HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use DUAC Gel safely and effectively. See full prescribing information for DUAC Gel.

DUAC (clindamycin phosphate and benzoyl peroxide) Gel, 1.2%/5% for topical use
Initial U.S. Approval: 2000

----------INDICATIONS AND USAGE----------

DUAC Gel is a combination of clindamycin phosphate (a lincosamide antibacterial) and benzoyl peroxide indicated for the topical treatment of inflammatory acne vulgaris. (1.1)

Limitation of Use:
DUAC Gel has not been demonstrated to have any additional benefit when compared with benzoyl peroxide alone in the same vehicle when used for the treatment of non-inflammatory acne. (1.2)

----------DOSAGE AND ADMINISTRATION----------

- Apply a thin layer of DUAC Gel to the face once daily, in the evening. (2)
- Not for oral, ophthalmic, or intravaginal use. (2)

----------DOSAGE FORMS AND STRENGTHS----------

Gel, 1.2%/5%: Each gram of DUAC Gel contains 12 mg clindamycin phosphate (equivalent to 10 mg of clindamycin) and 50 mg benzoyl peroxide. (3)

----------CONTRAINDICATIONS----------

DUAC Gel is contraindicated in:

- Patients who have demonstrated hypersensitivity (e.g., anaphylaxis) to clindamycin, benzoyl peroxide, any components of the formulation, or lincomycin. (4)
- Patients with a history of regional enteritis, ulcerative colitis, or antibiotic-associated colitis (including pseudomembranous colitis). (4)

----------WARNINGS AND PRECAUTIONS----------

- Colitis: Clindamycin can cause severe colitis, which may result in death. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of clindamycin. DUAC Gel should be discontinued if significant diarrhea occurs. (5.1)
- Ultraviolet light and environmental exposure (including use of tanning beds or sun lamps): Minimize sun exposure following drug application. (5.2)

----------ADVERSE REACTIONS----------

- The most common local adverse reactions (≥5%) are erythema, peeling, dryness, and burning. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Stiefel Laboratories, Inc. at 1-888-784-3335 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- DUAC Gel should not be used in combination with erythromycin-containing products because of its clindamycin component. (7.1)

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

Revised: 12/2013

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Indication

DUAC® (clindamycin phosphate and benzoyl peroxide) Gel, 1.2%/5% is indicated for the topical treatment of inflammatory acne vulgaris in patients 12 years and older.

1.2 Limitations of Use

DUAC Gel has not been demonstrated to have any additional benefit when compared with benzoyl peroxide alone in the same vehicle when used for the treatment of non-inflammatory acne.

2 DOSAGE AND ADMINISTRATION

Apply a thin layer of DUAC Gel to the face once daily, in the evening or as directed by the physician. The skin should be gently washed, rinsed with warm water, and patted dry before applying DUAC Gel. Avoid the eyes, mouth, lips, mucous membranes, or areas of broken skin.

DUAC Gel is not for oral, ophthalmic, or intravaginal use.

3 DOSAGE FORMS AND STRENGTHS

Gel, 1.2%/5%

DUAC Gel is a white to slightly yellow, opaque gel. Each gram of DUAC Gel contains 12 mg clindamycin phosphate (equivalent to 10 mg of clindamycin) and 50 mg benzoyl peroxide.

4 CONTRAINDICATIONS

4.1 Hypersensitivity

DUAC Gel is contraindicated in those individuals who have shown hypersensitivity to clindamycin, benzoyl peroxide, any components of the formulation, or lincomycin. Anaphylaxis, as well as allergic reactions leading to hospitalization, has been reported in postmarketing use with DUAC Gel. *[See Postmarketing Experience (6.2).]*

4.2 Colitis/Enteritis

DUAC Gel is contraindicated in those individuals with a history of regional enteritis, ulcerative colitis, pseudomembranous colitis, or antibiotic-associated colitis *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Colitis

Systemic absorption of clindamycin has been demonstrated following topical use of clindamycin. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of topical and systemic clindamycin. If significant diarrhea occurs, DUAC Gel should be discontinued.

Severe colitis has occurred following oral and parenteral administration of clindamycin with an onset of up to several weeks following cessation of therapy. Antiperistaltic agents such as opiates and diphenoxylate with atropine may prolong and/or worsen severe colitis. Severe colitis may result in death.

Studies indicate a toxin(s) produced by Clostridia is one primary cause of antibiotic-associated colitis. The colitis is usually characterized by severe persistent diarrhea and severe abdominal cramps and may be associated with the passage of blood and mucus. Stool cultures for *Clostridium difficile* and stool assay for *C. difficile* toxin may be helpful diagnostically.

5.2 Ultraviolet Light and Environmental Exposure

Benzoyl peroxide, a component of DUAC Gel, may cause increased sensitivity to sunlight. Minimize sun exposure (including use of tanning beds or sun lamps) following drug application. *[See Nonclinical Toxicology (13.1.)]* Patients who may be required to have considerable sun exposure due to occupation and those with inherent sensitivity to the sun should exercise particular caution.

6 ADVERSE REACTIONS

The following adverse reaction is described in more detail in the *Warnings and Precautions* section of the label:

- Colitis *[see Warnings and Precautions (5.1)]*.

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 with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

During clinical trials, 397 subjects used DUAC Gel once daily for 11 weeks for the treatment of moderate to moderately severe facial acne vulgaris. All subjects were graded for facial local skin reactions (erythema, peeling, burning, and dryness) on the following scale: 0 = absent, 1 = mild, 2 = moderate, and 3 = severe. The percentage of subjects that had symptoms present before treatment (at baseline) and during treatment is presented in Table 1.

Table 1. Local Skin Reactions With Use of DUAC Gel
Combined Results From Five Trials (n = 397)

	% of Subjects Using DUAC Gel With Symptom Present					
	Before Treatment (Baseline)			During Treatment		
Symptom	Mild	Moderate	Severe	Mild	Moderate	Severe
Erythema	28%	3%	0	26%	5%	0
Peeling	6%	<1%	0	17%	2%	0
Burning	3%	<1%	0	5%	<1%	0
Dryness	6%	<1%	0	15%	1%	0

(Percentages derived by number of subjects receiving DUAC Gel with symptom score/number of enrolled subjects receiving DUAC Gel).

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of DUAC 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.

Anaphylaxis, as well as allergic reactions leading to hospitalization, has been reported in postmarketing use with DUAC Gel.

7 DRUG INTERACTIONS

7.1 Erythromycin

Avoid using DUAC Gel in combination with erythromycin-containing products due to its clindamycin component. In vitro studies have shown antagonism between erythromycin and clindamycin. The clinical significance of this in vitro antagonism is not known.

7.2 Concomitant Topical Medications

Concomitant topical acne therapies should be used with caution since a possible cumulative irritancy effect may occur, especially with the use of peeling, desquamating, or abrasive agents. If irritancy or dermatitis occurs, reduce frequency of application or temporarily interrupt treatment and resume once the irritation subsides. Treatment should be discontinued if the irritation persists.

7.3 Neuromuscular Blocking Agents

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. DUAC Gel should be used with caution in patients receiving such agents.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C.

There are no adequate and well-controlled studies in pregnant women treated with DUAC Gel. DUAC Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Developmental toxicity studies performed in rats and mice using oral doses of clindamycin up to 600 mg/kg/day (240 and 120 times the amount of clindamycin in the highest recommended adult human dose based on mg/m^2, respectively) or subcutaneous doses of clindamycin up to 250 mg/kg/day (100 and 50 times the amount of clindamycin in the highest recommended adult human dose based on mg/m^2, respectively) revealed no evidence of teratogenicity.

8.3 Nursing Mothers

It is not known whether DUAC Gel is excreted into human milk after topical application. However, orally and parenterally administered clindamycin has been reported to appear in breast milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Because many drugs are excreted in human milk, caution should be exercised when DUAC Gel is administered to a nursing woman.

8.4 Pediatric Use

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

8.5 Geriatric Use

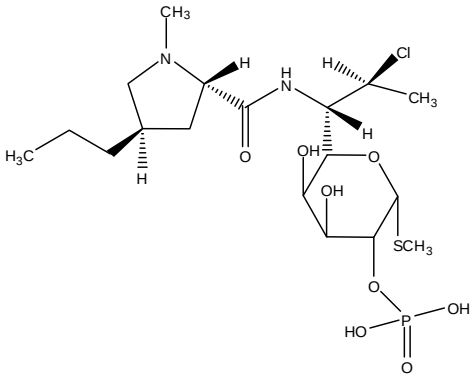
Clinical studies of DUAC Gel did not include sufficient numbers of subjects ages 65 and over to determine whether they respond differently from younger subjects.

11 DESCRIPTION

DUAC (clindamycin phosphate and benzoyl peroxide) Gel, 1.2%/5% is a fixed combination product with two active ingredients in a white to slightly yellow, opaque, aqueous gel formulation.

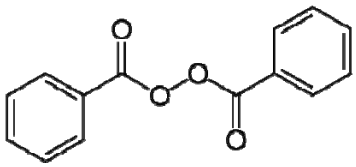
Clindamycin phosphate is a water soluble ester of the semi-synthetic antibiotic produced by a 7(S)-chloro-substitution of the 7(R)-hydroxyl group of the parent antibiotic lincomycin.

Clindamycin phosphate is $C_{18}H_{34}ClN_2O_8PS$. The structural formula for clindamycin phosphate is represented below:



Clindamycin phosphate has a molecular weight of 504.97 and its chemical name is methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-*trans*-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-*threo*-α-D-*galacto*-octopyranoside 2-(dihydrogen phosphate).

Benzoyl peroxide is $C_{14}H_{10}O_4$. It has the following structural formula:



Benzoyl peroxide has a molecular weight of 242.23.

Each gram of DUAC Gel contains 10 mg (1%) clindamycin, as clindamycin phosphate, and 50 mg (5%) benzoyl peroxide in a base consisting of carbomer homopolymer (type C), dimethicone, disodium lauryl sulfosuccinate, edetate disodium, glycerin, methylparaben, poloxamer 182, purified water, silicon dioxide, and sodium hydroxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Clindamycin: Clindamycin is a lincosamide antibacterial *[see Clinical Pharmacology (12.4)]*.

Benzoyl Peroxide: Benzoyl peroxide is an oxidizing agent with bacteriocidal and keratolytic effects, but the precise mechanism of action is unknown.

12.3 Pharmacokinetics

A comparative trial of the pharmacokinetics of DUAC Gel and 1% clindamycin solution alone in 78 subjects indicated that mean plasma clindamycin levels during the 4-week dosing period were <0.5 ng/mL for both treatment groups.

Benzoyl peroxide has been shown to be absorbed by the skin where it is converted to benzoic acid. Less than 2% of the dose enters systemic circulation as benzoic acid.

12.4 Microbiology

Clindamycin binds to the 50S ribosomal subunits of susceptible bacteria and prevents elongation of peptide chains by interfering with peptidyl transfer, thereby suppressing protein synthesis.

In Vivo Activity: No microbiology studies were conducted in the clinical trials with this product.

In Vitro Activity: The clindamycin and benzoyl peroxide components individually have been shown to have in vitro activity against *Propionibacterium acnes*, an organism which has been associated with acne vulgaris; however, the clinical significance of this in vitro activity is not known.

Drug Resistance: There are reports of an increase of P. acnes resistance to clindamycin in the treatment of acne. In patients with *P. acnes* resistant to clindamycin, the clindamycin component may provide no additional benefit beyond benzoyl peroxide alone.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Benzoyl peroxide has been shown to be a tumor promoter and progression agent in a number of animal studies. Benzoyl peroxide in acetone at doses of 5 and 10 mg administered twice per week induced squamous cell skin tumors in transgenic TgAC mice in a study using 20 weeks of topical treatment. The clinical significance of this is unknown.

In a 2-year dermal carcinogenicity study in mice, treatment with DUAC Gel at doses up to 8,000 mg/kg/day (16 times the highest recommended adult human dose of 2.5 g DUAC Gel, based on mg/m^2) did not cause an increase in skin tumors. However, topical treatment with another formulation containing 1% clindamycin and 5% benzoyl peroxide at doses of 100, 500, or 2,000 mg/kg/day caused a dose-dependent increase in the incidence of keratoacanthoma at the treated skin site of male rats in a 2-year dermal carcinogenicity study in rats.

In a 52-week photocarcinogenicity study in hairless mice (40 weeks of treatment followed by 12 weeks of observation), the median time to onset of skin tumor formation decreased and the number of tumors per mouse increased relative to controls following chronic concurrent topical treatment with DUAC Gel and exposure to ultraviolet radiation.

Genotoxicity studies were not conducted with DUAC Gel. Clindamycin phosphate was not genotoxic in *Salmonella typhimurium* or in a rat micronucleus test. Benzoyl peroxide has been found to cause DNA strand breaks in a variety of mammalian cell types, to be mutagenic in *Salmonella typhimurium* tests by some but not all investigators, and to cause sister chromatid exchanges in Chinese hamster ovary cells.

Studies have not been performed with DUAC Gel or benzoyl peroxide to evaluate the effect on fertility. Fertility studies in rats treated orally with up to 300 mg/kg/day of clindamycin (approximately 120 times the amount of clindamycin in the highest recommended adult human dose of 2.5 g DUAC Gel, based on mg/m^2) revealed no effects on fertility or mating ability.

14 CLINICAL STUDIES

In five randomized, double-blind clinical trials of 1,319 subjects, 397 used DUAC Gel, 396 used benzoyl peroxide, 349 used clindamycin, and 177 used vehicle. Subjects were instructed to wash the face, wait 10 to 20 minutes, and then apply medication to the entire face, once daily in the evening before retiring. DUAC Gel applied once daily for 11 weeks was significantly more effective than vehicle, benzoyl peroxide, and clindamycin in the treatment of inflammatory lesions of moderate to moderately severe facial acne vulgaris in three of the five trials (Trials 1, 2, and 5).

Subjects were evaluated and acne lesions counted at each clinical visit at Weeks 2, 5, 8, 11. The primary efficacy measures were the lesion counts and the investigator's global assessment evaluated at Week 11. Percent reductions in inflammatory lesion counts after treatment for 11 weeks in these 5 trials are shown in Table 2.

Table 2. Mean Percent Reduction in Inflammatory Lesion Counts

Treatment	Trial 1 (n = 120)	Trial 2 (n = 273)	Trial 3 (n = 280)	Trial 4 (n = 288)	Trial 5 (n = 358)
DUAC Gel	65%	56%	42%	57%	52%
Benzoyl Peroxide	36%	37%	32%	57%	41%
Clindamycin	34%	30%	38%	49%	33%
Vehicle	19%	-0.4%	29%	[redacted]	29%

The group treated with DUAC Gel showed greater overall improvement in the investigator's global assessment than the benzoyl peroxide, clindamycin, and vehicle groups in three of the five trials (Trials 1, 2, and 5).

Clinical trials have not adequately demonstrated the effectiveness of DUAC Gel versus benzoyl peroxide alone in the treatment of non-inflammatory lesions of acne.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

DUAC Gel is a white to slightly yellow, opaque gel. It is supplied as follows:

- 45 gram tube NDC 0145-2371-05

16.2 Storage and Handling

Pharmacist:

- Prior to Dispensing: Store in a cold place, preferably in a refrigerator, between 2°C and 8°C (36°F and 46°F). Do not freeze.

16.3 Dispensing Instructions for the Pharmacist

- Dispense DUAC Gel with a 60-day expiration date.
- Specify "Store at room temperature up to 25°C (77°F). Do not freeze."
- Keep tube tightly closed.
- Keep out of the reach of small children.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information).

- Patients who develop allergic reactions such as severe swelling or shortness of breath should discontinue use and contact their physician immediately.
- DUAC Gel may cause irritation such as erythema, scaling, itching, or burning, especially when used in combination with other topical acne therapies.
- Excessive or prolonged exposure to sunlight should be limited. To minimize exposure to sunlight, a hat or other clothing should be worn. Sunscreen may also be used.
- DUAC Gel may bleach hair or colored fabric.

DUAC is a registered trademark of Stiefel Laboratories, Inc.

Stiefel Laboratories, Inc.
Research Triangle Park, NC 27709

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PHARMACIST-DETACH HERE AND GIVE INSTRUCTIONS TO PATIENT

PATIENT INFORMATION
DUAC® (Doo-ack)
(clindamycin phosphate and benzoyl peroxide) Gel, 1.2%/5%

Important: For use on the skin only (topical use). Do not get DUAC Gel in your mouth, eyes, vagina, or on your lips.

Read this Patient Information before you start using DUAC Gel and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or your treatment.

What is DUAC Gel?

DUAC Gel is a prescription medicine used on the skin (topical) to treat inflamed acne in people 12 years and older.

Who should not use DUAC Gel?
Do not use DUAC Gel if you have:

- had an allergic reaction to clindamycin, lincomycin, benzoyl peroxide, or any of the ingredients in DUAC Gel. See the end of this leaflet for a complete list of ingredients in DUAC Gel.
- Crohn's disease or ulcerative colitis.
- had inflammation of the colon (colitis) with past antibiotic use.

What should I tell my healthcare provider before using DUAC Gel?
Before using DUAC Gel, tell your healthcare provider about all of your medical conditions, including if you:

- plan to have surgery with general anesthesia.
- are sensitive to sunlight.
- are pregnant or plan to become pregnant. It is not known if DUAC Gel will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if DUAC Gel passes into your breast milk. One of the medicines in DUAC Gel is clindamycin. Clindamycin when taken by mouth or by injection has been reported to appear in breast milk. You and your healthcare provider should decide if you will use DUAC Gel while breastfeeding.

Tell your healthcare provider about all the medicines you take, including prescription or over-the-counter medicines, vitamins, herbal supplements, and skin products you use. Using other topical acne products may increase the irritation of your skin when used with DUAC Gel.

- Especially tell your healthcare provider if you take a medicine that contains erythromycin. DUAC Gel should not be used with products that contain erythromycin.

How should I use DUAC Gel?

- Use DUAC Gel exactly as your healthcare provider tells you to use it.
- Before you apply DUAC Gel, wash your face gently with a mild soap, rinse with warm water, and pat the skin dry.
- Apply a thin layer of DUAC Gel to your face 1 time a day, in the evening or as directed by your healthcare provider. Wash your hands with soap and water after applying DUAC Gel.

- Do not get DUAC Gel in your mouth, eyes, nose, vagina, or on your lips. Do not get DUAC Gel on cuts or open wounds.

What should I avoid while using DUAC Gel?

- Limit your time in sunlight. Avoid using tanning beds or sun lamps. If you have to be in sunlight, wear a wide-brimmed hat or other protective clothing. Sunscreen may also be used.
- Talk to your healthcare provider if you spend a lot of time in the sun.
- DUAC Gel may bleach hair or colored fabric.

What are the possible side effects with DUAC Gel?

DUAC Gel may cause serious side effects, including:

- **Inflammation of the colon (colitis).** Stop using DUAC Gel and call your healthcare provider right away if you have severe watery diarrhea, or bloody diarrhea.
- **Allergic reactions.** Stop using DUAC Gel and call your healthcare provider or get help right away if you have any of the following symptoms:
    - o severe itching
    - o swelling of your face, eyes, lips, tongue, or throat
    - o trouble breathing

The most common side effects with DUAC Gel are skin reactions and may include redness, peeling, dryness, and burning. These are not all the possible side effects with DUAC 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 DUAC Gel?

- Store DUAC Gel at room temperature up to 25°C (77°F). Do not freeze DUAC Gel.
- The expiration date of DUAC Gel is 60 days from the date when you fill your prescription.
- Safely throw away expired DUAC Gel.
- Keep the tube tightly closed.

Keep DUAC Gel and all medicines out of the reach of children.

General information about DUAC Gel

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use DUAC Gel for a condition for which it was not

prescribed. Do not give DUAC Gel to other people, even if they have the same symptoms you have. It may harm them.

If you would like more information, talk with your healthcare provider. You can also ask your pharmacist or healthcare provider for information about DUAC Gel that is written for health professionals.

For more information, call 1-888-784-3335.

What are the ingredients in DUAC Gel?
Active Ingredients: clindamycin phosphate 1.2% and benzoyl peroxide 5%
Inactive ingredients: carbomer homopolymer (type C), dimethicone, disodium lauryl sulfosuccinate, edetate disodium, glycerin, methylparaben, poloxamer 182, purified water, silicon dioxide, and sodium hydroxide.

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

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Stiefel Laboratories, Inc.
Research Triangle Park, NC 27709

December 2013
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