

ADAPALENE AND BENZOYL PEROXIDE GEL, 0.1%/2.5% - adapalene and benzoyl peroxide gel, 0.1%/2.5% gel
Encube Ethicals Private Limited

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: 2008

INDICATIONS AND USAGE

Adapalene and benzoyl peroxide gel 0.1% / 2.5% is a combination of adapalene, a retinoid, and benzoyl peroxide, and is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older. (1)

DOSAGE AND ADMINISTRATION

Adapalene and benzoyl peroxide gel 0.1% / 2.5% is not for oral, ophthalmic, or intravaginal use. (2) Apply a thin film of adapalene and benzoyl peroxide gel 0.1% / 2.5% 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). Avoid the eyes, lips and mucous membranes. (2)

DOSAGE FORMS AND STRENGTHS

Each gram of adapalene and benzoyl peroxide gel 0.1% / 2.5% contains 1 mg (0.1%) adapalene and 25 mg (2.5%) benzoyl peroxide. (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

Ultraviolet Light and Environmental Exposure: Avoid exposure to sunlight and sunlamps. Wear sunscreen when sun exposure cannot be avoided. (5.1) Erythema, scaling, dryness, stinging/burning, irritant and allergic contact dermatitis may occur with use of adapalene and benzoyl peroxide gel 0.1% / 2.5% and may necessitate discontinuation. (5.2)

ADVERSE REACTIONS

Most commonly reported adverse events ($\geq 1\%$) in patients treated with adapalene and benzoyl peroxide gel 0.1% / 2.5% were dry skin, contact dermatitis, application site burning, application site irritation and skin irritation. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Encube Ethicals Private Limited, at 1-833-285-4151 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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

Revised: 8/2023

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Adapalene and benzoyl peroxide gel 0.1% / 2.5% is indicated for the topical treatment of acne vulgaris in patients 9 years of age and older.

2 DOSAGE AND ADMINISTRATION

For topical use only; adapalene and benzoyl peroxide gel 0.1% / 2.5% is not for oral, ophthalmic, or intravaginal use.

Apply a thin film of adapalene and benzoyl peroxide gel 0.1% / 2.5% 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). Avoid the eyes, lips and mucous membranes.

3 DOSAGE FORMS AND STRENGTHS

Each gram of adapalene and benzoyl peroxide gel 0.1% / 2.5% contains 1 mg (0.1%) adapalene and 25 mg (2.5%) benzoyl peroxide in a white to very pale yellow, opaque, aqueous based gel.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Ultraviolet Light and Environmental Exposure

Exposure to sunlight, including sunlamps, should be minimized during the use of adapalene and benzoyl peroxide gel 0.1% / 2.5%. Patients with high levels of sun exposure and those with inherent sensitivity to sun should exercise particular caution. Use of 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 0.1% / 2.5%.

5.2 Local Cutaneous Reactions

Erythema, scaling, dryness, and stinging/burning may be experienced with use of adapalene and benzoyl peroxide gel 0.1% / 2.5%. 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 0.1% / 2.5%, 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 0.1% / 2.5%.

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

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

During clinical trials, 1401 subjects were exposed to adapalene and benzoyl peroxide gel 0.1% / 2.5%. A total of 1036 subjects with acne vulgaris, 12 years and older, were treated once daily for 12 weeks to 12 months. Related adverse events reported within 12 weeks of treatment and in at least 1% of subjects treated with adapalene and benzoyl peroxide gel 0.1% / 2.5% and those reported in subjects treated with the vehicle gel are presented in **Table 1**:

Table 1. Drug Related Adverse Events Reported in Clinical Trials by At Least 1% of Patients Treated For 12 Weeks

System Organ Class/Preferred Term	Adapalene and Benzoyl Peroxide Gel 0.1% / 2.5% N=564	Vehicle gel N=489
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Subjects with AE (s)	14%	4%
Dry Skin	7%	2%
Contact dermatitis	3%	<1%
Application site burning	2%	<1%
Application site irritation	1%	<1%
Skin irritation	1%	0%

Local tolerability evaluations, presented in **Table 2**, were conducted at each study visit in clinical trials by assessment of erythema, scaling, dryness, burning, and stinging.

**Table 2. Incidence of Local Cutaneous Irritation in Controlled Clinical Trials (N=553)
Treatment Emergent Signs and Symptoms**

	Maximum Severity During Treatment			End of Treatment Severity (12 Weeks)		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Erythema	27%	13%	1%	8%	2%	1%
Scaling	35%	11%	1%	9%	1%	<1%
Dryness	41%	13%	1%	10%	2%	<1%
Stinging/burning	41%	15%	3%	7%	2%	1%

Analysis over the 12 week period showed that local tolerability scores for erythema, scaling, dryness, and stinging/burning peaked at Week 1 of therapy and decreased thereafter.

During a pediatric clinical trial, 285 children with acne vulgaris, 9 to 11 years of age were treated with adapalene and benzoyl peroxide gel 0.1% / 2.5% or with the vehicle gel once daily for 12 weeks. Overall, the safety profile of adapalene and benzoyl peroxide gel 0.1% / 2.5% in these subjects is comparable to the safety profile observed in older subjects 12 years of age and above, both in the nature and frequency of the observed adverse events.

Analysis of local tolerability evaluations shows similar incidence of treatment emergent signs and symptoms as in subjects 12 years of age and above, with local tolerability

signs and symptoms peaking during the first week and decreasing over time.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of adapalene and benzoyl peroxide gel 0.1% / 2.5%: eyelid edema, sunburn, blister, pain of skin, pruritus, swelling face, conjunctivitis, skin discoloration, rash, eczema, throat tightness and allergic contact dermatitis. 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.

7 DRUG INTERACTIONS

Concomitant topical acne therapy should be used with caution because a possible cumulative irritancy effect may occur, especially with the use of peeling, desquamating, or abrasive agents. No formal drug-drug interaction studies were conducted with adapalene and benzoyl peroxide gel 0.1% / 2.5%.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C. There are no well-controlled trials in pregnant women treated with adapalene and benzoyl peroxide gel 0.1% / 2.5%. Animal reproduction studies have not been conducted with the combination gel or benzoyl peroxide. Furthermore, such studies are not always predictive of human response; therefore, adapalene and benzoyl peroxide gel 0.1% / 2.5% should be used during pregnancy only if the potential benefit justifies the risk to the fetus.

No teratogenic effects were observed in rats treated with oral doses of 0.15 to 5.0 mg adapalene/kg/day, up to 25 times (mg/m²/day) the maximum recommended human dose (MRHD) of 2 grams of adapalene and benzoyl peroxide gel 0.1% / 2.5%. However, teratogenic changes were observed in rats and rabbits when treated with oral doses of \geq 25 mg adapalene/kg/day representing 123 and 246 times MRHD, respectively. Findings included cleft palate, microphthalmia, encephalocele and skeletal abnormalities in rats; and umbilical hernia, exophthalmos and kidney and skeletal abnormalities in rabbits.

Dermal teratology studies conducted in rats and rabbits at doses of 0.6 to 6.0 mg adapalene/kg/day [25 to 59 times (mg/m²) the MRHD] exhibited no fetotoxicity and only minimal increases in supernumerary ribs in both species and delayed ossification in rabbits.

8.3 Nursing Mothers

It is not known whether adapalene or benzoyl peroxide is excreted in human milk following use of adapalene and benzoyl peroxide gel 0.1% / 2.5%. Because many drugs are excreted in human milk, caution should be exercised when adapalene and benzoyl peroxide gel 0.1% / 2.5% is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness of adapalene and benzoyl peroxide gel 0.1% / 2.5% in pediatric patients under the age of 9 have not been established.

8.5 Geriatric Use

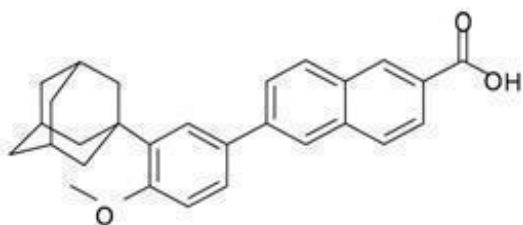
Clinical studies of adapalene and benzoyl peroxide gel 0.1% / 2.5% did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

11 DESCRIPTION

Adapalene and benzoyl peroxide gel 0.1% / 2.5% is a white to very pale yellow, opaque gel for topical use containing adapalene 0.1% and benzoyl peroxide 2.5%.

Adapalene, 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:

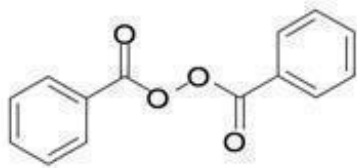
Adapalene:



Molecular formula: C₂₈H₂₈O₃ Molecular weight: 412.5

Benzoyl Peroxide 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: C₁₄H₁₀O₄ Molecular weight: 242.23

Adapalene and benzoyl peroxide gel 0.1% / 2.5% contains the following inactive ingredients: carbopol 980, d-limonene, docusate sodium solution, edetate disodium,

glycerin, poloxamer 182, polysorbate 80, propylene glycol, purified water, sodium hydroxide 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 0.1% / 2.5% is unknown.

12.3 Pharmacokinetics

A pharmacokinetic study was conducted in 10 adult subjects with acne vulgaris who were treated once daily for 30 days with 2 grams/day of adapalene and benzoyl peroxide gel 0.1% / 2.5% applied to 1000 cm² of acne involved skin, (face, chest, and upper back). Two subjects (20%) had quantifiable adapalene plasma concentrations above the limit of quantification (LOQ=0.1ng/mL). The highest adapalene C_{max} and AUC_{0-24h} was 0.21 ng/mL and 1.99 ng•h/mL, respectively. Excretion of adapalene appears to be primarily by the biliary route. Pharmacokinetics of adapalene and benzoyl peroxide gel 0.1% / 2.5% in pediatric subjects have not been evaluated.

Benzoyl peroxide is absorbed by the skin where it is converted to benzoic acid and eliminated in the urine.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity, photocarcinogenicity, genotoxicity, or fertility studies were conducted with adapalene and benzoyl peroxide gel 0.1% / 2.5%.

Carcinogenicity studies with adapalene have been conducted in mice at topical doses of 0.4, 1.3, and 4.0 mg/kg/day (1.2, 3.9, and 12 mg/m²/day), and in rats at oral doses of 0.15, 0.5, and 1.5 mg/kg/day (0.9, 3.0, and 9.0 mg/m²/day). In terms of body surface area, the highest dose levels are 9.8 (mice) and 7.4 times (rats) the MRHD of 2 grams of adapalene and benzoyl peroxide gel 0.1% / 2.5%. In the rat study, an increased incidence of benign and malignant pheochromocytomas 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 to 10 times the concentration of benzoyl peroxide in adapalene and benzoyl peroxide gel 0.1% / 2.5%) for two years. Rats received maximum daily applications of 138 (males) and 205 (females) mg benzoyl peroxide/kg. In terms of body surface area, these levels are 27 to 40 times the MRHD. 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 the rest of the 2 year study period, and in mice topically treated with 5% benzoyl peroxide carbopol gel for two years.

The role of benzoyl peroxide as a tumor promoter has been well established in several animal species. However, the significance of this finding in humans is unknown.

In a photocarcinogenicity study conducted with 5% benzoyl peroxide carbopol gel, no increase in UV-induced tumor formation was observed in hairless mice topically treated for 40 weeks.

No photocarcinogenicity studies were conducted with adapalene. However, 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 sunlight. Although the significance of these findings to humans is not clear, patients should be advised to avoid or minimize exposure to either sunlight or artificial irradiation sources.

Adapalene did not exhibit mutagenic or genotoxic effects in vitro (Ames test, Chinese hamster ovary cell assay, mouse lymphoma TK assay) or in vivo (mouse micronucleus test). Bacterial mutagenicity assays (Ames test) with benzoyl peroxide has provided mixed results, mutagenic potential was observed in a few but not in a majority of investigations. Benzoyl peroxide has been shown to produce single-strand DNA breaks in human bronchial epithelial and mouse epidermal cells, it has caused DNA-protein cross-links in the human cells, and has also induced a dose-dependent increase in sister chromatid exchanges in Chinese hamster ovary cells.

In rat oral studies, 20 mg adapalene/kg/day (120 mg/m²/day; 98 times the MRHD based on mg/m²/day comparison) did not affect the reproductive performance and fertility of F₀ males and females, or growth, development and reproductive function of F₁ offspring. No fertility studies were conducted with benzoyl peroxide.

14 CLINICAL STUDIES

The safety and efficacy of adapalene and benzoyl peroxide gel 0.1% / 2.5% applied once daily for the treatment of acne vulgaris were assessed in two 12 week, multicenter, controlled clinical studies of similar design, comparing adapalene and benzoyl peroxide gel 0.1% / 2.5% to the gel vehicle in acne subjects. Treatment response was defined as the percent of subjects who had a two grade improvement and rated 'Clear' and 'Almost Clear' at Week 12 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 residual hyperpigmentation and erythema may be present. An IGA score of 'Almost Clear' corresponded to a few

scattered comedones and a few small papules.

In Study 1, 517 subjects were randomized to adapalene and benzoyl peroxide gel 0.1% / 2.5%, adapalene 0.1% in vehicle gel, benzoyl peroxide 2.5% in vehicle gel, or vehicle gel. The median age of these 517 subjects was 15 years old and 60% were males.

At baseline, subjects had between 20 to 50 inflammatory lesions and 30 to 100 non-inflammatory lesions. The majority of subjects had a baseline IGA score of 'Moderate' which corresponded to more than half of the face is involved, many comedones, papules and pustules. The efficacy results at week 12 are presented in Table 3.

In Study 2, 1668 subjects were randomized to adapalene and benzoyl peroxide gel 0.1% / 2.5%, adapalene 0.1% in vehicle gel, benzoyl peroxide 2.5% in vehicle gel, or vehicle gel. The median age of subjects was 16 years old and 49% were males. At baseline, subjects had between 20 to 50 inflammatory lesions and 30 to 100 non-inflammatory lesions as well as an Investigator Global Assessment score of 'Moderate'. The efficacy results at week 12 are presented in Table 3.

In Study 3, 285 pediatric subjects 9 to 11 years of age were randomized to adapalene and benzoyl peroxide gel 0.1% / 2.5% or vehicle gel. The median age of subjects was 11 years and 24% were males. At baseline, subjects had a minimum of 20 but not more than 100 total lesions (inflammatory and/or non-inflammatory) with an Investigator Global Assessment score of 'Moderate'. The efficacy results at week 12 are presented in Table 3.

Table 3: Clinical Efficacy of Adapalene and Benzoyl Peroxide Gel 0.1% / 2.5% at Week 12

Study 1				
	Adapalene and Benzoyl Peroxide Gel 0.1% / 2.5% (N=149)	Adapalene 0.1% in Vehicle gel (N=148)	Benzoyl Peroxide 2.5% in Vehicle gel (N=149)	Vehicle gel (N=71)
IGA: Two Grade Improvement and Clear or Almost Clear	32 (21.5%)	18 (12.2%)	18 (12.1%)	4 (5.6%)
Inflammatory Lesions: Mean Absolute (Percent) Change	16.0 (52.4%)	11.4 (39.9%)	10.5 (35.8%)	9.5 (31.8%)
Non-inflammatory Lesions: Mean Absolute (Percent) Change	23.4 (45.9%)	15.2 (29.6%)	13.7 (32.2%)	13.2 (27.8%)

Study 2				
	Adapalene and Benzoyl Peroxide Gel 0.1% / 2.5% (N=415)	Adapalene 0.1% in Vehicle gel (N=420)	Benzoyl Peroxide 2.5% in Vehicle gel (N=415)	Vehicle gel (N=418)
IGA: Two Grade Improvement and Clear or Almost Clear	125 (30.1%)	83 (19.8%)	92 (22.2%)	47 (11.3%)
Inflammatory Lesions: Mean Absolute (Percent) Change	15.4 (53.4%)	12.3 (41.7%)	13.7 (47.6%)	8.7 (30.2%)
Non-inflammatory Lesions: Mean Absolute (Percent) Change	24.6 (48.1%)	21.0 (40.8%)	19.2 (37.2%)	11.3 (23.2%)

In both Studies 1 and 2 the treatment effect was smaller in subjects with a small number of baseline lesions than in subjects with a large number of baseline lesions.

Study 3		
	Adapalene and Benzoyl Peroxide Gel 0.1% / 2.5% N=142	Vehicle Gel N=143
IGA: Two Grade Improvement and Clear or Almost Clear	67 (47.2%)	22 (15.4%)
Inflammatory Lesions: Mean Absolute (Percent) Change	7.4 (36.0%)	0.7 (-13.2%)*
Non-inflammatory Lesions: Mean Absolute (Percent) Change	20.2 (54.7%)	2.9 (2.3%)

*That is, a mean percent increase of 13.2%

16 HOW SUPPLIED/STORAGE AND HANDLING

Adapalene and benzoyl peroxide gel 0.1% / 2.5% is white to very pale yellow in color and opaque in appearance, and is supplied as follows:

45 gram tube NDC 21922-052-65

45 gram pump NDC 21922-052-50

Storage and handling

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

17 PATIENT COUNSELING INFORMATION

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

Information for Patients

- Advise patients to cleanse the area to be treated with a mild or soapless cleanser; pat dry. Apply adapalene and benzoyl peroxide gel 0.1% / 2.5% 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.
- Adapalene and benzoyl peroxide gel 0.1% / 2.5% may cause irritation such as erythema, scaling, dryness, stinging or burning.
- Advise patients to minimize exposure to sunlight, including sunlamps.
- Recommend the use of sunscreen products and protective apparel, (e.g., hat) when exposure cannot be avoided.
- Adapalene and benzoyl peroxide gel 0.1% / 2.5% may bleach hair and colored fabric.

Manufactured by: **Encube Ethicals Private Limited**

Plot No. C-1, Madkaim Industrial Estate, Madkaim,

Post: Mardol, Ponda, Goa - 403 404, India.

Distributed by: **Encube Ethicals, Inc.**

200 Meredith Drive, Suite 202, Durham, NC 27713 USA

PATIENT INFORMATION

Adapalene (a dap' a leen) and Benzoyl (ben' zoe il) Peroxide Gel 0.1% / 2.5%

Important: For use on the skin only (topical). Do not use adapalene and benzoyl

peroxide gel 0.1% / 2.5% in or on your mouth, eyes, or vagina.

Read this Patient Information leaflet about adapalene and benzoyl peroxide gel 0.1% / 2.5% before you start using it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your doctor about your treatment or your medical condition. If you have any questions about adapalene and benzoyl peroxide gel 0.1% / 2.5%, talk with your doctor or pharmacist.

What is adapalene and benzoyl peroxide gel 0.1% / 2.5%?

Adapalene and benzoyl peroxide gel 0.1% / 2.5% is a prescription medicine for skin use only (topical) used to treat acne vulgaris in people 9 years of age and older.

Acne vulgaris is a condition in which the skin has blackheads, whiteheads and pimples.

It is not known if adapalene and benzoyl peroxide gel 0.1% / 2.5% is safe and effective in children younger than 9 years old.

What should I tell my doctor before using adapalene and benzoyl peroxide gel 0.1% / 2.5%?

Before you use adapalene and benzoyl peroxide gel 0.1% / 2.5%, tell your doctor if you:

- have other skin problems, including cuts or sunburn
- have any other medical conditions
- are pregnant or planning to become pregnant. It is not known if adapalene and benzoyl peroxide gel 0.1% / 2.5% can harm your unborn baby. Talk to your doctor if you are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed. It is not known if adapalene and benzoyl peroxide gel 0.1% / 2.5% 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 0.1% / 2.5%.

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

Especially tell your doctor if you use any other medicine for acne. Using adapalene and benzoyl peroxide gel 0.1% / 2.5% with topical medicines that contain sulfur, resorcinol or salicylic acid may cause skin irritation.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

How should I use adapalene and benzoyl peroxide gel 0.1% / 2.5%?

- Use adapalene and benzoyl peroxide gel 0.1% / 2.5% exactly as your doctor tells you to use it. Adapalene and benzoyl peroxide gel 0.1% / 2.5% is for skin use only. Do not

use adapalene and benzoyl peroxide gel 0.1% / 2.5% in or on your mouth, eyes, or vagina.

- Apply adapalene and benzoyl peroxide gel 0.1% / 2.5% 1 time a day.
- Do not use more adapalene and benzoyl peroxide gel 0.1% / 2.5% than you need to cover the treatment area. Using too much adapalene and benzoyl peroxide gel 0.1% / 2.5% or using it more than 1 time a day may increase your chance of skin irritation.

Applying adapalene and benzoyl peroxide gel 0.1% / 2.5%:

- Wash the area where the gel will be applied with a mild cleanser and pat dry.
- Adapalene and benzoyl peroxide gel 0.1% / 2.5% comes in a tube and a pump. If you have been prescribed the:
 - o Tube: Squeeze a small amount (about the size of a pea) of adapalene and benzoyl peroxide gel 0.1% / 2.5% onto your fingertips and spread a thin layer over the affected area.
 - o Pump: Depress the pump to dispense a small amount (about the size of a pea) of adapalene and benzoyl peroxide gel 0.1% / 2.5% and spread a thin layer over the affected area.

What should I avoid while using adapalene and benzoyl peroxide gel 0.1% / 2.5%?

- You should avoid spending time in sunlight or artificial sunlight, such as tanning beds or sunlamps. Adapalene and benzoyl peroxide gel 0.1% / 2.5% can make your skin sensitive to sun and the light from tanning beds and sunlamps. You should wear sunscreen and wear a hat and clothes that cover the areas treated with adapalene and benzoyl peroxide gel 0.1% / 2.5% if you have to be in sunlight.
- You should avoid weather extremes such as wind and cold as this may cause irritation to your skin.
- You should avoid applying adapalene and benzoyl peroxide gel 0.1% / 2.5% to cuts, abrasions and sunburned skin.
- You should avoid skin products that may dry or irritate your skin such as harsh soaps, astringents, cosmetics that have strong skin drying effects and products containing high levels of alcohol.
- You should avoid the use of “waxing” as a hair removal method on skin treated with adapalene and benzoyl peroxide gel 0.1% / 2.5%.
- Adapalene and benzoyl peroxide gel 0.1% / 2.5% may bleach your clothes or hair. Allow adapalene and benzoyl peroxide gel 0.1% / 2.5% to dry completely before dressing to prevent bleaching of your clothes.

What are the possible side effects of adapalene and benzoyl peroxide gel 0.1% / 2.5%?

Adapalene and benzoyl peroxide gel 0.1% / 2.5% may cause serious side effects including:

- Local skin reactions. Local skin reactions are most likely to happen during the first 4 weeks of treatment and usually lessen with continued use of adapalene and benzoyl peroxide gel 0.1% / 2.5%. Signs and symptoms of local skin reaction include:

- Redness
- Dryness
- Swelling
- Scaling
- Stinging or burning

Tell your doctor right away if these side effects continue for longer than 4 weeks or get worse, you may have to stop using adapalene and benzoyl peroxide gel 0.1% / 2.5%.

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of adapalene and benzoyl peroxide gel 0.1% / 2.5%. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088. You may also report side effects to Encube Ethicals Private Limited, at 1-833-285-4151.

How should I store adapalene and benzoyl peroxide gel 0.1% / 2.5%?

- Store adapalene and benzoyl peroxide gel 0.1% / 2.5% at room temperature, 68° – 77° F (20° – 25° C)
- Keep adapalene and benzoyl peroxide gel 0.1% / 2.5% inside container and out of light and away from heat.

Keep adapalene and benzoyl peroxide gel 0.1% / 2.5% and all medicines out of the reach of children.

General information about adapalene and benzoyl peroxide gel 0.1% / 2.5%

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information Leaflet. Do not use adapalene and benzoyl peroxide gel 0.1% / 2.5% for a condition for which it was not prescribed. Do not give adapalene and benzoyl peroxide gel 0.1% / 2.5% to other people, even if they have the same symptoms you have. It may harm them.

This Patient Information leaflet summarizes the most important information about adapalene and benzoyl peroxide gel 0.1% / 2.5%. If you would like more information, talk with your doctor. You can also ask your doctor or pharmacist for information about adapalene and benzoyl peroxide gel 0.1% / 2.5% that is written for health professionals.

What are the ingredients in adapalene and benzoyl peroxide gel 0.1% / 2.5%?

Active ingredient: adapalene and benzoyl peroxide

Inactive ingredients: carbopol 980, d-limonene, docusate sodium solution, edetate disodium, glycerin, poloxamer 182, polysorbate 80, propylene glycol, purified water, sodium hydroxide and sorbitan monooleate.

Manufactured by:

Encube Ethicals Private Limited

Plot No. C-1, Madkaim Industrial Estate,
Madkaim, Post: Mardol, Ponda,
Goa - 403 404, India.

Distributed by:

Encube Ethicals, Inc.
200 Meredith Drive, Suite 202
Durham, NC 27713 USA

Issued: 12/2022

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Carton Label

NDC 21922- **052**-50

Adapalene and Benzoyl Peroxide Gel, 0.1%/2.5%

PUMP

FOR TOPICAL USE ONLY

Net Wt. 45g

Rx only



Unvarnished Area
45 x 45 mm

2D Coding and Batch Details to be overcoded
(For Reference Only)



GTIN: XXXXXXXXXXXXX
S.NO.: XXXXXXXXXXX
EXP: XXXXXX
LOT: XXXXXXXXXXX

EAB3A/00



NDC 21922-052-50

Adapalene and Benzoyl Peroxide

Gel

0.1% / 2.5%

PUMP

FOR TOPICAL
USE ONLY.
Not for ophthalmic,
oral or intravaginal
use.

Net Wt. 45 g

Rx only

Usual dosage: Apply a thin film once a day to affected areas. See package insert for complete prescribing information.

Each gram contains: Adapalene 0.1% and benzoyl peroxide 2.5% in an aqueous gel consisting of carbopol 980, d-limonene, docusate sodium solution, edetate disodium, glycerin, poloxamer 182, polysorbate 80, propylene glycol, purified water, sodium hydroxide and sorbitan monooleate.

Storage: Store at 20° - 25°C (68° - 77°F); excursions permitted to 15° - 30°C (59° - 86°F) [see USP Controlled Room Temperature].

KEEP OUT OF THE REACH OF CHILDREN.



NDC 21922-052-50

Adapalene and Benzoyl Peroxide

Gel

0.1% / 2.5%

PUMP

FOR TOPICAL
USE ONLY.
Not for ophthalmic,
oral or intravaginal
use.

Net Wt. 45 g

Rx only



N 3 21922 05250 3

Rev. 12/22

See carton closure for lot number & expiration date.

Mfg. Lic. No. 361

Manufactured by:
Encube Ethicals Private Limited
Plot No. C-1, Madkaim Industrial Estate, Madkaim, Post: Mardol, Ponda, Goa - 403 404, India.

Distributed by:
Encube Ethicals, Inc.
200 Meredith Drive, Suite 202 Durham, NC 27713 USA

NDC 21922-052-50

Adapalene and Benzoyl Peroxide

Gel 0.1% / 2.5%

PUMP

FOR TOPICAL USE ONLY.
Not for ophthalmic, oral or intravaginal use.

Net Wt. 45 g

Rx only



Container Label

NDC 21922- 052-50


Adapalene and Benzoyl Peroxide Gel, 0.1%/2.5%

PUMP

FOR TOPICAL USE ONLY

Net Wt. 45g

Rx only



Each gram contains adapalene 0.1% and benzoyl peroxide 2.5% in an aqueous gel consisting of carbopol 980, d-limonene, docusate sodium solution, edetate disodium, glycerin, poloxamer 182, polysorbate 80, propylene glycol, purified water, sodium hydroxide and sorbitan monooleate.

NDC 21922-052-50

Adapalene and Benzoyl Peroxide Gel 0.1 % / 2.5%

PUMP

FOR TOPICAL USE ONLY.
Not for ophthalmic, oral or intravaginal use.

Net Wt. 45 g

Rx only

Usual Dosage: Apply a thin film once a day to affected areas. See package insert for complete prescribing information.

Storage: Store at 20° - 25°C (68° - 77°F); excursions permitted to 15° - 30°C (59° - 86°F) [see USP Controlled Room Temperature].

KEEP OUT OF THE REACH OF CHILDREN.

See lot number and expiration date below.


Mfg. Lic. No. 361

Manufactured by:
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200 Meredith Drive
Suite 202 Durham,
NC 27713 USA

EAB2A00

Rev. 12/22



N 3 21922 05250 3

NVZ Area
55.7 x 20 mm

ADAPALENE AND BENZOYL PEROXIDE GEL, 0.1%/2.5%

adapalene and benzoyl peroxide gel, 0.1%/2.5% gel

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:21922-052
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ADAPALENE (UNII: 1L4806J2QF) (ADAPALENE - UNII:1L4806J2QF)	ADAPALENE	1 mg in 1 g

BENZOYL PEROXIDE (UNII: W9WZ N9A0GM) (BENZOYL PEROXIDE - UNII:W9WZ N9A0GM)

BENZOYL PEROXIDE

25 mg
in 1 g

Inactive Ingredients

Ingredient Name	Strength
EDETATE DISODIUM (UNII: 7FLD91C86K)	
CARBOMER HOMOPOLYMER TYPE C (ALLYL PENTAERYTHRITOL CROSSLINKED) (UNII: 4Q93RCW27E)	
GLYCERIN (UNII: PDC6A3C0OX)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
DOCUSATE SODIUM (UNII: F05Q2T2JA0)	
POLOXAMER 182 (UNII: JX0HIX6OAG)	
POLYSORBATE 80 (UNII: 6OZP39ZG8H)	
SORBITAN MONOOLEATE (UNII: 06XEA2VD56)	
LIMONENE, (+)- (UNII: GFD7C86Q1W)	
SODIUM HYDROXIDE (UNII: 55X04QC32I)	
WATER (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:21922-052-50	1 in 1 CARTON	08/14/2023	
1		45 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	ANDA206164	08/14/2023	

Labeler - Encube Ethicals Private Limited (915834105)

Establishment

Name	Address	ID/FEI	Business Operations
Encube Ethicals Private Limited		725076298	ANALYSIS(21922-052) , LABEL(21922-052) , MANUFACTURE(21922-052) , PACK(21922-052)

Revised: 8/2023

Encube Ethicals Private Limited