PRODUCT MONOGRAPH

PrCLINDASOL®

clindamycin, octinoxate and avobenzone cream, 1%/7.5%/2% w/w
(clindamycin as clindamycin phosphate)

TOPICAL CREAM WITH SUNSCREENS

ACNE THERAPY

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THERAPEUTIC CLASSIFICATION

ACNE THERAPY

ACTION AND CLINICAL PHARMACOLOGY

CLINDASOL® Cream contains clindamycin 1% w/w (clindamycin as clindamycin phosphate USP), 7.5% w/w octinoxate and 2% w/w avobenzone cream.

Clindamycin phosphate is a water soluble ester from which the phosphate radical must be cleaved before it possesses antibiotic activity. *In vivo* clindamycin phosphate is hydrolysed into active clindamycin probably by the action of phosphatases contained in the skin.

Clindamycin is an inhibitor of protein synthesis which exerts its action at the ribosomal level. The primary effect is inhibition of initiation of the peptide chain synthesis by binding to the 50S subunit of ribosomes and blocking the access of transfer RNA to the bacterial ribosomal/messenger RNA complex. Susceptible micro organisms are thus unable to synthesize essential proteins.

Clindamycin has been shown to have *in vivo* activity against isolates of *Propionibacterium acnes*. This may account for its usefulness in the treatment of acne vulgaris. Cross-resistance has been demonstrated between clindamycin and lincomycin and between clindamycin and erythromycin. Studies have shown that a significantly greater reduction in the number of inflammatory lesions occurred in patients treated with topical clindamycin phosphate 1% compared to patients treated with the vehicle. The mean free clindamycin content of comedones extracted from subjects who used topical 1% clindamycin phosphate solution for a period of four weeks was 0.6 µg/mg.

Clindamycin is metabolized in the liver to both bio-active and inactive metabolites which are excreted in the urine. About 10% of active clindamycin is excreted unaltered in the urine and only small quantities are found in the faeces. The

clindamycin phosphate ester is virtually undetectable in serum one hour after intravenous administration but can still be detected three hours following intramuscular dosage. The half life of clindamycin phosphate is between 1.5 and 2 hours.

The sunscreens octinoxate, 7.5% w/w and avobenzone, 2% w/w may provide limited sun protection when CLINDASOL® is used as directed.

INDICATIONS AND CLINICAL USE

CLINDASOL® topical cream with sunscreens is indicated in the treatment of acne vulgaris.

CONTRAINDICATIONS

CLINDASOL® topical cream with sunscreens is contraindicated in persons who have shown hypersensitivity to clindamycin especially its phosphate ester, lincomycin, octinoxate, avobenzone or to any of the ingredients contained in CLINDASOL®.

CLINDASOL® is also contraindicated in patients with or with a history of previous regional enteritis, ulcerative colitis, spastic colitis or antibiotic-associated colitis (including pseudomembranous colitis).

WARNINGS

Skin

CLINDASOL® topical cream with sunscreens is known to be a mild irritant in humans and animals and is intended for external use only. Contact with the mouth, eyes, lips, other mucous membranes or areas of broken skin should be avoided. In the event of sensitization or severe local irritation from CLINDASOL® topical cream, usage should be discontinued immediately, the cream carefully washed off, and appropriate therapy initiated.

Clostridium Difficile-Associated Disease (CDAD)

Use of topical formulation of clindamycin results in absorption of clindamycin from the skin surface. *Clostridium difficile*-associated disease (CDAD), including pseudomembranous colitis has been reported with the use of topical, oral and parenteral administration of clindamycin (see ADVERSE REACTIONS). CDAD may range in severity from mild diarrhea to fatal colitis. It is important to consider this diagnosis in patients who present with diarrhea, or symptoms of colitis, pseudomembranous colitis, toxic mega colon, or perforation of colon subsequent to the administration of any antibacterial agent. CDAD has been reported to occur 2 months after the administration of antibacterial agents.

Treatment with antibacterial agents may alter the normal flora of the colon and may permit overgrowth of *Clostridium difficile*. *Clostridium difficile* produces toxins A and B, which contribute to the development of CDAD. CDAD may cause significant morbidity and mortality.

If the diagnosis of CDAD is suspected or confirmed, appropriate therapeutic measures should be initiated. Mild cases of CDAD usually respond to discontinuation of antibacterial agents not directed against *Clostridium difficile*. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial agent clinically effective against *Clostridium difficile*. Surgical evaluation should be instituted as clinically indicated, as surgical intervention may be required in certain severe cases.

PRECAUTIONS

The use of preparations containing antibiotics such as CLINDASOL® topical cream with sunscreens may be associated with overgrowth of antibiotic resistant microorganisms including those initially sensitive to the drug. The treatment of acne with topical antibiotics is associated with the development of antimicrobial resistance in *Propionibacterium acnes* as well as other bacteria (e.g. *Staphylococcus aureus, Streptococcus pyogenes*). The use of clindamycin may result in developing inducible resistance in these organisms. If this occurs, therapy should be discontinued and alternative acne therapy should be initiated. Resistance to clindamycin is often associated with resistance to erythromycin. It is therefore advisable to avoid concurrent use of the two agents either by topical or oral treatment.

Concomitant topical acne therapy 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, clindamycin should be discontinued.

Application of CLINDASOL® to affected areas may provide limited sun protection on treated areas for a limited time only. Patients should be instructed to use a broad spectrum sunscreen with an SPF of at least 15 on all areas of the skin that will be exposed to sunlight.

Use in pregnancy: The safety of CLINDASOL® during pregnancy has not been established. No adequate and well-controlled data in pregnant women treated with % topical clindamycin 1% (clindamycin as clindamycin phosphate USP) are available. Systemic absorption of clindamycin following topical application of clindamycin phosphate is less than 5%. Clindamycin readily crosses the placental barrier. It is not known whether CLINDASOL® Topical Cream can

cause fetal harm if administered to pregnant women or can affect reproductive potential. CLINDASOL® Topical Cream should not be administered to a pregnant woman unless the potential benefits to the mother clearly outweigh the possible risk to the fetus.

Subcutaneous administration of clindamycin phosphate at 100 and 180 mg/kg/day in Sprague-Dawley rats had no teratogenic effects (see TOXICOLOGY).

Use in nursing mothers: The safety of CLINDASOL® in nursing women has not been established. No adequate and well-controlled data in nursing women treated with topical clindamycin 1% (clindamycin as clindamycin phosphate USP) are available. It is not known whether clindamycin is excreted in human milk following topical use of CLINDASOL® topical cream. Orally and parenterally administered clindamycin is excreted 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 CLINDASOL® topical cream therapy to the mother. If used during lactation, clindamycin should not be applied to the breast area to avoid accidental ingestion by the infant.

Pediatric Use: Safety and effectiveness of topical clindamycin phosphate in the pediatric population under the age of 12 have not been established.

Drug Interactions
Clindamycin and erythromycin have been shown to be antagonistic *in vitro*.

Systemic clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, clindamycin should be used with caution in patients receiving such agents.

ADVERSE REACTIONS

Clinical Trial Adverse Drug Reactions
The safety was assessed in patients receiving twice daily administration of CLINDASOL®, or placebo cream with sunscreen, or an active comparator (topical clindamycin phosphate solution; equivalent to 1% clindamycin) over a period of 12 weeks. The data from N=276 acne vulgaris patients was collected from one placebo-controlled and one active-controlled studies. The most common drug-related adverse reactions reported by ≥ 1% of patients from these two studies are provided in Table 1.

Table 1: Most common drug-related adverse reactions reported by ≥ 1% of patients

Adverse Drug Reactions		Clindasol$^{\phi}$ n/N (%)			Placebo n/N (%)			Active comparator n/N (%)		
		4 wk	8 wk	12 wk	4 wk	8 wk	12 wk	4 wk	8 wk	12 wk
General disorders and administrative site conditions	Burning or Itching	17/134 (12.7)	17/119 (14.3)	10/114 (8.8)	9/62 (14.5)	5/58 (8.6)	3/57 (5.3)	13/68 (19.1)	12/62 (19.4)	8/62 (12.9)
	Peeling or Dryness	23/134 (17.2)	19/119 (16.0)	13/114 (11.4)	7/62 (11.3)	9/58 (15.5)	10/57 (17.5)	18/68 (26.5)	18/62 (29.0)	11/62 (17.7)
	Oiliness	64/134 (47.8)	44/119 (37.0)	28/114 (24.6)	16/62 (25.8)	14/58 (24.1)	10/57 (17.5)	29/68 (42.6)	25/62 (40.3)	21/62 (33.9)
	Erythema	24/134 (17.9)	14/119 (11.8)	12/114 (10.5)	4/62 (6.4)	3/58 (5.2)	3/57 (5.3)	17/68 (25.0)	18/62 (29.0)	12/62 (19.4)
	Stinging	1/63 (1.6)	1/54 (1.9)	2/114 (1.7)	---	---	---	---	---	---
	Small red bumps	2/63* (3.2)	---	1/51 (2.0)	---	---	---	---	---	---
Immune system disorders	Urticaria	---	1/65 (1.5)	---	---	---	---	---	---	---
	Whealing	---	---	---	---	---	---	---	1/62 (1.6)	1/62 (1.6)
	Swollen lips	---	---	---	---	---	---	1/68 (1.5)	---	---
Gastrointestinal disorders	Diarrhea	3/134 (2.2)	---	---	1/62 (1.6)	---	---	---	1/62** (1.6)	---
	Abdominal Cramping	2/63 (3.2)	---	1/51 (2.0)	---	---	---	---	---	---

*Includes report of bumpiness and pustules; pustules identified as containing gram negative folliculitis
**Reported by one patient as "loose stools" between weeks 2 and 9 of the treatment
$^{\phi}$ CLINDASOL® arm represents adverse drug reactions combined from two clinical studies (placebo-controlled SCI-90-02, and active-controlled SCI-94-02); therefore, the total number of patients (N) differs from control arms.

Additional adverse drug reactions reported in clindamycin phosphate clinical trials

The following additional common adverse drug reactions (≥ 1%) have been reported in clinical trials involving other clindamycin phosphate formulations:

Skin and subcutaneous disorders: rash

Nervous system disorders: headache

Gastrointestinal disorders: nausea

Post-Market Adverse Drug Reactions

Gastrointestinal disorders: bloody diarrhea, colitis (including pseudomembranous colitis) (See WARNINGS – CDAD).

SYMPTOMS AND TREATMENT OF OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Symptoms:

Topically applied clindamycin phosphate from CLINDASOL® topical cream can be absorbed in sufficient amounts to cause systemic gastrointestinal side effects including abdominal pain, nausea, vomiting and diarrhea. In the case of excessive application or accidental ingestion of CLINDASOL® topical cream, the use of the cream should be discontinued for several days before resuming therapy (see WARNINGS).

Treatment:

No specific antidote is available. In the case of excessive application or accidental ingestion of CLINDASOL® topical cream the application site should be washed off with lukewarm water and the use of the cream should be discontinued for several days before resuming therapy (see WARNINGS).

DOSAGE AND ADMINISTRATION

CLINDASOL® (clindamycin as clindamycin phosphate USP) cream with sunscreens should be applied twice daily to areas affected by acne. These areas should be washed first with a mild soap, rinsed well, and patted dry. The cream should then be applied using fingertips in a gentle rubbing motion. Hands

should be washed thoroughly after application. CLINDASOL® topical cream is not for oral, ophthalmic, or intravaginal use. Care should be taken to avoid eyes, nostrils, mouth, other mucous membranes or areas of broken skin.

CLINDASOL® contains sunscreens and may provide limited sun protection for a limited time (see PRECAUTIONS). The method of application to affected areas only may not lead to a full sun protection. Patients should be instructed to use a broad spectrum sunscreen with an SPF of at least 15 on all areas of the skin that will be exposed to sunlight.

If there has been no improvement after 6 to 8 weeks, or if the condition becomes worse, treatment should be discontinued.

Due to increased risk of antimicrobial resistance, the benefit of continuing treatment beyond 12 weeks should be evaluated.

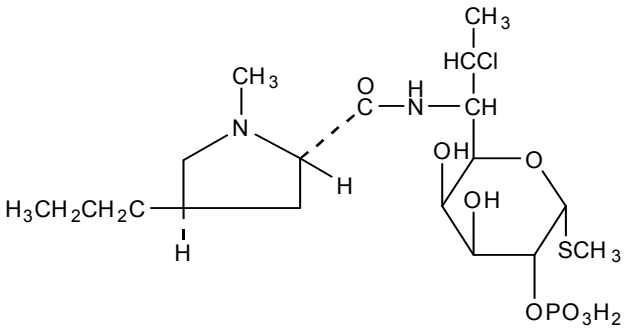
PHARMACEUTICAL INFORMATION

DRUG SUBSTANCE

Proper Name: Clindamycin phosphate

Chemical Name: 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)

Structural Formula:



Molecular Formula: $C_{18}H_{34}ClN_2O_8PS$ **Molecular Weight:** 504.96

Description: Clindamycin is a white to off-white, odourless or almost odourless, hygroscopic, crystalline powder with a bitter taste, soluble in water (1 in 2.5); slightly soluble in dehydrated alcohol and very slightly soluble in acetone. 1.2 g of clindamycin phosphate is approximately equivalent to 1 g of clindamycin base.

COMPOSITION: CLINDASOL® cream contains 1% w/w clindamycin (clindamycin as clindamycin phosphate USP) in a cream base with 7.5% octinoxate and 2% avobenzone . It also contains elefac I-205, glycerin, diisopropyl adipate, stearyl alcohol, sorbitan monostearate, D.C. fluid Nos. 556 and 344, light mineral oil, polysorbate 60, carbomer 934, germaben II, sodium hydroxide as pH adjustor and purified water.

STORAGE: Store CLINDASOL® between 15°- 30°C. Do not freeze.

AVAILABILITY OF DOSAGE FORMS

CLINDASOL®: 25 g tubes containing clindamycin 1% w/w (clindamycin as clindamycin phosphate USP) and sunscreens in an oil-in-water emulsion with Germaben II as a preservative.

INFORMATION FOR THE PATIENT

Your physician has prescribed CLINDASOL® topical cream with sunscreens to treat your acne. It is important to read and follow the directions below:

When it should not be used:

1. You should not use CLINDASOL® if you have hypersensitivity to clindamycin phosphate, lincomycin, octinoxate, avobenzone or to any of the ingredients contained in CLINDASOL®.
2. You should also not use CLINDASOL® if you have a history of regional enteritis, ulcerative colitis, spastic colitis or antibiotic-associated colitis (including pseudomembranous colitis).

Directions for use:

1. Wash the affected areas with a mild soap (not medicated), rinse well and pat dry.
2. With your fingertips, apply a thin film of CLINDASOL® to the areas affected by acne. Gently spread the medication and rub in slightly, carefully avoiding the eyes, mouth, nostrils, other mucous membranes or areas of broken skin.
3. Do not use any other acne medications unless your physician instructs you to do so.
4. Wash your hands thoroughly after using the medication.
5. Apply the medication in the morning and at night or as directed by your physician.
6. CLINDASOL® contains sunscreens and may provide limited sun protection for a limited time. To obtain complete sunscreen protection, use a broad spectrum sunscreen with a sun protection factor (SPF) of at least 15 on all areas of the skin that will be exposed to sunlight.

Precautions:

1. Keep your medication in a safe place, out of the reach of children.
2. CLINDASOL® is for external use only.
3. Keep CLINDASOL® away from your eyes, nostrils, mouth, other mucous membranes or areas of broken skin.
4. Do not use any other acne medications unless your physician instructs you to do so.

5. Avoid contact with eyes. If contact occurs, flush eyes with copious amounts of water for at least five minutes. If discomfort persists, consult your physician.
6. Tell your physician if you are pregnant or breastfeeding a baby. If you are pregnant or breastfeeding, your physician may decide not to prescribe this medicine, although, there may be circumstances when your physician advises you differently.
7. Do not use CLINDASOL® if you have had a reaction to clindamycin or the sunscreens contained in this product. CLINDASOL® contains the following sunscreens: avobenzone and octinoxate.

If you have a problem:

1. Immediately inform your physician if you develop any of the following very rare side effects:
   - abdominal or stomach cramps, severe pain or bloating
   - severe watery or prolonged diarrhea which may be bloody
   - nausea or vomiting
2. If you experience excessive peeling, burning, oily skin, redness, tenderness, drying, itching or irritation, discontinue use and consult your physician for advice.
3. Do not expect to see immediate improvement of your acne. Be patient and apply your medication as your physician has directed.
4. Do not use CLINDASOL® for more than 12 weeks. If there has been no improvement after 6 to 8 weeks, or if the condition becomes worse, discontinue treatment and contact your physician.

REMEMBER: CLINDASOL® has been prescribed by your physician for you; do not allow other people to use it.

MICROBIOLOGY

Clindamycin is active against anaerobic Gram-positive bacilli such as *Corynebacteria* but resistant subspecies of *Clostridium* may occur. Aerobic Gram-negative bacteria are nearly all resistant to clindamycin.

The *in vitro* susceptibility of *P. acnes* and related species to clindamycin is shown in the following table:

Species	No. of strains	Cumulative % of strains inhibited at MICs (mg/L)				
		<0.02	**0.04**	**0.1**	**0.2**	**0.4**
P. acnes	38	--	34	87	95	100
P. granulosum	15	7	87	93	100	--
C. avidum	16	--	56	69	81	100
C. minutissimum	3	--	--	--	100	--
C. parvum	1	--	--	--	100	--

During clinical use of topical erythromycin, strains of *P. acnes* resistant to erythromycin have been recovered in about 20% of subjects. The resistant organisms recovered were also resistant to clindamycin.

PHARMACOLOGY

HUMAN STUDIES

Topical clindamycin phosphate seems less prone to be systemically absorbed than clindamycin hydrochloride. It was found that less than 1% of a 20 mg-dose (1 mL b.i.d.; 0.25 mg/kg/day) of clindamycin phosphate was absorbed, with a peak serum level of only 1.7 ng/mL.

Bioassay on urine samples from patients who used topical 1% clindamycin phosphate b.i.d. for eight weeks did not detect the presence of clindamycin phosphate in the urine. If systemic absorption of clindamycin occurred, the amount excreted in urine was below the bioassay detectable limits of 0.25 mg/mL.

Skin surface counts of *Propionibacterium acnes* in human volunteers who used topical 1% clindamycin phosphate solution for eleven days show that clindamycin phosphate significantly reduces *P. acnes* count; the mean log reduction from baseline to day eleven was 0.70 (81%). Concurrent measurement of free fatty acid levels did not show significant changes over time.

After four weeks of therapy with topical 1% clindamycin phosphate solution, comedones from 18 out of 20 treated subjects contained free clindamycin. The mean clindamycin content was 0.60 µg/mg.

In patients receiving b.i.d. application of a 1% clindamycin phosphate solution for eight weeks, 60% of the staphylococcal and enterococcal isolates became resistant to clindamycin during therapy (MIC > 4 mg/L). All *propionibacteria* were sensitive to clindamycin. Eight weeks after stopping the treatment, the skin flora was normalized in most patients.

B.i.d. application of a 1% clindamycin phosphate solution for eight weeks did not change the colon microflora. None of the ten patients enrolled had *Clostridium difficile* nor its toxins present in their stool. No increased resistance to clindamycin was observed.

Clindamycin concentrations in the mother, umbilical cord and neonate were assayed in 54 caesarean section human patients receiving perioperative clindamycin and gentamicin for prophylaxis. Each patient received 5.5 to 11.1 mg/kg of intravenous clindamycin. A half hour after the injection, the average level of clindamycin in the mother's blood was around 5.5 µg/mL and gradually declined over six to eight hours. About twenty minutes after the injection, the peak concentration of clindamycin in the venous blood of the umbilical cord was 3 µg/mL. Neonatal venous blood concentrations of clindamycin during the first six hours of life were below 2 µg/mL. Amniotic fluid samples obtained thirty and sixty minutes after injection showed no antibiotics.

TOXICOLOGY

ACUTE TOXICITY STUDIES

LD_{50} FOR CLINDAMYCIN PHOSPHATE

Route of Administration	Species	LD_{50} (mg/kg)
Intraperitoneal	Mouse	1145
Intravenous	Mouse	855
Subcutaneous	Neonatal Rat	179
Oral	Rat	1832
Subcutaneous	Rat	>2000

Primary Cutaneous Irritation

The degree of cutaneous irritation produced following a single application of CLINDASOL® (clindamycin phosphate) cream with sunscreens was evaluated in six rabbits over a period of seven days.

All rabbits showed mild erythema which was somewhat more pronounced on the non-scarified side. By day 6, only one rabbit showed mild erythema which persisted up to the seventh day.

Following observations at 24 and 72 hours, the primary cutaneous irritation index for CLINDASOL® was calculated to be 1.1 with respect to a maximum index of 8.0. CLINDASOL® was considered as very slightly irritant in rabbits.

Primary Ocular Irritation

The degree of ocular irritation produced following a single instillation in one eye of three rabbits was evaluated over a period of three days.

For all observation periods, the cornea and the iris of all three rabbits showed no positive reactions to CLINDASOL®.

Minor erythema of the conjunctiva was observed in all three rabbits at one hour and in two rabbits at four hours. Observation taken at a later time showed no erythema. There was no edema or suppuration of the conjunctiva for all observation periods.

The acute ocular irritation index was equal to two and was found at one hour. The mean ocular irritation index was equal to 0 at 24 hours.

From these results, CLINDASOL® was considered as almost non-irritant.

SUBACUTE TOXICITY STUDIES

RATS

One month subcutaneous tolerance study

Repeated injections of 30 mg/kg of clindamycin phosphate for one month, in the interscapular site, produced low grade inflammatory changes. A daily regimen of 60 and 90 mg/kg produced more extensive inflammatory changes and was more frequently accompanied by focal necrosis of the subcutaneous tissue and overlying epidermis. No systemic effects, due to the drug, were observed.

DOGS

One month intramuscular tolerance study

Following repeated intramuscular injections, in the posterior thigh muscles of dogs, at doses of 30, 60 and 90 mg/kg for 32 days clindamycin phosphate was found to be mildly to moderately irritating. As long as the injections were continued, scarring of the muscle bundle was observed in a dose-dependent manner. At the end of the study, elevations of the serum activity of glutamic-oxaloacetic transaminase (SGOT) were found in all dogs of the treated groups and slight increases in the serum activities of glutamic pyruvic transaminase (SGPT) were also reported. A slight dose related increase in liver weight was indicated on the basis of percentage of body weight. Other blood constituents, liver function parameters and final urinalysis were normal.

Intravenous tolerance studies

Twice daily IV injections of 60 or 120 mg/kg of clindamycin phosphate in dogs for one month produced essentially no inflammation at the site of injection in all twelve dogs. There were no significant deviations in the hemograms, blood chemistry or urinalyses of the treated dogs compared to the control animals. In vitro studies performed on blood samples collected from treated and control animals showed no evidence of clindamycin phosphate induced hemolysis. In addition, no Heinz body formation or increased fragility of erythrocytes was observed in blood samples of treated animals.

TERATOLOGY

Teratological studies were not conducted with CLINDASOL® (clindamycin phosphate) cream with sunscreens.

Subcutaneous injections of clindamycin phosphate at 100 and 180 mg/kg/day on gestation days six through fifteen in ICR and CF1 mice and Sprague-Dawley rats had no detrimental effects on the litter weight, live pup weight, number of live and dead pups per litter and the number of resorptions per litter. Fetuses of rats and DV1 mice showed no sign of teratogenic activity as evidenced by examination for gross external, visceral and skeletal malformations. In fetus of ICR mice, a low incidence of cleft palate was observed. This incidence of cleft palate in the clindamycin phosphate treated litter was not significantly different from the incidence reported in the control litter.

BIBLIOGRAPHY

Crawford, WW, Crawford, IP, Stoughton, RB, Cornell, RC. Laboratory induction and clinical occurrence of combined clindamycin and erythromycin resistance in corynebacterium acnes. J Inv Derm 1979;72:187-190.

Guin, JD. Treatment of acne vulgaris with topical clindamycin phosphate: A double-blind study. Int Journal Dermatol 1981;20:286-288.

Guin, JD, Lummis, WL. Comedonal levels of free clindamycin following topical treatment with a 1% solution of clindamycin phosphate. Journal Amer Acad Dermatol 1982;7:265-268.

Keusch, GT, Present, DH. Summary of a workshop on clindamycin colitis. J Am Inf Diseases May 1976;133:578-587.

Kuhlman, DS, Callen, JP. A comparison of clindamycin phosphate 1 percent topical lotion and placebo in the treatment of acne vulgaris. Cutis 1986;Sept:203-206.

Leigh, DA. Antibacterial activity and pharmacokinetics of clindamycin. J Antimicrobial Chemotherapy 1981;7(Suppl A):3-9

Parry, MF, Rha, CK. Pseudomembranous colitis caused by topical clindamycin phosphate. Arch Dermatol 1986:122:583-584.

Rothman, KF, Pochi, PE. Use of oral and topical agents for acne in pregnancy. J Am Acad Dermatol 1988;19:431-42.

Weinstein, AJ, Gibbs, R, Gallagher, M. Placental transfer of clindamycin and gentamicin in term pregnancy. Am J Obstet Genecol 1976 April:688-691.