

**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 (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. 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 Mylan at 1-877-446-3679 (1-877-4-INFO-RX) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

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

**Revised: 04/2018**

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## **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.

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

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

### **3 DOSAGE FORMS AND STRENGTHS**

EVOCLIN (clindamycin phosphate) is a white to off-white thermolabile foam. EVOCLIN Foam, 1% contains 10 mg of clindamycin as clindamycin phosphate, USP per gram.

### **4 CONTRAINDICATIONS**

EVOCLIN Foam is contraindicated in individuals with a history of regional enteritis or ulcerative colitis, or a history of antibiotic-associated colitis (including pseudomembranous 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. 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 irritation or dermatitis occurs, clindamycin should be discontinued.

Avoid contact of EVOCLIN Foam with eyes, mouth, lips, other mucous membranes or areas of broken skin. If contact occurs, rinse 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  $\geq 1\%$  of the subjects in clinical trials comparing EVOCLIN Foam and its vehicle is presented in Table 1.

**Table 1: Adverse Reactions Occurring in  $\geq 1\%$  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, pain of skin, colitis (including pseudomembranous colitis), and hemorrhagic diarrhea. 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

#### Risk Summary

There are no available data on EVOCLIN Foam use in pregnant women to inform a drug-associated risk for adverse developmental outcomes.

Animal reproduction studies have not been conducted with EVOCLIN Foam. No evidence of fetal harm or malformations was observed in pregnant rats and mice administered daily subcutaneous or oral doses of clindamycin salts during organogenesis at doses that produced exposures up to 84 and 42 times, respectively, the maximum recommended human dose (MRHD) of EVOCLIN Foam based on body surface area (BSA) comparisons and assuming 100% absorption [*see Data*].

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

#### Data

##### *Animal Data*

Reproduction studies have been conducted in rats and mice using subcutaneous or oral doses of clindamycin phosphate, clindamycin hydrochloride or clindamycin palmitate hydrochloride administered daily during organogenesis at doses up to the equivalent of 432 mg/kg/day clindamycin phosphate. These studies produced no evidence of fetal harm or malformations in rats or mice at exposures 84 or 42 times, respectively, the MRHD of clindamycin phosphate (i.e., 5 milliliters of EVOCLIN Foam) based on BSA comparison and assuming 100% absorption.

### 8.2 Lactation

#### Risk Summary

There is no information on the presence of clindamycin in human milk, or the effects on the breast-fed child, or the effects on milk production following use of EVOCLIN Foam. However, orally and parenterally administered clindamycin has been reported to appear in breast milk.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for EVOCLIN Foam and any potential adverse effects on the breast-fed child from EVOCLIN Foam or from the underlying maternal condition.

#### Clinical Considerations

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

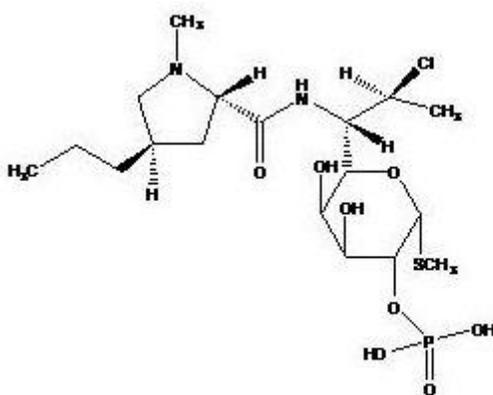
The clinical study with EVOCLIN Foam did not include sufficient numbers of subjects aged 65 and over to determine if they respond differently than younger subjects.

## 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*- $\alpha$ -D-galacto-octopyranoside 2-(dihydrogen phosphate). The structural formula for clindamycin phosphate is represented below:



Molecular Formula: C<sub>18</sub>H<sub>34</sub>ClN<sub>2</sub>O<sub>8</sub>PS

Molecular Weight: 504.97 g/mol

EVOCLIN Foam contains clindamycin (1%) as clindamycin phosphate, USP 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 of clindamycin 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<sub>max</sub> and AUC<sub>(0-12)</sub> 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 topical administration to mice for two years. The topical doses used in this study were approximately 3 and 15 times higher than the MRHD of clindamycin phosphate from EVOCLIN Foam, based on BSA comparison and assuming 100% absorption. No significant increase in tumors was noted in the treated animals.

The genotoxic potential of clindamycin was evaluated in an in vitro Ames assay and in an in vivo rat micronucleus test. Both tests were negative.

Reproduction studies in rats using oral doses of clindamycin hydrochloride or 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%*
<b>Percent reduction in lesion counts</b>		
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 (clindamycin phosphate) Foam, 1% contains 10 mg of clindamycin as clindamycin phosphate, USP per gram. The white to off-white thermolabile foam is available as follows:

NDC 0378-8134-50  
50 gram aerosol can

NDC 0378-8134-01  
100 gram aerosol can

### **16.2 Storage and Handling**

**Store at 20° to 25°C (68° to 77°F). [See USP Controlled Room Temperature.]**

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. Patients should be advised to discontinue use if excessive irritancy or dermatitis occur.

### **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.

Revised: 04/2018

Manufactured for:

Mylan Pharmaceuticals Inc., Morgantown, WV 26505 U.S.A.

By DPT Laboratories, Ltd., San Antonio, TX 78215 U.S.A.

EVOCLIN is a registered trademark of Stiefel Laboratories, Inc., a GSK Company, exclusively licensed to the Mylan Companies.

**PATIENT INFORMATION**

**EVOCLIN (Ev-o-clin)  
(clindamycin phosphate)  
Foam, 1%**

**Important Information: EVOCLIN Foam is for use on the skin only. Do not use EVOCLIN Foam in your eyes, mouth or vagina.**

**What is EVOCLIN Foam?**

EVOCLIN Foam is a prescription medicine used on the skin (topical) to treat acne vulgaris in people 12 years and older.

It is not known if EVOCLIN Foam is safe and effective in children under 12 years of age.

**Who should not use EVOCLIN Foam?**

**Do not use EVOCLIN Foam if you:**

- have Crohn's disease
- have ulcerative colitis
- have had inflammation of the colon (colitis) or severe diarrhea with past antibiotic use

Tell your doctor if you are not sure if you have any of the conditions listed above.

**What should I tell my doctor before using EVOCLIN Foam?**

**Before using EVOCLIN Foam, tell your doctor about all of your medical conditions, including if you:**

- have or have had bowel problems (such as Crohn's disease, ulcerative colitis, colitis)
- have or have had eczema or other skin problems
- are planning to have surgery. EVOCLIN Foam may affect how certain medicines work that may be given during surgery.
- are pregnant or plan to become pregnant. It is not known if EVOCLIN Foam may harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if EVOCLIN Foam passes into your breast milk. Talk to your doctor about using EVOCLIN Foam while breastfeeding. If you use EVOCLIN Foam while breastfeeding and EVOCLIN Foam is applied on the chest, take care to avoid getting EVOCLIN Foam into your baby's mouth.

**Tell your doctor about all the medicines you take** including prescription and over-the-counter medicines, vitamins and herbal supplements.

EVOCLIN Foam may affect the way other medicines work and other medicines may affect how EVOCLIN Foam works.

Especially tell your doctor if you take medicine by mouth that contains erythromycin or use products on your skin that contain erythromycin.

Know the medicines you take. Keep a list of them to show your doctor and pharmacist when you get a new medicine.

#### **How should I use EVOCLIN Foam?**

- Use EVOCLIN Foam exactly as your doctor tells you to use it. See the detailed “Instructions for Use” for directions about how to apply EVOCLIN Foam correctly.
- Wash your skin with mild soap and water and dry before applying EVOCLIN Foam.
- Apply EVOCLIN Foam 1 time each day to the affected skin area. You should apply enough EVOCLIN Foam to cover the entire affected area.
- Dispense EVOCLIN Foam directly into the cap. **Do not** dispense EVOCLIN Foam directly onto your hands or face, because the foam will begin to melt on contact with warm skin.
- Wash your hands after applying EVOCLIN Foam.

#### **What should I avoid while using EVOCLIN Foam?**

- EVOCLIN Foam is flammable. Avoid fire, flames, or smoking during and right after you apply EVOCLIN Foam to your skin.
- Avoid getting EVOCLIN Foam in or near your eyes, mouth, lips, or broken skin. If you get EVOCLIN Foam in your eyes, mouth, on lips or broken skin, rinse well with water.

#### **What are possible side effects with EVOCLIN Foam?**

##### **EVOCLIN Foam may cause serious side effects, including:**

- **Inflammation of the colon (colitis).** Diarrhea, bloody diarrhea, and colitis has happened in people who use EVOCLIN Foam. Stop using EVOCLIN Foam and call your doctor right away if you have severe stomach (abdominal) cramps, watery diarrhea, or bloody diarrhea during treatment, and for several weeks after treatment, with EVOCLIN Foam.
- **Skin irritation.** Stop using EVOCLIN Foam and call your doctor if you develop skin irritation during treatment with EVOCLIN Foam.

**The most common side effects of EVOCLIN Foam include** headache and application site reactions (including burning, itching, and dryness).

These are not all the possible side effects of EVOCLIN Foam.

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 EVOCLIN Foam?**

- Store EVOCLIN Foam at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep EVOCLIN Foam away from heat. Never throw the can into a fire, even if the can is empty.
- Do not store EVOCLIN Foam at temperatures above 120°F (49°C).
- Do not break through (puncture) the EVOCLIN Foam can.

**Keep EVOCLIN Foam and all medicines out of the reach of children.**

#### **General information about the safe and effective use of EVOCLIN Foam.**

Medicines are sometimes prescribed for purposes other than those listed in Patient Information leaflet. Do not use EVOCLIN Foam for a condition for which it was not prescribed. Do not give EVOCLIN Foam to other people, even if they have the same symptoms you have. It may harm them. You can also ask your pharmacist or doctor for information about EVOCLIN Foam that is written for health professionals.

#### **What are the ingredients in EVOCLIN Foam?**

**Active ingredient:** clindamycin phosphate

**Inactive ingredients:** cetyl alcohol, ethanol (58%), polysorbate 60, potassium hydroxide, propylene glycol, purified water, and stearyl alcohol. The can is pressurized with a hydrocarbon (propane/butane) propellant.

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

Revised: 04/2018

Manufactured for:

Mylan Pharmaceuticals Inc., Morgantown, WV 26505 U.S.A.

By DPT Laboratories, Ltd., San Antonio, TX 78215 U.S.A.

EVOCLIN is a registered trademark of Stiefel Laboratories, Inc., a GSK Company, exclusively licensed to the Mylan Companies.

**Instructions for Use  
EVOCLIN (Ev-o-clin)  
(clindamycin phosphate)  
Foam, 1%**

**Important Information:** EVOCLIN Foam is for use on the skin only. Do not use EVOCLIN Foam in your eyes, mouth or vagina.

**Step 1:** Remove the clear cap from the EVOCLIN Foam can.



**Step 2:** Line up the black circle with the nozzle.



**Step 3:** Hold the can upright and firmly press the nozzle to dispense EVOCLIN Foam into the clear cap.

- Dispense enough EVOCLIN Foam to cover the entire affected area.



- If the can seems warm or the foam seems runny, run the can under cold water.



**Step 4:** Pick up small amounts of EVOCLIN Foam with your fingertips and gently rub the foam into the affected area until the foam disappears.



**Step 5:** Wash your hands after applying EVOCLIN Foam.

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| <ul style="list-style-type: none"><li>• Throw away any of the unused medicine that you dispensed out of the can.</li></ul> |  |
|--|--|

**How should I store EVOCLIN Foam?**

- Store EVOCLIN Foam at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep EVOCLIN Foam away from heat. Never throw the can into a fire, even if the can is empty.
- Do not store EVOCLIN Foam at temperatures above 120°F (49°C).
- Do not break through (puncture) the EVOCLIN Foam can.

**Keep EVOCLIN Foam and all medicines out of the reach of children.**

The Patient Information and Instructions for Use have been approved by the U.S. Food and Drug Administration.

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