

# ADAPALENE AND BENZOYL PEROXIDE- adapalene and benzoyl peroxide gel

## Viona Pharmaceuticals Inc

-----

### HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ADAPALENE AND BENZOYL PEROXIDE GEL safely and effectively. See full prescribing information for ADAPALENE AND BENZOYL PEROXIDE GEL.

ADAPALENE and BENZOYL PEROXIDE gel, for topical use

Initial U.S. Approval: 2015

### INDICATIONS AND USAGE

Adapalene and benzoyl peroxide gel, is a combination of adapalene, a retinoid and benzoyl peroxide and is indicated for the topical treatment of acne vulgaris in adults and pediatric patients 12 years of age and older. (1)

### DOSAGE AND ADMINISTRATION

- For topical use only
- Adapalene and benzoyl peroxide gel is not for oral, ophthalmic or intravaginal use. (2)
- Apply a thin layer of adapalene and benzoyl peroxide gel to affected areas of the face and/or trunk once daily after washing. (2)
- Use a pea-sized amount for each area of the face (e.g., forehead, chin, each cheek). (2)
- Avoid the eyes, lips, and mucous membranes. (2)

### DOSAGE FORMS AND STRENGTHS

Topical Gel, 0.3%/2.5%. (3)

### CONTRAINDICATIONS

Adapalene and benzoyl peroxide gel is contraindicated in patients with a history of hypersensitivity reactions to benzoyl peroxide or any components of the formulation in adapalene and benzoyl peroxide gel. (4)

### WARNINGS AND PRECAUTIONS

- **Hypersensitivity:** Severe hypersensitivity reactions, including anaphylaxis and angioedema, have been reported with the use of benzoyl peroxide products. (5.1)
- **Photosensitivity:** Avoid exposure to sunlight and sunlamps. Wear broad spectrum sunscreen and protective clothing when sun exposure cannot be avoided. (5.2)
- **Skin Irritation:** Erythema, scaling, dryness, stinging/burning, irritant and allergic contact dermatitis may occur with use of adapalene and benzoyl peroxide gel and may necessitate discontinuation. (5.3)

### ADVERSE REACTIONS

The most common adverse reactions (incidence  $\geq 1\%$ ) are skin irritation, eczema, atopic dermatitis and skin burning sensation. (6)

**To report SUSPECTED ADVERSE REACTIONS, contact Viona Pharmaceuticals Inc. at 1-888-304-5011 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.**

Revised: 6/2025

---

## FULL PRESCRIBING INFORMATION: CONTENTS\*

### 1 INDICATIONS AND USAGE

### 2 DOSAGE AND ADMINISTRATION

### 3 DOSAGE FORMS AND STRENGTHS

### 4 CONTRAINDICATIONS

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Hypersensitivity

- 5.2 Photosensitivity
- 5.3 Skin Irritation/Contact Dermatitis

## **6 ADVERSE REACTIONS**

- 6.1 Clinical Trials Experience
- 6.2 Postmarketing Experience

## **8 USE IN SPECIFIC POPULATIONS**

- 8.1 Pregnancy
- 8.2 Lactation
- 8.4 Pediatric Use
- 8.5 Geriatric Use

## **11 DESCRIPTION**

## **12 CLINICAL PHARMACOLOGY**

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

## **13 NONCLINICAL TOXICOLOGY**

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

## **14 CLINICAL STUDIES**

## **16 HOW SUPPLIED/STORAGE AND HANDLING**

- 16.1 How Supplied
- 16.2 Storage and Handling

## **17 PATIENT COUNSELING INFORMATION**

\* Sections or subsections omitted from the full prescribing information are not listed.

---

## **FULL PRESCRIBING INFORMATION**

### **1 INDICATIONS AND USAGE**

Adapalene and benzoyl peroxide gel is indicated for the topical treatment of acne vulgaris in adults and pediatric patients 12 years of age and older.

### **2 DOSAGE AND ADMINISTRATION**

- For topical use only. Adapalene and benzoyl peroxide gel is not for oral, ophthalmic, or intravaginal use.
- Apply a thin layer of adapalene and benzoyl peroxide gel to affected areas of the face and/or trunk once daily after washing.
- Use a pea-sized amount for each area of the face (e.g., forehead, chin, each cheek).
- Wash hands after application as adapalene and benzoyl peroxide gel may bleach hair or colored fabrics.
- Avoid the eyes, lips and mucous membranes.

### **3 DOSAGE FORMS AND STRENGTHS**

Each gram of adapalene and benzoyl peroxide gel, USP contains 3 mg (0.3%) adapalene, USP and 25 mg (2.5%) benzoyl peroxide, USP in a white to very pale yellow opaque gel.

Adapalene and benzoyl peroxide gel, USP is available in pumps containing 45 g or 60 g.

## **4 CONTRAINDICATIONS**

Adapalene and benzoyl peroxide gel is contraindicated in patients with a history of hypersensitivity reactions to benzoyl peroxide or any components of the formulation in adapalene and benzoyl peroxide gel.

## **5 WARNINGS AND PRECAUTIONS**

### **5.1 Hypersensitivity**

Hypersensitivity reactions, including anaphylaxis, angioedema, and urticaria, have been reported with the use of benzoyl peroxide products. If a serious hypersensitivity reaction occurs, discontinue adapalene and benzoyl peroxide gel immediately and initiate appropriate therapy.

### **5.2 Photosensitivity**

Avoid exposure to sunlight, including sunlamps, during the use of adapalene and benzoyl peroxide gel. Patients with high levels of sun exposure and those with inherent sensitivity to sun should exercise particular caution. Use of broad spectrum sunscreen products and protective apparel (e.g., hat) are recommended when exposure cannot be avoided. Weather extremes, such as wind or cold, may be irritating to patients under treatment with adapalene and benzoyl peroxide gel.

### **5.3 Skin Irritation/Contact Dermatitis**

Erythema, scaling, dryness and stinging/burning may be experienced with use of adapalene and benzoyl peroxide gel. These are most likely to occur during the first four weeks of treatment, are mostly mild to moderate in intensity and usually lessen with continued use of the medication. Irritant and allergic contact dermatitis may occur. Depending upon the severity of these adverse reactions, patients should be instructed to use a moisturizer, reduce the frequency of the application of adapalene and benzoyl peroxide gel or discontinue use. The product should not be applied to cuts, abrasions, eczematous or sunburned skin. As with other retinoids, use of "waxing" as a depilatory method should be avoided on skin treated with adapalene and benzoyl peroxide gel.

Avoid concomitant use of other potentially irritating topical products (medicated or abrasive soaps and cleansers, soaps and cosmetics that have strong skin-drying effect and products with high concentrations of alcohol, astringents, spices or limes).

## **6 ADVERSE REACTIONS**

### **6.1 Clinical Trials Experience**

The following adverse reactions are discussed in greater detail elsewhere in the labeling:

- Hypersensitivity [see *Warnings and Precautions (5.1)*]
- Skin Irritation/Contact Dermatitis [see *Warnings and Precautions (5.3)*]

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

During the randomized, double-blind, vehicle- and active-controlled clinical trial, 217 subjects were exposed to adapalene and benzoyl peroxide gel. A total of 197 subjects with acne vulgaris, 12 years and older, were treated once daily for 12 weeks. Adverse reactions reported within 12 weeks of treatment in at least 1% of subjects treated with adapalene and benzoyl peroxide gel and for which the rate with adapalene and benzoyl peroxide gel exceeded the rate for the vehicle are presented in Table 1:

**Table 1 Adverse Reactions Occurring in  $\geq$  1% of Subjects with Acne Vulgaris in a 12 week Clinical Trial**

	<b>Adapalene and Benzoyl Peroxide Gel, 0.3%/2.5% (N=217)</b>	<b>Adapalene and Benzoyl Peroxide Gel, 0.1%/2.5% (N=217)</b>	<b>Vehicle (N=69)</b>
Skin irritation	4%	< 1%	0%
Eczema	1%	0%	0%
Dermatitis atopic	1%	0%	0%
Skin burning sensation	1%	0%	0%

Local tolerability evaluations presented in Table 2, were conducted at each trial visit in the clinical trial by assessment of erythema, scaling, dryness and stinging/burning, which peaked at Week 1 of therapy and decreased thereafter.

**Table 2 Incidence of Local Cutaneous Irritation in 12 week Clinical Trial in Subjects with Acne Vulgaris**

	<b>Maximum Severity During Treatment</b>		<b>End of Treatment Severity (Final Score)</b>	
	<b>Moderate</b>	<b>Severe</b>	<b>Moderate</b>	<b>Severe</b>
<b>Adapalene and Benzoyl Peroxide Gel, 0.3%/2.5% (N=213)</b>				
Erythema	20%	1%	4%	< 1%
Scaling	17%	1%	1%	< 1%
Dryness	15%	2%	3%	< 1%
Stinging/burning	19%	6%	1%	1%
<b>Adapalene and Benzoyl Peroxide Gel, 0.1%/2.5% (N=212)</b>				
Erythema	15%	1%	2%	< 1%
Scaling	12%	< 1%	2%	0%
Dryness	13%	1%	2%	0%
Stinging/burning	14%	9%	3%	0%
<b>Vehicle (N=68)</b>				
Erythema	6%	1%	1%	0%
Scaling	6%	0%	1%	0%
Dryness	4%	1%	1%	0%

Stinging/burning	3%	1%	0%	0%
------------------	----	----	----	----

## 6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of adapalene and benzoyl peroxide gel. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

***Skin and subcutaneous tissue disorders:*** sunburn, blister (including vesicles and bullae), pruritus, hyperpigmentation and hypopigmentation.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

#### ***Risk Summary***

Available pharmacovigilance data with adapalene and benzoyl peroxide gel use in pregnant women are insufficient to establish a drug associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted with the combination gel.

#### *Adapalene gel, 0.3%*

Available data from clinical trials with adapalene gel 0.3% use in pregnant women are insufficient to establish a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of adapalene to pregnant rats and rabbits during organogenesis at dose exposures 41 and 81 times, respectively, the human exposure at the maximum recommended human dose (MRHD) of 2 g resulted in fetal skeletal and visceral malformations (*see Data*).

#### *Benzoyl peroxide gel, 2.5%*

The systemic exposure of benzoyl peroxide is unknown. Based on published literature, benzoyl peroxide is rapidly metabolized to benzoic acid (an endogenous substance), which is eliminated in the urine. Hence, maternal use is not expected to result in fetal exposure of the drug.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

#### ***Data***

##### *Animal Data*

No malformations were observed in rats treated with oral adapalene doses of 0.15 mg/kg/day to 5 mg/kg/day, up to 8 times the MRHD of 2 grams of adapalene and benzoyl peroxide gel based on a mg/m<sup>2</sup> comparison. However, malformations were observed in rats and rabbits when treated with oral doses of  $\geq$  25 mg/kg/day adapalene

(41 and 81 times the MRHD, respectively, based on a mg/m<sup>2</sup> comparison). Findings included cleft palate, microphthalmia, encephalocele, and skeletal abnormalities in rats and umbilical hernia, exophthalmos, and kidney and skeletal abnormalities in rabbits.

Dermal adapalene embryofetal development studies in rats and rabbits at doses up to 6 mg/kg/day (9.7 and 19.5 times the MRHD, respectively, based on a mg/m<sup>2</sup> comparison) exhibited no fetotoxicity and only minimal increases in skeletal variations (supernumerary ribs in both species and delayed ossification in rabbits).

## **8.2 Lactation**

### ***Risk Summary***

#### *Adapalene gel, 0.3%*

There are no data on the presence of adapalene gel or its metabolite in human milk, the effects on the breastfed infant, or the effects on milk production. In animal studies, adapalene is present in rat milk with oral administration of the drug. When a drug is present in animal milk, it is likely that the drug will be present in human milk. It is possible that topical administration of large amounts of adapalene could result in sufficient systemic absorption to produce detectable quantities in human milk (*see Clinical Considerations*).

#### *Benzoyl peroxide gel, 2.5%*

The systemic exposure of benzoyl peroxide is unknown. Based on the published literature, benzoyl peroxide is rapidly metabolized to benzoic acid (an endogenous substance), which is eliminated in the urine. Any amount of benzoyl peroxide excreted into human milk by a nursing mother would be expected to be rapidly metabolized by tissue and stomach esterases. There are no data on the presence of benzoyl peroxide in human milk, its effects on the breastfed infant or its effects on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for adapalene and benzoyl peroxide gel and any potential adverse effects on the breastfed child from adapalene and benzoyl peroxide gel or from the underlying maternal condition.

#### *Clinical Considerations*

To minimize potential exposure to the breastfed infant via breastmilk, use adapalene and benzoyl peroxide gel on the smallest area of skin and for the shortest duration possible while breastfeeding. Advise breastfeeding women not to apply adapalene and benzoyl peroxide gel directly to the nipple and areola to avoid direct infant exposure.

## **8.4 Pediatric Use**

Safety and effectiveness of adapalene and benzoyl peroxide gel in pediatric patients under the age of 12 have not been established.

## **8.5 Geriatric Use**

Clinical studies of adapalene and benzoyl peroxide gel did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from younger subjects.

## 11 DESCRIPTION

Adapalene and benzoyl peroxide gel 0.3%/2.5% is a white to very pale yellow opaque gel for topical use containing adapalene, USP 0.3% and benzoyl peroxide 2.5%.

Adapalene USP, a synthetic retinoid, is a naphthoic acid derivative with retinoid-like properties. The chemical name for adapalene is (6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthoic acid). It has the following structural formula:

Adapalene:

Molecular formula:  $C_{28}H_{28}O_3$

Molecular weight: 412.5

Hydrous benzoyl peroxide, USP is a highly lipophilic oxidizing agent that localizes in both bacterial and keratinocyte cell membranes. The chemical name for benzoyl peroxide is dibenzoyl peroxide. It has the following structural formula:

Benzoyl Peroxide:

Molecular formula:  $C_{14}H_{10}O_4$

Molecular weight: 242.23

Adapalene and benzoyl peroxide gel, USP contains the following inactive ingredients: acrylamide/sodium acryloyldimethyl taurate copolymer, docusate sodium, edetate disodium, glycerin, isohexadecane, poloxamer 124, polysorbate 80, propylene glycol, purified water and sorbitan monooleate.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

*Adapalene*

Adapalene binds to specific retinoic acid nuclear receptors but does not bind to cytosolic

receptor protein. Biochemical and pharmacological profile studies have demonstrated that adapalene is a modulator of cellular differentiation, keratinization and inflammatory processes. However, the significance of these findings with regard to the mechanism of action of adapalene for the treatment of acne is unknown.

### *Benzoyl peroxide*

Benzoyl peroxide is an oxidizing agent with bactericidal and keratolytic effects.

## **12.2 Pharmacodynamics**

Pharmacodynamics of adapalene and benzoyl peroxide gel is unknown.

## **12.3 Pharmacokinetics**

A pharmacokinetic trial was conducted in 26 adult and adolescent subjects (12 years to 33 years of age) with severe acne vulgaris who were treated with once-daily applications during a 4 week period with, on average, 2.3 grams/day (range 1.6 grams/day to 3.1 grams/day) of adapalene and benzoyl peroxide gel applied as a thin layer to the face, shoulders, upper chest and upper back. After a 4 week treatment, 16 subjects (62%) had quantifiable adapalene plasma concentrations above the limit of quantification of 0.1 ng/mL, with a mean  $C_{max}$  of  $0.16 \pm 0.08$  ng/mL and a mean  $AUC_{0-24hr}$  of  $2.49 \pm 1.21$  ng.h/mL. The most exposed subject had adapalene  $C_{max}$  and  $AUC_{0-24hr}$  of 0.35 ng/mL and 6.41 ng.h/mL, respectively. Excretion of adapalene appears to be primarily by the biliary route. Benzoyl peroxide is absorbed by the skin where it is converted to benzoic acid and eliminated in the urine.

### *Drug Interactions*

No formal drug-drug interaction studies were conducted with adapalene and benzoyl peroxide gel.

## **13 NONCLINICAL TOXICOLOGY**

### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

No carcinogenicity, genotoxicity or fertility studies were conducted with adapalene and benzoyl peroxide gel.

Carcinogenicity studies with adapalene were conducted in mice at topical doses of 0.4 mg/kg/day, 1.3 mg/kg/day and 4 mg/kg/day (1.2 mg/m<sup>2</sup>/day, 3.9 mg/m<sup>2</sup>/day, 12 mg/m<sup>2</sup>/day) and in rats at oral doses of 0.15 mg/kg/day, 0.5 mg/kg/day and 1.5 mg/kg/day (0.9 mg/m<sup>2</sup>/day, 3 mg/m<sup>2</sup>/day and 9 mg/m<sup>2</sup>/day). The highest dose levels are 3.2 (mice) and 2.4 (rats) times the MRHD of adapalene and benzoyl peroxide gel based on a mg/m<sup>2</sup> comparison. In the rat study, an increased incidence of benign and malignant pheochromocytomas reported in the adrenal medulla of male rats was observed.

No significant increase in tumor formation was observed in rodents topically treated with 15% to 25% benzoyl peroxide carbopol gel (6 times to 10 times the concentration of benzoyl peroxide in adapalene and benzoyl peroxide gel) for two years. Rats received maximum daily applications of 138 (males) and 205 (females) mg/kg benzoyl peroxide (27 times to 40 times the MRHD based on a mg/m<sup>2</sup> comparison). Similar results were

obtained in mice topically treated with 25% benzoyl peroxide carbopol gel for 56 weeks followed by intermittent treatment with 15% benzoyl peroxide carbopol gel for rest of the 2 year study period and in mice topically treated with 5% benzoyl peroxide carbopol gel for two years.

Benzoyl peroxide is a tumor promoter in several animal species. The significance of this finding in humans is unknown.

Adapalene was not mutagenic or genotoxic *in vitro* (Ames test, Chinese hamster ovary cell assay or mouse lymphoma TK assay) or *in vivo* (mouse micronucleus test).

Benzoyl peroxide caused DNA strand breaks and DNA-protein cross-links in mammalian cells, increased sister chromatid exchanges in Chinese hamster ovary cells and was mutagenic in a few, but not all, *in vitro* bacterial mutagenicity assays (Ames tests) conducted.

In rat oral studies, 20 mg/kg/day adapalene (32 times the MRHD based on a mg/m<sup>2</sup> comparison) did not affect the reproductive performance and fertility of F<sub>0</sub> males and females or the growth, development or reproductive function of F<sub>1</sub> offspring.

No fertility studies were conducted with benzoyl peroxide.

## 14 CLINICAL STUDIES

The safety and efficacy of adapalene and benzoyl peroxide gel applied once daily for 12 weeks for the treatment of acne vulgaris were assessed in a multicenter, randomized, double-blind, vehicle-controlled trial, comparing adapalene and benzoyl peroxide gel to vehicle gel in subjects with acne vulgaris. The trial also evaluated adapalene and benzoyl peroxide gel, 0.1%/2.5%, a lower strength product than adapalene and benzoyl peroxide gel, 0.3%/2.5%. In this trial, 217 subjects were treated with adapalene and benzoyl peroxide gel, 217 subjects with adapalene and benzoyl peroxide, gel, 0.1%/2.5% and 69 subjects with the vehicle gel.

Treatment response was defined as the percent of subjects who were rated "clear" or "almost clear" at Week 12 with at least a two-grade improvement based on the Investigator's Global Assessment (IGA) and mean absolute change from baseline at Week 12 in both inflammatory and non-inflammatory lesion counts. An IGA score of 'Clear' corresponded to clear skin with no inflammatory or non-inflammatory lesions. An IGA score of "almost clear" corresponded to a few scattered comedones and a few small papules.

At baseline, 50% of subjects were graded as "moderate" (IGA Grade 3) and 50% were graded as "severe" (IGA Grade 4) on the IGA scale. Subjects had an average of 98 (range 51 to 226) total lesions of which the mean number of inflammatory lesions was 38 (range: 20 to 99) and the mean number of non-inflammatory lesions was 60 (range 30 to 149). Subjects ranged in age from 12 years to 57 years, with 273 (54%) of subjects 12 to 17 years of age. Approximately equal number of males (48%) and females (52%) were enrolled.

The IGA success rate, mean reduction and percent reduction in acne lesion counts from baseline after 12 weeks of treatment are presented in the following table.

### Table 3 Clinical Efficacy of Adapalene and Benzoyl Peroxide Gel at

## Week 12 in Subjects with Acne Vulgaris

	<b>Adapalene and Benzoyl Peroxide Gel, 0.3%/2.5% (N=217)</b>	<b>Adapalene and Benzoyl Peroxide Gel, 0.1%/2.5% (N=217)*</b>	<b>Vehicle (N=69)</b>
IGA: two-grade improvement and "clear" or "almost clear"	33.7%	27.3%	11%
Inflammatory lesions: mean absolute (percent) reduction	27.8 (68.7%)	26.5 (69.3%)	13.2 (39.2%)
Non-inflammatory lesions: mean absolute (percent) reduction	40.5 (68.3%)	40 (68%)	19.7 (37.4%)

\*This trial was not designed or powered to compare the efficacy of adapalene and benzoyl peroxide gel to the lower strength adapalene and benzoyl peroxide gel, 0.1%/2.5%, nor to compare the lower strength adapalene and benzoyl peroxide gel, 0.1%/2.5% to the vehicle control.

In subjects graded as "severe" (IGA Grade 4), efficacy was observed in the adapalene and benzoyl peroxide gel group.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

### 16.1 How Supplied

Adapalene and benzoyl peroxide gel, USP 0.3%/2.5% is white to very pale yellow in color and opaque in appearance and is supplied as follows:

45 gram pump            NDC 72578-119-04  
60 gram pump            NDC 72578-119-02

### 16.2 Storage and Handling

- Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature].
- Keep away from heat.
- Protect from light.
- Keep out of reach of children.

## 17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA approved patient labeling (Patient Information).

### Hypersensitivity

Inform patients that serious hypersensitivity reactions occurred with the use of benzoyl peroxide products. If a patient experiences a serious hypersensitivity reaction, instruct

patient to discontinue adapalene and benzoyl peroxide gel immediately and seek medical help [see *Warnings and Precautions (5.1)*].

### **Photosensitivity**

Advise patients to minimize or avoid exposure to natural or artificial light, including tanning beds or UVA/B treatment. Recommend the use of broad spectrum sunscreen products and protective apparel (e.g., hat) when exposure cannot be avoided [see *Warnings and Precautions (5.2)*].

### **Skin Irritation/Contact Dermatitis**

Inform patients that adapalene and benzoyl peroxide gel may cause irritation such as erythema, scaling, dryness, stinging or burning [see *Warnings and Precautions (5.3)*].

### **Lactation**

Use adapalene and benzoyl peroxide gel on the smallest part of the skin and for the shortest duration possible while breastfeeding. Advise breastfeeding women not to apply adapalene and benzoyl peroxide gel directly to the nipple and areola to avoid direct infant exposure [see *Use in Specific Populations (8.2)*].

### **Administration Instructions**

- Advise patients to cleanse the area to be treated with a mild or soapless cleanser; pat dry. Apply adapalene and benzoyl peroxide gel as a thin layer, avoiding the eyes, lips and mucous membranes.
- Advise patients not to use more than the recommended amount and not to apply more than once daily as this will not produce faster results, but may increase irritation.
- Wash hands after application as adapalene and benzoyl peroxide gel may bleach hair and colored fabric.

### **Manufactured by:**

#### **Zydus Lifesciences Ltd.**

Changodar, Ahmedabad, India.

### **Distributed by:**

#### **Viona Pharmaceuticals Inc.**

Cranford, NJ 07016

Rev.: 05/25

<b>Patient Information</b>
<b>Adapalene (a dap' a leen) and Benzoyl Peroxide (ben' zoe il per ox' ide) Gel, USP</b>
<b>Important information:</b> Adapalene and benzoyl peroxide gel is for use on the skin only (topical). Do not use adapalene and benzoyl peroxide gel in or on your mouth, eyes or vagina.
<b>What is adapalene and benzoyl peroxide gel?</b> Adapalene and benzoyl peroxide gel is a prescription medicine used on the skin (topical) to treat acne vulgaris. It is not known if adapalene and benzoyl peroxide gel is safe and effective in

children under 12 years of age.

**Do not use adapalene and benzoyl peroxide gel if you** have had an allergic reaction to benzoyl peroxide or any of the ingredients in adapalene and benzoyl peroxide gel. See the end of this Patient Information leaflet for a complete list of ingredients in adapalene and benzoyl peroxide gel.

**Before using adapalene and benzoyl peroxide gel, tell your doctor about all of your medical conditions, including if you:**

- have other skin problems, including cuts, abrasions, sunburn or eczema.
- are pregnant or plan to become pregnant. It is not known if adapalene and benzoyl peroxide gel can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if adapalene and benzoyl peroxide passes into your breast milk and if it can harm your baby. Talk to your doctor about the best way to feed your baby if you use adapalene and benzoyl peroxide gel. If you use adapalene and benzoyl peroxide gel while breastfeeding, use adapalene and benzoyl peroxide gel on the smallest area of the skin and for the shortest time needed. Do not apply adapalene and benzoyl peroxide gel directly to the nipple and the areola to minimize contact with your baby.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements.

**How should I use adapalene and benzoyl peroxide gel?**

- Use adapalene and benzoyl peroxide gel exactly as your doctor tells you to use it.
- Apply adapalene and benzoyl peroxide gel 1 time a day.
- Do not use more adapalene and benzoyl peroxide gel than you need to cover the treatment area. Using too much adapalene and benzoyl peroxide gel or using it more than 1 time a day may increase your chance of skin irritation.

**Applying adapalene and benzoyl peroxide gel:**

- Wash the area where the gel will be applied with a mild or soapless cleanser and pat dry.
- Adapalene and benzoyl peroxide gel comes in a pump. Depress the pump to dispense a small amount (about the size of a pea) of adapalene and benzoyl peroxide gel and spread a thin layer over the treatment area. Use a pea-sized amount for each area of the face (forehead, chin, and each cheek).
- Wash your hands right away after applying the gel. Adapalene and benzoyl peroxide gel may bleach your hair or colored fabrics. Allow adapalene and benzoyl peroxide gel to dry completely before dressing to prevent bleaching of your clothes.

**What should I avoid while using adapalene and benzoyl peroxide gel?**

- Avoid spending time in sunlight or artificial sunlight, such as tanning beds or sunlamps. Adapalene and benzoyl peroxide gel can make your skin sensitive to sun and the light from tanning beds and sunlamps. Use sunscreen and wear a hat and clothes that cover the areas treated with adapalene and benzoyl peroxide gel if you have to be in sunlight.

- Cold weather and wind may irritate skin treated with adapalene and benzoyl peroxide gel.
- Avoid applying adapalene and benzoyl peroxide gel to cuts, abrasions and sunburned skin.
- Avoid skin products that may dry or irritate your skin such as medicated or harsh soaps, astringents, cosmetics that make your skin dry and products containing high levels of alcohol, spices or limes.
- Avoid the use of "waxing" as a hair removal method on skin treated with adapalene and benzoyl peroxide gel.

## **What are the possible side effects of adapalene and benzoyl peroxide gel?**

### **Adapalene and benzoyl peroxide gel may cause serious side effects including:**

- **Allergic reactions.** Stop using adapalene and benzoyl peroxide gel and get medical help right away if you have any of the following symptoms during treatment with adapalene and benzoyl peroxide gel:
  - hives, rash or severe itching
  - swelling of your face, eyes, lips, tongue, or throat
  - trouble breathing or throat tightness
  - feeling faint, dizzy, or lightheaded
- **Skin irritation.** Skin irritation is common with adapalene and benzoyl peroxide gel and is most likely to happen during the first 4 weeks of treatment, and usually lessen with continued use of adapalene and benzoyl peroxide gel. Skin reactions at the treatment area include redness, scaling, dryness, stinging, burning, itching and swelling. Tell your doctor if you get any skin reactions.
- **Sensitivity to sunlight.** See " **What should I avoid while using adapalene and benzoyl peroxide gel?** "

These are not all of the possible side effects of adapalene and benzoyl peroxide gel.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

### **How should I store adapalene and benzoyl peroxide gel?**

- Store adapalene and benzoyl peroxide gel at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep adapalene and benzoyl peroxide gel out of light and away from heat.

### **Keep adapalene and benzoyl peroxide gel and all medicines out of the reach of children.**

### **General information about the safe and effective use of adapalene and benzoyl peroxide gel**

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use adapalene and benzoyl peroxide gel for a condition for which it was not prescribed. Do not give adapalene and benzoyl peroxide gel to other people, even if they have the same symptoms you have. It may harm them. You can ask your doctor or pharmacist for information about

adapalene and benzoyl peroxide gel that is written for health professionals.

**What are the ingredients in adapalene and benzoyl peroxide gel?**

**Active ingredient:** adapalene, USP and benzoyl peroxide, USP

**Inactive ingredients:** acrylamide/sodium acryloyldimethyl taurate copolymer, docusate sodium, edetate disodium, glycerin, isohexadecane, poloxamer 124, polysorbate 80, propylene glycol, purified water and sorbitan monooleate.

For more information, call Viona Pharmaceuticals Inc. at 1-888-304-5011.

**Manufactured by:**  
**Zydus Lifesciences Ltd.**  
Changodar, Ahmedabad, India.  
**Distributed by:**  
**Viona Pharmaceuticals Inc.**  
Cranford, NJ 07016

Rev.: 05/25

This Patient Information has been approved by the U.S. Food and Drug Administration.

**PACKAGE LABEL.PRINCIPAL DISPLAY PANEL**

Adapalene and benzoyl peroxide gel, USP 0.3%/2.5%

NDC 72578-119-04

45 g

Rx only

**ADAPALENE AND BENZOYL PEROXIDE**

adapalene and benzoyl peroxide gel

**Product Information**

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:72578-119
<b>Route of Administration</b>	TOPICAL		

**Active Ingredient/Active Moiety**

Ingredient Name	Basis of Strength	Strength
<b>ADAPALENE</b> (UNII: 1L4806J2QF) (ADAPALENE - UNII:1L4806J2QF)	ADAPALENE	3 mg in 1 g
<b>BENZOYL PEROXIDE</b> (UNII: W9WZN9A0GM) (BENZOYL PEROXIDE - UNII:W9WZN9A0GM)	BENZOYL PEROXIDE	25 mg in 1 g

**Inactive Ingredients**

Ingredient Name	Strength
<b>1-PROPANESULFONIC ACID, 2-METHYL-2-((1-OXO-2-PROPEN-1-YL)AMINO)-, SODIUM SALT (1:1), POLYMER WITH 2-PROPENAMIDE</b> (UNII: 5F4963KLHS)	
<b>DOCUSATE SODIUM</b> (UNII: F05Q2T2JA0)	
<b>EDETATE DISODIUM</b> (UNII: 7FLD91C86K)	
<b>GLYCERIN</b> (UNII: PDC6A3C0OX)	
<b>ISOHEXADECANE</b> (UNII: 918X1OUF1E)	
<b>POLOXAMER 124</b> (UNII: 1S66E28KXA)	
<b>POLYSORBATE 80</b> (UNII: 6OZP39ZG8H)	
<b>PROPYLENE GLYCOL</b> (UNII: 6DC9Q167V3)	
<b>SORBITAN MONOOLEATE</b> (UNII: 06XEA2VD56)	
<b>WATER</b> (UNII: 059QF0KO0R)	

**Product Characteristics**

<b>Color</b>	WHITE (white to very pale yellow)	<b>Score</b>	
<b>Shape</b>		<b>Size</b>	
<b>Flavor</b>		<b>Imprint Code</b>	
<b>Contains</b>			

**Packaging**

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:72578-119-04	1 in 1 BOTTLE, PUMP	06/06/2022	
1		45 g in 1 BOTTLE, PUMP; Type 0: Not a Combination Product		
2	NDC:72578-119-02	1 in 1 BOTTLE, PUMP	06/06/2022	
2		60 g in 1 BOTTLE, PUMP; Type 0: Not a Combination Product		

## Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA214553	06/06/2022	

**Labeler** - Viona Pharmaceuticals Inc (081468959)

## Establishment

Name	Address	ID/FEI	Business Operations
Zydus Lifesciences Limited		650650802	ANALYSIS(72578-119) , MANUFACTURE(72578-119)

Revised: 6/2025

Viona Pharmaceuticals Inc