

ADAPALENE- adapalene gel
PruGen, Inc.

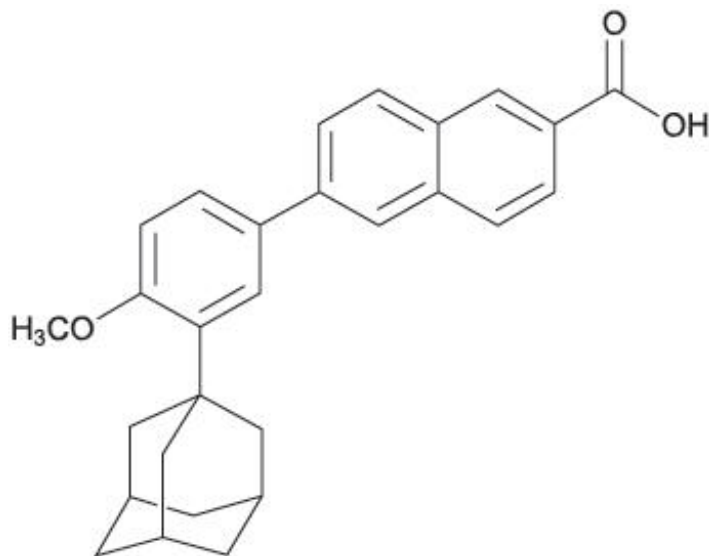
Adapalene Gel, 0.1%

Rx Only

DESCRIPTION

Adapalene gel 0.1%, containing adapalene USP, is used for the topical treatment of acne vulgaris. Each gram of adapalene gel 0.1% contains adapalene USP 0.1% (1 mg) in a vehicle consisting of carbomer homopolymer, edetate disodium, methylparaben, poloxamer 182, propylene glycol, purified water and sodium hydroxide.

The chemical name of adapalene USP is 6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthoic acid. Adapalene USP is a white to off-white powder which is sparingly soluble in tetrahydrofuran, very slightly soluble in diethyl ether. The molecular formula is $C_{28}H_{28}O_3$ and molecular weight is 412.52. Adapalene USP is represented by the following structural formula:



CLINICAL PHARMACOLOGY

Adapalene is a chemically stable, retinoid-like compound. Biochemical and pharmacological profile studies have demonstrated that adapalene is a modulator of cellular differentiation, keratinization, and inflammatory processes all of which represent important features in the pathology of acne vulgaris.

Mechanistically, adapalene binds to specific retinoic acid nuclear receptors but does not bind to the cytosolic receptor protein. Although the exact mode of action of adapalene is unknown, it is suggested that topical adapalene may normalize the differentiation of follicular epithelial cells resulting in decreased microcomedone formation.

Pharmacokinetics

Absorption of adapalene through human skin is low. Only trace amounts (<0.25 ng/mL) of parent substance have been found in the plasma of acne patients following chronic topical application of adapalene in controlled clinical trials. Excretion appears to be primarily by the biliary route.

INDICATIONS AND USAGE

Adapalene gel, 0.1% is indicated for the topical treatment of acne vulgaris.

CONTRAINDICATIONS

Adapalene gel should not be administered to individuals who are hypersensitive to adapalene or any of the components in the vehicle gel.

WARNINGS

Use of adapalene gel should be discontinued if hypersensitivity to any of the ingredients is noted. Patients with sunburn should be advised not to use the product until fully recovered.

PRECAUTIONS

General

If a reaction suggesting sensitivity or chemical irritation occurs, use of the medication should be discontinued. Exposure to sunlight, including sunlamps, should be minimized during the use of adapalene. Patients who normally experience high levels of sun exposure, and those with inherent sensitivity to sun, should be warned to exercise caution. Use of sunscreen products and protective clothing over treated areas is recommended when exposure cannot be avoided. Weather extremes, such as wind or cold, also may be irritating to patients under treatment with adapalene. Avoid contact with the eyes, lips, angles of the nose, and mucous membranes. The product should not be applied to cuts, abrasions, eczematous skin, or sunburned skin.

Certain cutaneous signs and symptoms such as erythema, dryness, scaling, burning, or pruritus may be experienced during treatment. These are most likely to occur during the first two to four weeks and will usually lessen with continued use of the medication. Depending upon the severity of adverse events, patients should be instructed to reduce the frequency of application or discontinue use.

Drug Interactions

As adapalene gel has the potential to produce local irritation in some patients, concomitant use of other potentially irritating topical products (medicated or abrasive soaps and cleansers, soaps and cosmetics that have a strong drying effect, and products with high concentrations of alcohol, astringents, spices, or lime) should be approached with caution. Particular caution should be exercised in using preparations containing sulfur, resorcinol, or salicylic acid in combination with adapalene gel. If these preparations have been used, it is advisable not to start therapy with adapalene gel until the effects of such preparations in the skin have subsided.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies with adapalene have been conducted in mice at topical doses of 0.3, 0.9, and 2.6 mg/kg/day and in rats at oral doses of 0.15, 0.5, and 1.5 mg/kg/day, approximately 4-75 times the maximal daily human topical dose. In the oral study, positive linear trends were observed in the incidence of follicular cell adenomas and carcinomas in the thyroid glands of female rats, and in the incidence of benign and malignant pheochromocytomas in the adrenal medullas of male rats.

No photocarcinogenicity studies were conducted. Animal studies have shown an increased tumorigenic risk with the use of pharmacologically similar drugs (e.g., retinoids) when exposed to UV irradiation in the laboratory or to sunlight. Although the significance of these studies to human use is not clear, patients should be advised to avoid or minimize exposure to either sunlight or artificial UV irradiation sources.

In a series of *in vivo* and *in vitro* studies, adapalene did not exhibit mutagenic or genotoxic activities.

Pregnancy

Teratogenic effects

Pregnancy Category C

No teratogenic effects were seen in rats at oral doses of adapalene 0.15 to 5.0 mg/kg/day, up to 120 times the maximal daily human topical dose. Cutaneous route teratology studies conducted in rats and rabbits at doses of 0.6, 2.0, and 6.0 mg/kg/day, up to 150 times the maximal daily human topical dose exhibited no fetotoxicity and only minimal increases in supernumerary ribs in rats. There are no adequate and well-controlled studies in pregnant women. Adapalene should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when adapalene gel is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients below the age of 12 have not been established.

ADVERSE REACTIONS

Some adverse effects such as erythema, scaling, dryness, pruritus, and burning will occur in 10-40% of patients. Pruritus or burning immediately after application also occurs in approximately 20% of patients. The following additional adverse experiences were reported in approximately 1% or less of patients: skin irritation, burning/stinging, erythema, sunburn, and acne flares. These are most commonly seen during the first month of therapy and decrease in frequency and severity thereafter. All adverse effects with use of adapalene gel during clinical trials were reversible upon discontinuation of therapy.

OVERDOSAGE

Adapalene gel is intended for cutaneous use only. If the medication is applied excessively, no more rapid or better results will be obtained and marked redness, peeling, or discomfort may occur. The acute oral toxicity of adapalene gel in mice and rats is greater than 10 mL/kg. Chronic ingestion of the drug may lead to the same side effects as those associated with excessive oral intake of Vitamin A.

DOSAGE AND ADMINISTRATION

Adapalene gel 0.1% should be applied once a day to affected areas after washing in the evening before retiring. A thin film of the gel should be applied, avoiding eyes, lips, and mucous membranes.

During the early weeks of therapy, an apparent exacerbation of acne may occur. This is due to the action of the medication on previously unseen lesions and should not be considered a reason to discontinue therapy. Therapeutic results should be noticed after eight to twelve weeks of treatment.

HOW SUPPLIED

Adapalene gel, 0.1% is supplied in the following size:

45 g laminate tube NDC 42546-720-45

Storage

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Protect from freezing.

Manufactured by:

Glenmark Pharmaceuticals Ltd.
Colvale-Bardez, Goa 403 513, India

Manufactured for:

PruGen Pharmaceuticals
Scottsdale, AZ 85255

Questions? (866) 696-8525
www.prugen.com

June 2015

PE304260914-1

PRINCIPAL DISPLAY PANEL - 45 grams Tube Carton

NDC 42546-720-45

Rx only

PRUGEN™
PHARMACEUTICALS

ADAPALENE Gel 0.1%

45 grams

For External Use Only. Not For Ophthalmic Use.

Manufactured by:
Glenmark Pharmaceuticals Ltd
 Colvale-Bardez,
 Goa 403513, India
 GO/DRUGS/648

Manufactured for:
PruGen Pharmaceuticals
 Scottsdale, AZ 85255
 06/15 Rev 1.0

Questions? (866) 696-8525
 www.prugen.com

NDC 42546-720-45

Rx only



ADAPALENE Gel 0.1%

45 grams

For External Use Only. Not For Ophthalmic Use.

For External Use Only. Not For Ophthalmic Use.

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Protect from freezing.

Usual dosage: Apply a thin film once a day to affected areas after washing in the evening before retiring.

See package insert for complete prescribing information.

Each gram contains: adapalene USP 0.1% (1 mg) in a vehicle consisting of carbomer homopolymer, edetate disodium, methylparaben, poloxamer 182, propylene glycol, purified water, and sodium hydroxide.

NDC 42546-720-45

Rx only



ADAPALENE Gel 0.1%

45 grams

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ADAPALENE

adapalene gel

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:42546-720
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
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ADAPALENE (UNII: 1L4806J2QF) (ADAPALENE - UNII:1L4806J2QF)		ADAPALENE	45 g in 1 g	
Inactive Ingredients				
Ingredient Name			Strength	
CARBOXYPOLYMETHYLENE (UNII: 0A5MM307FC)				
EDETATE DISODIUM (UNII: 7FLD91C86K)				
METHYL PARABEN (UNII: A2I8C7HI9T)				
POLOXAMER 182 (UNII: JX0HIX6OAG)				
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)				
WATER (UNII: 059QF0K00R)				
SODIUM HYDROXIDE (UNII: 55X04QC32I)				
Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:42546-720-45	1 in 1 CARTON	03/04/2016	
1		45 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	ANDA091314	03/04/2016		

Labeler - PruGen, Inc. (929922750)

Establishment

Name	Address	ID/FEI	Business Operations
GLENMARK PHARMACEUTICALS INC., USA		079922908	MANUFACTURE(42546-720)

Revised: 1/2018

PruGen, Inc.