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Each gram of clindamycin phosphate and benzoyl peroxide gel, 1.2%/5% 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 clindamycin phosphate and benzoyl peroxide gel and 1% clindamycin solution alone in 78 subjects indicated that mean plasma clindamycin levels during the 4-week dosing period were less than 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 clindamycin phosphate and benzoyl peroxide gel at doses up to 8,000 mg per kg per day (16 times the highest recommended adult human dose of 2.5 g clindamycin phosphate and benzoyl peroxide gel, based on mg per m²) 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 per kg per 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 clindamycin phosphate and benzoyl peroxide gel and exposure to ultraviolet radiation.

Genotoxicity studies were not conducted with clindamycin phosphate and benzoyl peroxide 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 clindamycin phosphate and benzoyl peroxide gel or benzoyl peroxide to evaluate the effect on fertility. Fertility studies in rats treated orally with up to 300 mg per kg per day of clindamycin (approximately 120 times the amount of clindamycin in the highest recommended adult human dose of 2.5 g clindamycin phosphate and benzoyl peroxide gel, based on mg per m²) revealed no effects on fertility or mating ability.

14 CLINICAL STUDIES

In five randomized, double-blind clinical trials of 1,319 subjects, 397 used clindamycin phosphate and benzoyl peroxide 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. Clindamycin phosphate and benzoyl peroxide 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)
Clindamycin phosphate and benzoyl peroxide gel	65%	56%	42%	57%	52%
Benzoyl Peroxide	36%	37%	32%	57%	41%
Clindamycin	34%	30%	38%	49%	33%
Vehicle	19%	-0.4%	29%		29%

The group treated with clindamycin phosphate and benzoyl peroxide 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 clindamycin phosphate and benzoyl peroxide gel versus benzoyl peroxide alone in the treatment of non-inflammatory lesions of acne.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Clindamycin Phosphate and Benzoyl Peroxide Gel, 1.2%/5% is a white to slightly yellow, opaque gel. It is supplied as follows:

- 45 gram tube NDC 51672-1366-6

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 clindamycin phosphate and benzoyl peroxide 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.
- Clindamycin phosphate and benzoyl peroxide 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.
- Clindamycin phosphate and benzoyl peroxide gel may bleach hair or colored fabric.
- Clindamycin phosphate and benzoyl peroxide gel may cause skin and facial hair to temporarily change color (yellow/orange) when used with topical sulfone products.

Manufactured by: Taro Pharmaceuticals Inc., Brampton, Ontario, Canada L6T 1C1
Distributed by: **Taro Pharmaceuticals U.S.A., Inc.**, Hawthorne, NY 10532

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PATIENT INFORMATION

Clindamycin Phosphate (klin'' da mye' sin fos' fate) and Benzoyl Peroxide (BEN-zoe-il per-OX-ide) Gel, 1.2%/5%

Important: For use on the skin only (topical use). Do not get clindamycin phosphate and benzoyl peroxide gel in your mouth, eyes, vagina, or on your lips.

Read this Patient Information before you start using clindamycin phosphate and benzoyl peroxide 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 Clindamycin Phosphate and Benzoyl Peroxide Gel?

Clindamycin phosphate and benzoyl peroxide gel is a prescription medicine used on the skin (topical) to treat inflamed acne in people 12 years and older.

Who should not use Clindamycin Phosphate and Benzoyl Peroxide Gel?

Do not use Clindamycin Phosphate and Benzoyl Peroxide Gel if you have:

- had an allergic reaction to clindamycin, lincomycin, benzoyl peroxide, or any of the ingredients in clindamycin phosphate and benzoyl peroxide gel. See the end of this leaflet for a complete list of ingredients in clindamycin phosphate and benzoyl peroxide 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 Clindamycin Phosphate and Benzoyl Peroxide Gel?

Before using Clindamycin Phosphate and Benzoyl Peroxide 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 clindamycin phosphate and benzoyl peroxide gel will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if clindamycin phosphate and benzoyl peroxide gel passes into your breast milk. One of the medicines in clindamycin phosphate and benzoyl peroxide 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 clindamycin phosphate and benzoyl peroxide 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 clindamycin phosphate and benzoyl peroxide gel.

- Especially tell your healthcare provider if you take a medicine that contains erythromycin. Clindamycin phosphate and benzoyl peroxide gel should not be used with products that contain erythromycin.
- Clindamycin phosphate and benzoyl peroxide gel may cause skin and facial hair to temporarily change color (yellow or orange) when used with topical products that contain sulfones.

How should I use Clindamycin Phosphate and Benzoyl Peroxide Gel?

- Use clindamycin phosphate and benzoyl peroxide gel exactly as your healthcare provider tells you to use it.
- Before you apply clindamycin phosphate and benzoyl peroxide gel, wash your face gently with a mild soap, rinse with warm water, and pat the skin dry.
- Apply a thin layer of clindamycin phosphate and benzoyl peroxide 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 clindamycin phosphate and benzoyl peroxide gel.
- Do not get clindamycin phosphate and benzoyl peroxide gel in your mouth, eyes, nose, vagina, or on your lips. Do not get clindamycin phosphate and benzoyl peroxide gel on cuts or open wounds.

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What should I avoid while using Clindamycin Phosphate and Benzoyl Peroxide 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.
- Clindamycin phosphate and benzoyl peroxide gel may bleach hair or colored fabric.

What are the possible side effects with Clindamycin Phosphate and Benzoyl Peroxide Gel?

Clindamycin Phosphate and Benzoyl Peroxide Gel may cause serious side effects, including:

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

The most common side effects with Clindamycin Phosphate and Benzoyl Peroxide Gel

are skin reactions and may include redness, peeling, dryness, and burning. These are not all the possible side effects with clindamycin phosphate 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 Clindamycin Phosphate and Benzoyl Peroxide Gel?

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

Keep Clindamycin Phosphate and Benzoyl Peroxide Gel and all medicines out of the reach of children.

General information about Clindamycin Phosphate and Benzoyl Peroxide Gel

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use clindamycin phosphate and benzoyl peroxide gel for a condition for which it was not prescribed. Do not give clindamycin phosphate and benzoyl peroxide 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 clindamycin phosphate and benzoyl peroxide gel that is written for health professionals.

For more information, call 1-866-923-4914.

What are the ingredients in Clindamycin Phosphate and Benzoyl Peroxide 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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