CLINDAMYCIN PHOSPHATE 1.2% AND TRETINOIN 0.025%- clindamycin phosphate and tretinoin gel
Oceanside Pharmaceuticals

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use CLINDAMYCIN PHOSPHATE 1.2% and TRETINOIN 0.025% Gel safely and effectively. See full prescribing information for CLINDAMYCIN PHOSPHATE 1.2% and TRETINOIN 0.025% Gel.

CLINDAMYCIN PHOSPHATE 1.2% and TRETINOIN 0.025% gel

For topical use only
Initial U.S. Approval: 2006

INDICATIONS AND USAGE

Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel is a lincosamide antibiotic and retinoid combination product indicated for the topical treatment of acne vulgaris in patients 12 years or older. (1)

DOSAGE AND ADMINISTRATION

- Apply a pea-sized amount to the entire face once daily at bedtime. Do not apply to eyes, mouth, angles of the nose, or mucous membranes. (2)
- Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel is not for oral, ophthalmic, or intravaginal use. (2)

DOSAGE FORMS AND STRENGTHS

Topical gel: Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel in 30 and 60 gram tubes. (3)

CONTRAINDICATIONS

Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel is contraindicated in patients with regional enteritis, ulcerative colitis, or history of antibiotic-associated 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. Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel should be discontinued if significant diarrhea occurs. (5.1)
- Ultraviolet Light and Environmental Exposures: Avoid exposure to sunlight and sunlamps. Wear sunscreen daily. (5.2)

ADVERSE REACTIONS

Observed local adverse reactions in patients treated with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel were skin erythema, scaling, itching, burning, and stinging. Other most commonly reported adverse events (≥1% in patients treated with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel) were nasopharyngitis, pharyngolaryngeal pain, dry skin, cough, and sinusitis. (6.1)
To report SUSPECTED ADVERSE REACTIONS, contact Oceanside Pharmaceuticals at 1-800-321-4576 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Concomitant use of topical medications with a strong drying effect can increase skin irritation. Use with caution. (7.1)
- Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel should not be used in combination with erythromycin-containing products because of its clindamycin component. (7.2)

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

Revised: 4/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel is indicated for the topical treatment of acne vulgaris in patients 12 years or older.

2 DOSAGE AND ADMINISTRATION

At bedtime, squeeze a pea-sized amount of medication onto one fingertip, dot onto the chin, cheeks, nose, and forehead, then gently rub over the entire face. Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel should be kept away from the eyes, the mouth, angles of the nose, and mucous membranes.

Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel is not for oral, ophthalmic, or intravaginal use.

3 DOSAGE FORMS AND STRENGTHS

Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel, a combination of a lincosamide antibiotic and a retinoid, contains clindamycin phosphate 1.2% and tretinoin 0.025%, formulated as a topical gel. Each gram of Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel contains, as dispensed, 10 mg (1%) clindamycin as phosphate, and 0.25 mg (0.025%) tretinoin in an aqueous-based gel. Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel is available in 30 gram and 60 gram tubes.

4 CONTRAINDICATIONS

Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel is contraindicated in patients with regional enteritis, ulcerative colitis, or history of antibiotic-associated colitis.

5 WARNINGS AND PRECAUTIONS

5.1 Colitis

Systemic absorption of clindamycin has been demonstrated following topical use of this product. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of topical clindamycin. When significant diarrhea occurs, Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel should be discontinued.

Severe colitis has occurred following oral or 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

Exposure to sunlight, including sunlamps, should be avoided during the use of Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel, and patients with sunburn should be advised not to use the product until fully recovered because of heightened susceptibility to sunlight as a result of the use of tretinoin. 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. Daily use of sunscreen products and protective apparel (e.g., a hat) are recommended. Weather extremes, such as wind or cold, also may be irritating to patients under treatment with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

Because clinical trials are conducted under prescribed conditions, adverse reaction rates observed in the clinical trial may not reflect the rates observed in practice. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse reactions that appear to be related to drug use for approximating rates.

The safety data presented in Table 1 (below) reflects exposure to Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel in 1853 patients with acne vulgaris. Patients were 12 years and older and were treated once daily for 12 weeks. Adverse reactions that were reported in ≥1% of patients treated with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel were compared to adverse reactions in patients treated with clindamycin phosphate 1.2% in vehicle gel, tretinoin 0.025% in vehicle gel, and the vehicle gel alone:

Table 1: Adverse Reactions Reported in at Least 1% of Patients Treated with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel: 12-Week Studies

	Clindamycin Phosphate 1.2% and Tretinoin			

	0.025% Gel N=1853 N (%)	Clindamycin N=1428 N (%)	Tretinoin N=846 N (%)	Vehicle N=423 N (%)
PATIENTS WITH AT LEAST ONE AR	497 (27)	342 (24)	225 (27)	91 (22)
Nasopharyngitis	65 (4)	64 (5)	16 (2)	5 (1)
Pharyngolaryngeal pain	29 (2)	18 (1)	5 (1)	7 (2)
Dry skin	23 (1)	7 (1)	3 (<1)	0 (0)
Cough	19 (1)	21 (2)	9 (1)	2 (1)
Sinusitis	19 (1)	19 (1)	15 (2)	4 (1)
NOTE: Formulations used in all treatment arms were in the Clindamycin Phosphate 1.2% and Tretinoin 0.025% vehicle gel.				

Cutaneous safety and tolerance evaluations were conducted at each study visit in all of the clinical trials by assessment of erythema, scaling, itching, burning, and stinging:

Table 2: Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel-Treated Patients with Local Skin Reactions

Local Reaction	Baseline N=1835 N (%)	End of Treatment N=1614 N (%)
Erythema	636 (35)	416 (26)
Scaling	237 (13)	280 (17)
Itching	189 (10)	70 (4)
Burning	38 (2)	56 (4)
Stinging	33 (2)	27 (2)

At each study visit, application site reactions on a scale of 0 (none), 1 (mild), 2 (moderate), and 3 (severe), and the mean scores were calculated for each of the local skin reactions. In Studies 1 and 2, 1277 subjects enrolled with moderate to severe acne, 854 subjects treated with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel and 423 treated with vehicle. Analysis over the 12-week period demonstrated that cutaneous irritation scores for erythema, scaling, itching, burning, and stinging peaked at 2 weeks of therapy, and were slightly higher for the Clindamycin Phosphate 1.2% and Tretinoin 0.025%-treated group, decreasing thereafter.

One open-label 12-month safety study for Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel showed a similar adverse reaction profile as seen in the 12-week studies. Eighteen out of 442 subjects (4%) reported gastrointestinal symptoms.

7 DRUG INTERACTIONS

7.1 Concomitant Topical Medication

Concomitant topical medication, medicated or abrasive soaps and cleansers, soaps and cosmetics that have a strong drying effect, and products with high concentrations of alcohol, astringents, spices or lime should be used with caution. When used with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel, there may be increased skin irritation.

7.2 Erythromycin

Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel should not be used in combination with erythromycin-containing products due to its clindamycin component. In vitro studies have shown

antagonism between these two antimicrobials. The clinical significance of this in vitro antagonism is not known.

7.3 Neuromuscular Blocking Agents

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, Clindamycin Phosphate 1.2% and Tretinoin 0.025% 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 well-controlled trials in pregnant women treated with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel. Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel was tested for maternal and developmental toxicity in New Zealand White Rabbits with topical doses of 60, 180 and 600 mg/kg/day. Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel at 600 mg/kg/day (approximately 12 times the recommended clinical dose assuming 100% absorption and based on body surface area comparison) was considered to be the no-observed-adverse-effect level (NOAEL) for maternal and developmental toxicity following dermal administration of Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel for 2 weeks prior to artificial insemination and continuing until gestation day 18, inclusive. For purposes of comparisons of the animal exposure to human exposure, the recommended clinical dose is defined as 1 g of Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel applied daily to a 60 kg person.

Clindamycin

Teratology (Segment II) studies using clindamycin were performed orally in rats (up to 600 mg/kg/day) and mice (up to 100 mg/kg/day) (583 and 49 times amount of clindamycin in the recommended clinical dose based on body surface area comparison, respectively) or with subcutaneous doses of clindamycin up to 180 mg/kg/day (175 and 88 times the amount of clindamycin in the recommended clinical dose based on body surface area comparison, respectively) revealed no evidence of teratogenicity.

Tretinoin

In oral Segment III studies in rats with tretinoin, decreased survival of neonates and growth retardation were observed at doses in excess of 2 mg/kg/day (~78 times the recommended clinical dose assuming 100% absorption and based on body surface area comparison).

With widespread use of any drug, a small number of birth defect reports associated temporally with the administration of the drug would be expected by chance alone. Thirty cases of temporally associated congenital malformations have been reported during two decades of clinical use of another formulation of topical tretinoin. Although no definite pattern of teratogenicity and no causal association have been established from these cases, five of the reports describe the rare birth defect category, holoprosencephaly (defects associated with incomplete midline development of the forebrain). The significance of these spontaneous reports in terms of risk to the fetus is not known.

Dermal tretinoin has been shown to be fetotoxic in rabbits when administered in doses 40 times the recommended human clinical dose based on body surface area comparison. Oral tretinoin has been shown to be fetotoxic in rats when administered in doses 78 times the recommended clinical dose based on body surface area comparison.

8.3 Nursing Mothers

It is not known whether clindamycin is excreted in human milk following use of Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel. 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. It is not known whether tretinoin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness of Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel in pediatric patients under the age of 12 have not been established.

Clinical trials of Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel included patients 12-17 years of age. *[See Clinical Studies (14).]*

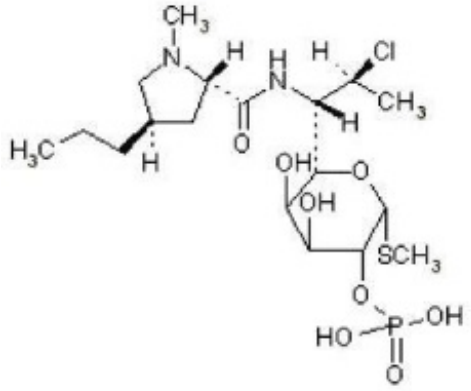
8.5 Geriatric Use

Clinical studies of Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

11 DESCRIPTION

Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel is an antibiotic and retinoid combination gel product with two active ingredients. 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.

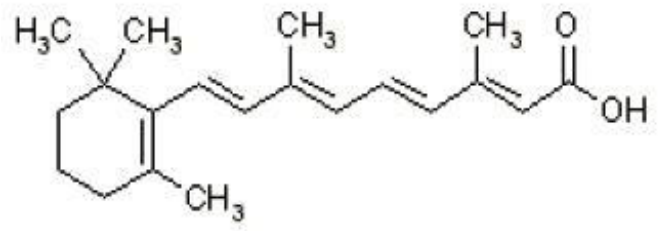
The chemical name for clindamycin phosphate is Methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-*trans*-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-*threo*-α-D-*galacto*-octopyranoside 2-(dihydrogen phosphate). The structural formula for clindamycin phosphate is represented below:



Clindamycin phosphate:
Molecular Formula: $C_{18}H_{34}ClN_2O_8PS$ Molecular Weight: 504.97

The chemical name for tretinoin is 3,7-Dimethyl-9-(2,6,6-trimethyl-1-cyclohexen-1-yl)-2,4,6,8 nonatetraenoic acid (all-*trans* form). The structural formula for tretinoin is represented below:

Tretinoin:



Molecular Formula: $C_{20}H_{28}O_2$ Molecular Weight: 300.44

Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel contains the following inactive ingredients: butylated hydroxytoluene NF, carbomer 981 NF, citric acid USP, edetate disodium USP, glycerin USP, methylparaben NF, polysorbate 80 NF, propylparaben NF, purified water USP and tromethamine USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Clindamycin

[See Microbiology (12.4).]

Tretinoin

Although the exact mode of action of tretinoin is unknown, current evidence suggests that topical tretinoin decreases cohesiveness of follicular epithelial cells with decreased microcomedo formation.

Additionally, tretinoin stimulates mitotic activity and increased turnover of follicular epithelial cells causing extrusion of the comedones.

12.3 Pharmacokinetics

In an open-label, multiple-dose study treating 12 subjects with moderate to severe acne, the percutaneous absorption of tretinoin following 14 consecutive daily applications of approximately 4 g of Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel was minimal. Quantifiable tretinoin plasma concentrations ranged from 1.0 to 1.6 ng/mL, with unquantifiable plasma concentrations in 50% to 92% of subjects at any given timepoint following administration. The plasma concentrations of the key tretinoin metabolites, 13-cis-retinoic acid and 4-oxo-13-cis-retinoic acid, ranged from 1.0 to 1.4 ng/mL and from 1.6 to 6.5 ng/mL, respectively. Plasma concentrations for clindamycin generally did not exceed 3.5 ng/mL, with the exception of one subject whose plasma concentration reached 13.1 ng/mL.

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 bacterial protein synthesis. Clindamycin has 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 activity against *P. acnes* was not examined in clinical trials with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel. *P. acnes* resistance to clindamycin has been documented. Resistance to clindamycin is often associated with resistance to erythromycin.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity, mutagenicity and impairment of fertility testing of Clindamycin Phosphate 1.2% and

Tretinoin 0.025% Gel have not been performed in any species.

Clindamycin

The carcinogenicity of a 1% clindamycin phosphate gel similar to Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel was evaluated by daily application to mice for 2 years. The daily doses used in this study were approximately 13 and 72 times higher than the human dose of clindamycin phosphate from Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel, assuming complete absorption and based on body surface area comparison. No significant increase in tumors was noted in the treated animals. For purposes of comparisons of the animal exposure to human exposure, the recommended human topical clinical dose is defined as 1 g of Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel applied daily to a 60 kg person.

Fertility (Segment 1) studies in rats treated orally with up to 300 mg/kg/day of clindamycin (approximately 290 times the amount of clindamycin delivered from the recommended clinical dose for Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel, based on body surface area comparison) revealed no effects on fertility or mating ability.

Tretinoin

In two independent studies with long-term topical application of tretinoin in mice, carcinogenicity was not observed. In both studies, tretinoin was administered topically (0.025% or 0.1%) three times per week for up to 2 years. No carcinogenicity was observed with maximum effects of dermal amyloidosis in the basal layer of the skin.

Tretinoin has been shown to enhance photo co-carcinogenicity in properly performed specific studies, employing concurrent or intercurrent exposure to the drug and UV radiation. The contribution of clindamycin to that effect is unknown. Although the significance of these studies to humans is not clear, patients should minimize exposure to sun.

The genotoxic potential of tretinoin was evaluated in an in vitro Ames Salmonella reversion test and an in vitro chromosomal aberration assay in Chinese hamster ovary cells. Both tests were negative.

In oral Segment 1 studies in rats treated with tretinoin, the no-observed-effect-level was 2 mg/kg/day (~78 times the recommended clinical dose assuming 100% absorption and based on body surface area comparison).

14 CLINICAL STUDIES

The safety and efficacy of once daily use of Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel for treatment of acne vulgaris were assessed in three 12-week prospective, multi-center, randomized, blinded studies in patients 12 years and older. Studies 1 and 2 were of identical design, and compared Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel to clindamycin in the vehicle gel, tretinoin in the vehicle gel, and the vehicle gel alone. Patients with mild, moderate, or severe acne were enrolled in the studies. The co-primary efficacy variables were:

(1) Mean percent change from baseline at Week 12 in

- inflammatory lesion counts,
- non-inflammatory lesion counts, and
- total lesion counts

(2) Percent of subjects who cleared or almost cleared at Week 12 as judged by an Evaluator’s Global Severity (EGS) score.

The EGS scoring scale used in all of the clinical trials for Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel is as follows:

Grade	Description
Clear	Normal, clear skin with no evidence of acne vulgaris
Almost Clear	Rare non-inflammatory lesions present, with rare non-inflamed papules (papules must be resolving and may be hyperpigmented, though not pink-red)
Mild	Some non-inflammatory lesions are present, with few inflammatory lesions (papules/pustules only; no nodulocystic lesions)
Moderate	Non-inflammatory lesions predominate, with multiple inflammatory lesions evident: several to many comedones and papules/pustules, and there may or may not be one small nodulo-cystic lesion
Severe	Inflammatory lesions are more apparent, many comedones and papules/pustules, there may or may not be a few nodulocystic lesions
Very Severe	Highly inflammatory lesions predominate, variable number of comedones, many papules/pustules and many nodulocystic lesions

In Study 1, a total of 1252 patients were enrolled, and in Study 2, a total of 1288 patients were enrolled. The combined results are presented in Table 3.

Table 3: Efficacy Results at Week 12 in Studies 1 and 2

	Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel N=845	Clindamycin N=426	Tretinoin N=846	Vehicle N=423
Evaluator's Global Severity: N (%)				
Patients achieving success*	180 (21%)	70 (16%)	122 (14%)	34 (8%)
Inflammatory Lesion Count (% reduction from baseline)				
Mean	48%	42%	39%	26%
Non-inflammatory Lesion Count (% reduction from baseline)				
Mean	36%	27%	31%	16%
Total Lesion Count (% reduction from baseline)				
Mean	41%	34%	34%	20%

* Success was defined as cleared or almost cleared at Week 12.

In Study 3, Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel was compared to clindamycin gel in a total of 2010 patients with moderate or severe acne vulgaris (see Table 3). As with Studies 1 and 2, the co-primary endpoints were mean percent reduction in lesion counts (inflammatory, non-inflammatory and total) and the EGS score. In Study 3, success on the EGS score was assessed by the percentage of subjects who had at least 2 grades of improvement from Baseline to Week 12.

Table 4: Efficacy Results at Week 12 in Study 3

	Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel N=1008	Clindamycin N=1002
Evaluator's Global Severity: N (%)		
Patients achieving success*	415 (41%)	345 (34%)
Inflammatory Lesion Count (% reduction from baseline)		
Mean	61%	55%
Non-inflammatory Lesion Count (% reduction from baseline)		
Mean	50%	41%
Total Lesion Count (% reduction from baseline)		
Mean	54%	47%

* Success was defined as at least a 2-grade improvement at Week 12 from baseline.

16 HOW SUPPLIED/STORAGE AND HANDLING

Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel is supplied as follows:

30 gram tube NDC 68682-300-30
60 gram tube NDC 68682-300-60

Storage and Handling

- Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].
- Protect from light.
- Protect from freezing.
- Keep out of the 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).

Instructions for Use

- At bedtime, the face should be gently washed with a mild soap and warm water. After patting the skin dry, apply Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel as a thin layer over the entire face (excluding the eyes and lips).
- Patients should be advised not to use more than the recommended pea-sized amount and not to apply more often than once daily (at bedtime) as this will not make for faster results and may increase irritation.
- A sunscreen should be applied every morning and reapplied over the course of the day as needed. Patients should be advised to avoid exposure to sunlight, sunlamp, ultraviolet light, and other medicines that may increase sensitivity to sunlight.

Skin Irritation

Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel may cause irritation such as erythema, scaling, itching, burning, or stinging.

Colitis

In the event a patient treated with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel experiences severe diarrhea or gastrointestinal discomfort, Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel should be discontinued and a physician should be contacted.

Distributed by:
Oceanside Pharmaceuticals, a division of
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Bridgewater, NJ 08807 USA

Manufactured by:
Bausch Health Companies Inc.
Laval, Quebec H7L 4A8, Canada

9704800

PATIENT INFORMATION
Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel

IMPORTANT: Not for mouth, eye, or vaginal use.

Read the Patient Information that comes with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel 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 acne or treatment.

What is Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel?

Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel is an antibiotic and retinoid combination medicine used for the skin treatment of acne in patients 12 years and older.

Who should not use Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel?

Do not use Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel if you:

- have Crohn's Disease
- have Ulcerative Colitis
- have developed colitis with past antibiotic use

Tell your doctor:

- **if you are pregnant or planning to become pregnant.** It is not known if Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel may harm your unborn baby.
- **if you are breastfeeding.** Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel may pass through your milk and may harm your baby.
- **about all the medicines and skin products you use:**
    - Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel should not be used with erythromycin-containing products.
    - Avoid medicated or abrasive soaps and cleansers, soaps and cosmetics that have a strong drying effect, and skin products that contain alcohol, astringents, spices or lime. These products may cause increased skin irritation if used with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel.

How should I use Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel?

Use Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel exactly as prescribed. It may take some time for you to see improvement of your acne with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel. Your doctor will tell you how long to use Clindamycin Phosphate 1.2% and Tretinoin

0.025% Gel.

At bedtime:

- Wash your face gently with a mild soap and warm water.
- Pat the skin dry.
- Apply a pea-size amount of Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel to your fingertip and spread it over your face. Gently, smooth it into your skin. **Do not get Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel in your eyes or mouth, on your lips, on the corners of your nose, or on open wounds.**

In the morning:

- Apply a sunscreen and reapply during the day as needed.
- **Do not** apply Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel more than once a day.
- **Do not** use too much Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel. Too much Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel may irritate your skin.
- **Do not** wash your face more than 2 to 3 times a day. Washing your face too often or scrubbing it may make your acne worse.

Avoid:

- **excessive exposure to the sun, cold, and wind.** Weather extremes can dry and burn the skin. Always use a sunscreen on Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel treated skin, even on cloudy days. Use other protective clothing such as a hat when you are in the sun.
- **the use of sunlamps and tanning booths.**

If your face becomes sunburned, stop Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel until your skin has healed.

What are possible side effects with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel?

- **Skin irritation.** Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel may cause skin irritation such as dryness, redness, peeling, burning, or stinging. **Stop Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel and call your doctor if your skin becomes very red, swollen, blistered, or crusted.**
- **Change in skin color.** Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel may cause a temporary skin color change (lighter or darker).
- **Colitis.** This occurs rarely.Stop Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel and call your doctor if you develop severe watery diarrhea, or bloody diarrhea.

Talk to your doctor about any side effect that bothers you or that does not go away.

These are not all the side effects with Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel. Ask your doctor or pharmacist for more information.

How should I store Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel?

- **Store Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel at room temperature, 59° to 86°F (15° to 30°C). Do not freeze.**
- **Keep Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel away from heat and light.**
- **Keep the tube tightly closed.**
- **Keep Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel and all medicines out of reach**

of children.

General information about Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel

Medicines are sometimes prescribed for purposes other than those listed in patient information leaflet. Do not use Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel for a condition for which it was not prescribed. **Do not give Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel to other people, even if they have the same symptoms you have. It may harm them.**

This leaflet summarizes the most important information about Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel. If you would like more information, talk with your doctor. You can also ask your pharmacist or doctor for information about Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel that is written for healthcare professionals.

If you have questions about Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel you can also call: 1-800-321-4576 (this is a toll-free number) between 10:00 a.m. and 4:00 p.m. Eastern Time, Monday through Friday.

What are the ingredients in Clindamycin Phosphate 1.2% and Tretinoin 0.025% Gel?

Active Ingredients: clindamycin phosphate 1.2% and tretinoin 0.025%

Inactive Ingredients: butylated hydroxytoluene NF, carbomer 981 NF, citric acid USP, edetate disodium USP, glycerin USP, methylparaben NF, polysorbate 80 NF, propylparaben NF, purified water USP and tromethamine USP.

Distributed by:
Oceanside Pharmaceuticals, a division of
Bausch Health US, LLC
Bridgewater, NJ 08807 USA

Manufactured by:
Bausch Health Companies Inc.
Laval, Quebec H7L 4A8, Canada

9704800
Revised: 04/2020

PRINCIPAL DISPLAY PANEL - 60 g Carton

NDC 68682-300-60

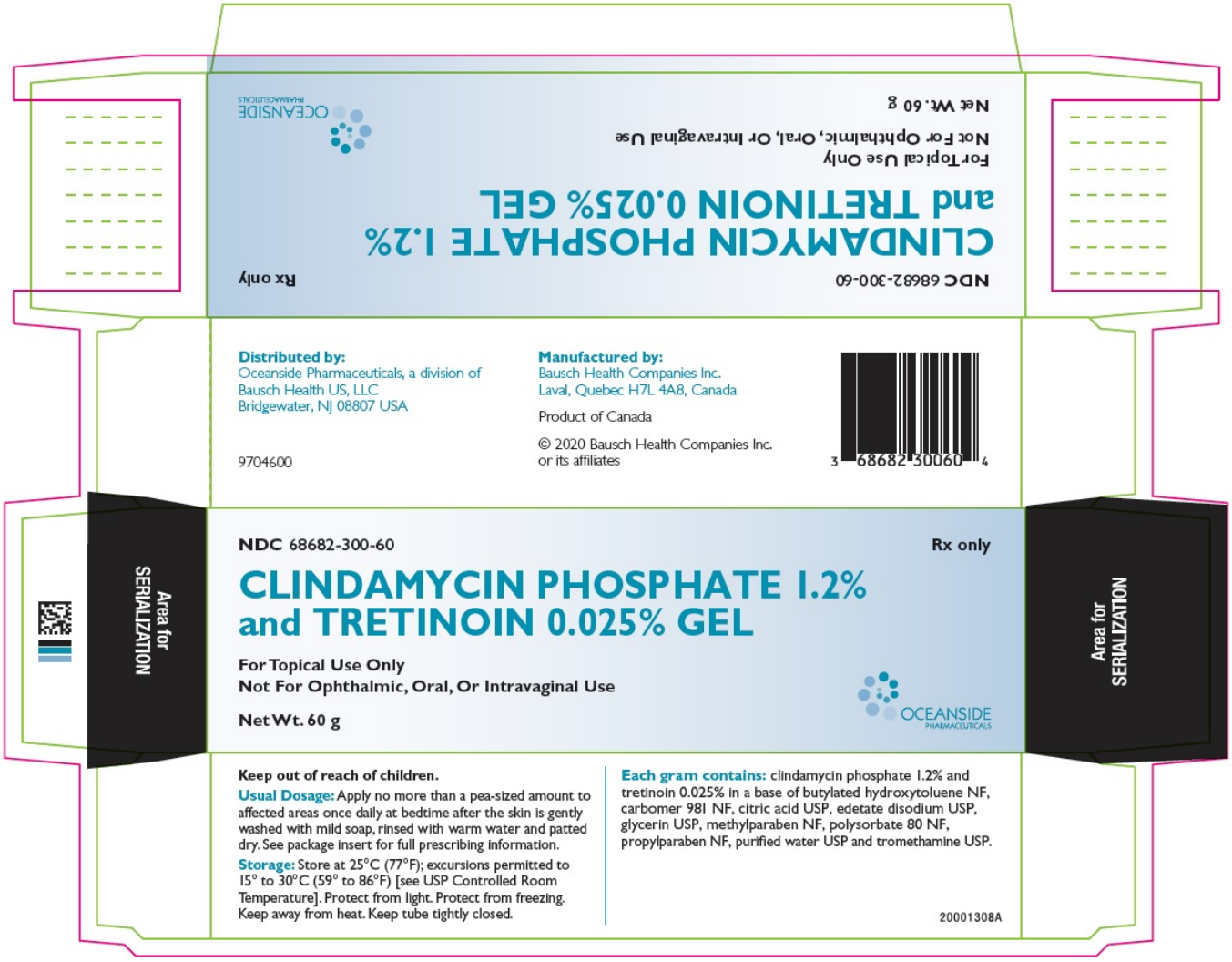
Rx only

**CLINDAMYCIN PHOSPHATE 1.2%
and TRETINOIN 0.025% GEL**

**For Topical Use Only
Not For Ophthalmic, Oral, Or Intravaginal Use**

Net Wt. 60 g

**OCEANSIDE
PHARMACEUTICALS**



CLINDAMYCIN PHOSPHATE 1.2% AND TRETINOIN 0.025%

clindamycin phosphate and tretinoin gel

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:68682-300
Route of Administration	TOPICAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
clindamycin phosphate (UNII: EH6D7113I8) (clindamycin - UNII:3U02EL437C)	clindamycin	12 mg in 1 g
tretinoin (UNII: 5688UTC01R) (tretinoin - UNII:5688UTC01R)	tretinoin	0.25 mg in 1 g

Inactive Ingredients	
Ingredient Name	**Strength**
water (UNII: 059QF0KO0R)	
glycerin (UNII: PDC6A3C0OX)	
CARBOMER HOMOPOLYMER TYPE A (ALLYL PENTAERYTHRITOL CROSSLINKED) (UNII: F68VH75CJC)	

methylparaben (UNII: A2I8C7HI9T)	
polysorbate 80 (UNII: 6OZP39ZG8H)	
edetate disodium (UNII: 7FLD91C86K)	
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	
propylparaben (UNII: Z8IX2SC1OH)	
butylated hydroxytoluene (UNII: 1P9D0Z171K)	
tromethamine (UNII: 023C2WHX2V)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:68682-300-30	1 in 1 CARTON	08/04/2020	
1		30 g in 1 TUBE; Type 0: Not a Combination Product		
2	NDC:68682-300-60	1 in 1 CARTON	08/04/2020	
2		60 g in 1 TUBE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA authorized generic	NDA050802	08/04/2020	

Labeler - Oceanside Pharmaceuticals (832011691)

Establishment

Name	Address	ID/FEI	Business Operations
Contract Pharmaceuticals Limited Canada		248761249	MANUFACTURE(68682-300) , PACK(68682-300)

Establishment

Name	Address	ID/FEI	Business Operations
DPT Laboratories, Ltd.		832224526	MANUFACTURE(68682-300) , PACK(68682-300)

Establishment

Name	Address	ID/FEI	Business Operations
Bausch Health Companies Inc.		245141858	MANUFACTURE(68682-300) , PACK(68682-300)

Revised: 4/2020 Oceanside Pharmaceuticals