HIGHLIGHTS OF PRESCRIBING INFORMATION

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

EVOCLIN® (clindamycin phosphate) Foam, 1%
For Topical Use
Initial U.S. Approval: 1970

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

EVOCLIN Foam is a lincosamide product indicated for acne vulgaris in patients 12 years and older. (1)

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

- For topical use only; not for oral, ophthalmic, or intravaginal use. (2)
- Apply EVOCLIN Foam once daily to affected areas. (2)
- Flammable; avoid fire, flame and/or smoking during and immediately following application. (2)

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

Foam containing 1% clindamycin as clindamycin phosphate. (3)

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

EVOCLIN Foam is contraindicated in individuals with a history of regional enteritis or ulcerative colitis, or a 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. EVOCLIN Foam should be discontinued if significant diarrhea occurs. (5.1)

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

The most common adverse reactions (>1%) are headache and application site reactions including burning, pruritus, and dryness. (6.1)

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

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

Revised: 12/2010

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

EVOCLIN Foam is indicated for topical application in the treatment of acne vulgaris in patients 12 years and older.

2 DOSAGE AND ADMINISTRATION

EVOCLIN Foam is for topical use only, and not for oral, ophthalmic, or intravaginal use.

Apply EVOCLIN Foam once daily to affected areas after the skin is washed with mild soap and allowed to fully dry. Use enough to cover the entire affected area.

The contents of EVOCLIN Foam are flammable; avoid fire, flame and/or smoking during and immediately following application.

3 DOSAGE FORMS AND STRENGTHS

White to off-white thermolabile foam. Each gram of EVOCLIN Foam contains, as dispensed, 12 mg (1.2%) of clindamycin phosphate, equivalent to 10 mg (1%) of clindamycin.

4 CONTRAINDICATIONS

EVOCLIN Foam is contraindicated in individuals with a history of regional enteritis or ulcerative colitis, or a 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. If significant diarrhea occurs, EVOCLIN Foam should be discontinued. [*See Adverse Reactions (6.2).*]

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 Irritation

EVOCLIN Foam can cause irritation.

Avoid contact of EVOCLIN Foam with eyes. If contact occurs, rinse eyes thoroughly with water.

EVOCLIN Foam should be prescribed with caution in atopic individuals.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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

A total of 439 subjects with mild to moderate acne vulgaris were treated once daily for 12 weeks with EVOCLIN Foam.

The incidence of adverse reactions occurring in ≥1% of the subjects in clinical trials comparing EVOCLIN Foam and its vehicle is presented in Table 1.

Table 1: Adverse Reactions Occurring in ≥1% of Subjects

Adverse Reactions	Number (%) of Subjects	
	EVOCLIN Foam N = 439	Vehicle Foam N = 154
Headache	12 (3%)	1 (1%)
Application site burning	27 (6%)	14 (9%)
Application site pruritus	5 (1%)	5 (3%)
Application site dryness	4 (1%)	5 (3%)
Application site reaction, not otherwise specified	3 (1%)	4 (3%)

In a contact sensitization study, none of the 203 subjects developed evidence of allergic contact sensitization to EVOCLIN Foam.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of EVOCLIN Foam: application site pain, application site erythema, diarrhea, urticaria, abdominal pain, hypersensitivity, rash, abdominal discomfort, nausea, seborrhea, application site rash, , dizziness, and pain of skin. 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.

Abdominal pain and gastrointestinal disturbances, as well as gram-negative folliculitis, have also been reported in association with the use of topical formulations of clindamycin. Orally and parenterally administered clindamycin have been associated with severe colitis, which may end fatally.

7 DRUG INTERACTIONS

7.1 Erythromycin

EVOCLIN Foam should not be used in combination with topical or oral erythromycin-containing products due to possible antagonism 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.

7.2 Neuromuscular Blocking Agents

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B: There are no adequate and well-controlled studies in pregnant women treated with EVOCLIN Foam. EVOCLIN Foam should be used during pregnancy only if the potential benefit clearly outweighs the potential risk to the fetus.

Reproduction studies have been performed in rats and mice using subcutaneous and oral doses of clindamycin phosphate, clindamycin hydrochloride and clindamycin palmitate hydrochloride. These studies revealed no evidence of fetal harm. The highest dose used in the rat and mouse teratogenicity studies was equivalent to a clindamycin phosphate dose of 432 mg/kg. For a rat, this dose is 84 fold higher, and for a mouse 42 fold higher, than the anticipated human dose of clindamycin phosphate from EVOCLIN Foam based on a mg/m^2 comparison.

8.3 Nursing Mothers

It is not known whether clindamycin is excreted in human milk following use of EVOCLIN Foam. 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.

If used during lactation and EVOCLIN Foam is applied to the chest, care should be taken to avoid accidental ingestion by the infant.

8.4 Pediatric Use

Safety and effectiveness of EVOCLIN Foam in children under the age of 12 have not been studied.

8.5 Geriatric Use

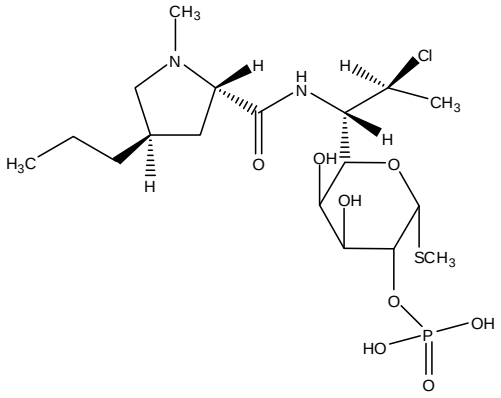
The clinical study with EVOCLIN Foam did not include sufficient numbers of subjects aged 65 and over to determine if they respond differently than younger subjects.

11 DESCRIPTION

EVOCLIN (clindamycin phosphate) Foam contains clindamycin (1%) as clindamycin phosphate.

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:



Molecular Formula: $C_{18}H_{34}ClN_2O_8PS$ Molecular Weight: 504.97 g/mol

EVOCLIN Foam contains clindamycin (1%) as clindamycin phosphate, at a concentration equivalent to 10 mg clindamycin per gram in a thermolabile hydroethanolic foam vehicle consisting of cetyl alcohol, ethanol (58%), polysorbate 60, potassium hydroxide, propylene glycol, purified water, and stearyl alcohol pressurized with a hydrocarbon (propane/butane) propellant.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Mechanism of action in acne vulgaris is unknown. *[See Microbiology (12.4)]*

12.2 Pharmacodynamics

Pharmacodynamics of EVOCLIN Foam is unknown.

12.3 Pharmacokinetics

In an open label, parallel group study in 24 subjects with acne vulgaris, 12 subjects (3 male and 9 female) applied 4 grams of EVOCLIN Foam once-daily for five days, and 12 subjects (7 male and 5 female) applied 4 grams of a clindamycin gel, 1%, once daily for five days. On Day 5, the mean C_{max} and $AUC_{(0-12)}$ were 23% and 9% lower, respectively, for EVOCLIN Foam than for the clindamycin gel, 1%.

Following multiple applications of EVOCLIN Foam, less than 0.024% of the total dose was excreted unchanged in the urine over 12 hours on Day 5.

12.4 Microbiology

No microbiology studies were conducted in the clinical trials with this product.

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. Clindamycin has been shown to have *in vitro* activity against *Propionibacterium acnes* (*P. acnes*), an organism that has been associated with acne vulgaris; however, the clinical significance of this activity against *P. acnes* was not examined in clinical studies with EVOCLIN Foam**.** *P. acnes* resistance to clindamycin has been documented.

Inducible Clindamycin Resistance

The treatment of acne with antimicrobials is associated with the development of antimicrobial resistance in *P. 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. This resistance is not detected by routine susceptibility testing.

Cross Resistance

Resistance to clindamycin is often associated with resistance to erythromycin.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenicity of a 1.2% clindamycin phosphate gel similar to EVOCLIN Foam was evaluated by daily application to mice for two years. The daily doses used in this study were approximately 3 and 15 times higher than the human dose of clindamycin phosphate from 5 milliliters of EVOCLIN Foam, assuming complete absorption and based on a body surface area comparison. No significant increase in tumors was noted in the treated animals.

A 1.2% clindamycin phosphate gel similar to EVOCLIN Foam caused a statistically significant shortening of the median time to tumor onset in a study in hairless mice in which tumors were induced by exposure to simulated sunlight.

Genotoxicity tests performed included a rat micronucleus test and an Ames Salmonella reversion test. Both tests were negative.

Reproduction studies in rats using oral doses of clindamycin hydrochloride and clindamycin palmitate hydrochloride have revealed no evidence of impaired fertility.

14 CLINICAL STUDIES

In one multicenter, randomized, double-blind, vehicle-controlled clinical trial, subjects with mild to moderate acne vulgaris used EVOCLIN Foam or the vehicle Foam once daily for twelve weeks. Treatment response, defined as the proportion of subjects clear or almost clear, based on the Investigator Static Global Assessment (ISGA), and the mean percent reductions in lesion counts at the end of treatment in this study are shown in Table 2.

Table 2: Efficacy Results at Week 12

Efficacy Parameters	**EVOCLIN Foam N=386**	**Vehicle Foam N=127**
Treatment response (ISGA)	31%	18%*
Percent reduction in lesion counts		
Inflammatory Lesions	49%	35%*
Noninflammatory Lesions	38%	27%*
Total Lesions	43%	31%*

* $P<0.05$

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

EVOCLIN Foam containing clindamycin phosphate equivalent to 10 mg clindamycin per gram, is white to off-white in color and thermolabile. It is available in the following sizes:

- 100 gram aerosol can - NDC 0145-0061-00
- 50 gram aerosol can - NDC 0145-0061-50

16.2 Storage and Handling

Store at controlled room temperature between 68° to 77°F (20° to 25°C).

Flammable. avoid fire, flame or smoking during and immediately following application.

Contents under pressure. Do not puncture or incinerate. Do not expose to heat or store at temperature above 120°F (49°C).

Keep out of reach of children.

17 PATIENT COUNSELING INFORMATION

See FDA-Approved patient labeling (Patient Information).

17.1 Instructions for Use

- Patients should be advised to wash their skin with mild soap and allow it to dry before applying EVOCLIN Foam.
- Patients should use enough EVOCLIN Foam to cover the face and to apply once daily.
- Patients should dispense EVOCLIN Foam directly into the cap or onto a cool surface.
- Patients should wash their hands after applying EVOCLIN Foam.

17.2 Skin Irritation

EVOCLIN Foam may cause irritation such as erythema, scaling, itching, burning, or stinging.

17.3 Colitis

In the event a patient treated with EVOCLIN Foam experiences severe diarrhea or gastrointestinal discomfort, EVOCLIN Foam should be discontinued and a physician should be contacted.

EVC:1PI