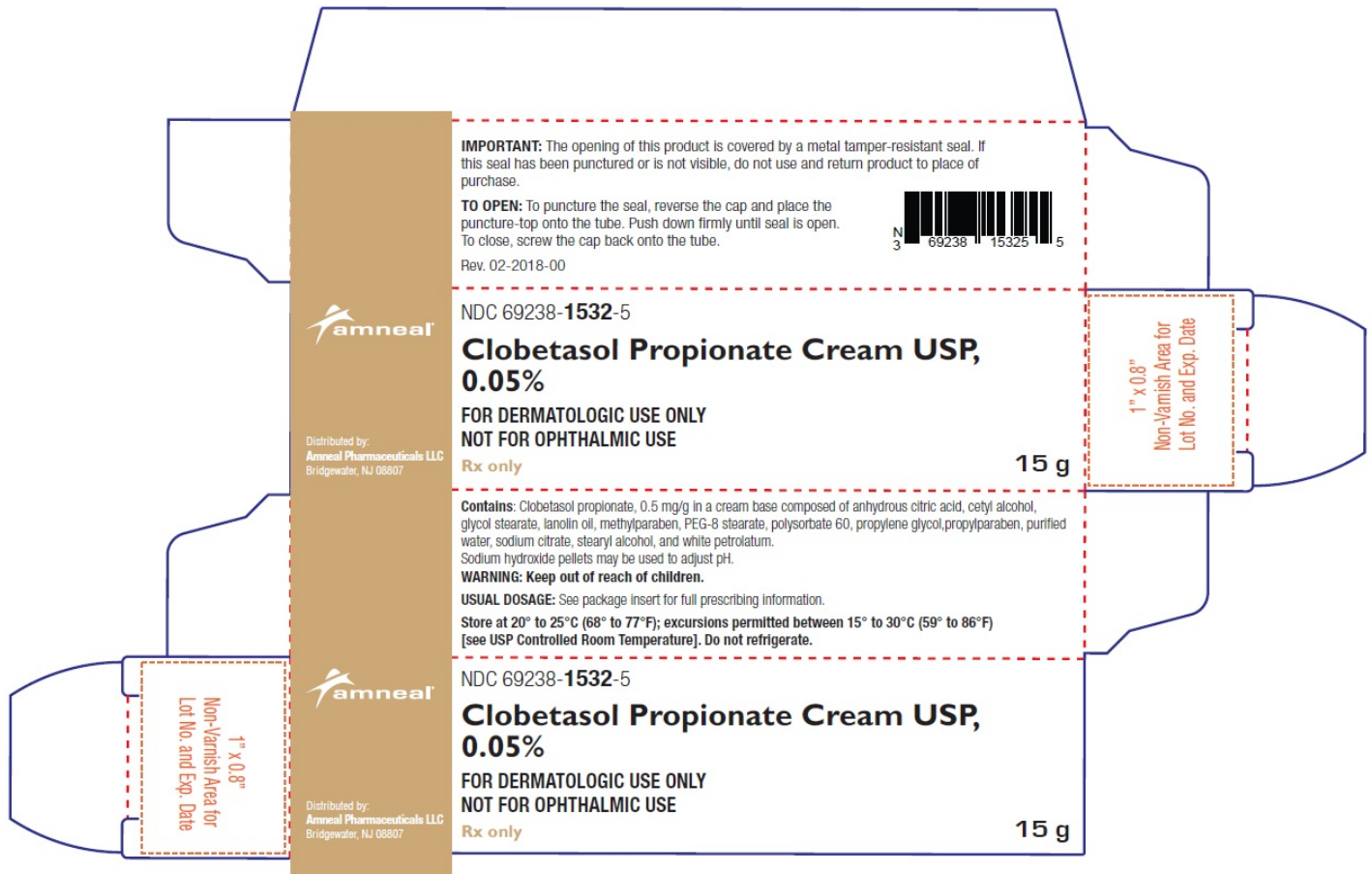
Important: Do not use if seal has been punctured or is not visible. **To Open:** Use cap to puncture seal.

Distributed by: **Amneal Pharmaceuticals LLC**, Bridgewater, NJ 08807

Rev. 02-2018-00



PRINCIPAL DISPLAY PANEL



CLOBETASOL PROPIONATE

clobetasol propionate cream

Product Information

Product Type

HUMAN PRESCRIPTION DRUG

Item Code (Source)

NDC:69238-1532

| | |
|--------------------------------|---------|
| 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 |
|--|----------|
| ANHYDROUS CITRIC ACID (UNII: XF417D3PSL) | |
| CETYL ALCOHOL (UNII: 936JST6JCN) | |
| GLYCOL STEARATE (UNII: 0324G66D0E) | |
| LANOLIN OIL (UNII: OVV5IJ58F) | |
| METHYLPARABEN (UNII: A2I8C7HI9T) | |
| POLYSORBATE 60 (UNII: CAL22UVI4M) | |
| PROPYLENE GLYCOL (UNII: 6DC9Q167V3) | |
| PROPYLPARABEN (UNII: Z8IX2SC1OH) | |
| WATER (UNII: 059QF0K00R) | |
| SODIUM CITRATE (UNII: 1Q73Q2JULR) | |
| STEARYL ALCOHOL (UNII: 2KR89I4HIY) | |
| PETROLATUM (UNII: 4T6HI2BN9U) | |
| POLYOXYL 8 STEARATE (UNII: 2P9L47VI5E) | |
| SODIUM HYDROXIDE (UNII: 55X04QC32I) | |

Product Characteristics

| | | | |
|-----------------|----------------------------|---------------------|--|
| Color | WHITE (White to off-white) | Score | |
| Shape | | Size | |
| Flavor | | Imprint Code | |
| Contains | | | |

Packaging

| # | Item Code | Package Description | Marketing Start Date | Marketing End Date |
|---|------------------|---|----------------------|--------------------|
| 1 | NDC:69238-1532-5 | 1 in 1 CARTON | 12/28/2018 | |
| 1 | | 15 g in 1 TUBE; Type 0: Not a Combination Product | | |
| 2 | NDC:69238-1532-3 | 1 in 1 CARTON | 12/28/2018 | |
| 2 | | 30 g in 1 TUBE; Type 0: Not a Combination Product | | |
| 3 | NDC:69238-1532-4 | 1 in 1 CARTON | 12/28/2018 | |
| 3 | | 45 g in 1 TUBE; Type 0: Not a Combination Product | | |
| 4 | NDC:69238-1532-6 | 1 in 1 CARTON | 12/28/2018 | |
| 4 | | 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 |
|--------------------|--|----------------------|--------------------|
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| ANDA | ANDA211256 | 12/28/2018 | |
|------|------------|------------|--|

Labeler - Amneal Pharmaceuticals NY LLC (123797875)

Establishment

| Name | Address | ID/FEI | Business Operations |
|-----------------------------|---------|-----------|---|
| Amneal Pharmaceuticals, LLC | | 053542455 | ANALYSIS(69238-1532) , LABEL(69238-1532) , MANUFACTURE(69238-1532) , PACK(69238-1532) |

Revised: 5/2019

Amneal Pharmaceuticals NY LLC