



BY WILLIAM G. WILKOFF, M.D.

## LETTERS FROM MAINE

### Mi Casa Es Su Casa

Let me ask you a question. Your receptionist receives a call from the mother of a 7-month-old who has been feverish and irritable for 3 days. She is visiting from out of state and staying with a

family whose three children have been your patients for 13 years. The mother is "pretty sure" that her insurance will cover an out-of-network visit.

Would your receptionist: (a) schedule an appointment, (b) ask you if it is okay to book the appointment and then warn the mother that she will have to pay at the time of the visit, or (c) suggest that the family take the child to the emergency department?

What would your answer be if the scenario included that this child from out of town also was the niece of one of your nurses?

I ask this question because the issue of how one manages visiting families comes up almost weekly in our office. Because our license plates here in Maine include the slogan "Vacationland" and because Brunswick sits on the shores of scenic Casco Bay, we have lots of visitors.

Our policy has always been to find an appointment slot for someone who tells us they are visiting from out of town regardless of whether they have been referred by a family that we know. I hope that the bulk of our motivation is just old-fashioned New England hospitality. But, a lot of it is just habit. In the not-so-good old days before there were such things as emergency department physicians, we were going to end up seeing the patients from out of town anyway. And it was usually more convenient for us to have them come to our office.

Even when staffed with well-trained physicians, an emergency department is usually not the optimal diagnostic or therapeutic setting for a moderately ill young child or infant. And most families who are accustomed to good office care at a medical home know this.

Although it's hard for me to imagine why anyone who lives in Vacationland would want to travel out of state, from time to time it does happen. And, when our patients' families return we occasionally hear horror stories of their attempts to find pediatric care. I recently had a mother tell me that a referral from a current patient and an offer to pay cash failed to unlock the tightly guarded pediatric office in the suburban community where she was visiting her parents.

I am sure that there are some communities with large transient populations in which our visitor-friendly office policy might be committing economic suicide. And, I suspect that many larger communities have emergency departments that can offer nonurgent pediatric care that would pass my "Is it good enough for my granddaughter?" test.

However, it troubles me to hear how shabbily some of our families are treated when they venture far from their children's medical home.

When we became fellows, the American Academy of Pediatrics didn't ask us to promise that we would see any patient who has a medical home supervised by one of our brother or sister pediatricians. Nor do any of us have written contracts with the families in our practices stating that we will agree to see any child who comes to visit them. But, if you have found yourself in a strange town with a sick child as I have, you know what you should do when a distraught mother visiting from out of town calls your office. ■

#### BenzaClin® Topical Gel

(clindamycin - benzoyl peroxide gel)

**Brief summary. Please see full prescribing information for complete product information.**

**Topical Gel: clindamycin (1%) as clindamycin phosphate, benzoyl peroxide (5%)**

**For Dermatological Use Only - Not for Ophthalmic Use**

**\*Reconstitute Before Dispensing\***

#### INDICATIONS AND USAGE

**BenzaClin Topical Gel** is indicated for the topical treatment of acne vulgaris.

#### CONTRAINDICATIONS

**BenzaClin Topical Gel** is contraindicated in those individuals who have shown hypersensitivity to any of its components or to lincomycin. It is also contraindicated in those having a history of regional enteritis, ulcerative colitis, or antibiotic-associated colitis.

#### WARNINGS

**ORALLY AND PARENTERALLY ADMINISTERED CLINDAMYCIN HAS BEEN ASSOCIATED WITH SEVERE COLITIS WHICH MAY RESULT IN PATIENT DEATH. USE OF THE TOPICAL FORMULATION OF CLINDAMYCIN RESULTS IN ABSORPTION OF THE ANTIBIOTIC FROM THE SKIN SURFACE. DIARRHEA, BLOODY DIARRHEA, AND COLITIS (INCLUDING PSEUDOMEMBRANOUS COLITIS) HAVE BEEN REPORTED WITH THE USE OF TOPICAL AND SYSTEMIC CLINDAMYCIN. 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. ENDOSCOPIC EXAMINATION MAY REVEAL PSEUDOMEMBRANOUS COLITIS. STOOL CULTURE FOR *Clostridium Difficile* AND STOOL ASSAY FOR *C. difficile* TOXIN MAY BE HELPFUL DIAGNOSTICALLY. WHEN SIGNIFICANT DIARRHEA OCCURS, THE DRUG SHOULD BE DISCONTINUED. LARGE BOWEL ENDOSCOPY SHOULD BE CONSIDERED TO ESTABLISH A DEFINITIVE DIAGNOSIS IN CASES OF SEVERE DIARRHEA. ANTIPERISTALTIC AGENTS SUCH AS OPIATES AND DIPHENOXYLATE WITH ATROPINE MAY PROLONG AND/OR WORSEN THE CONDITION. DIARRHEA, COLITIS, AND PSEUDOMEMBRANOUS COLITIS HAVE BEEN OBSERVED TO BEGIN UP TO SEVERAL WEEKS FOLLOWING CESSATION OF ORAL AND PARENTERAL THERAPY WITH CLINDAMYCIN.**

Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation and treatment with an antibacterial drug clinically effective against *C. difficile* colitis.

#### PRECAUTIONS

**General:** For dermatological use only; not for ophthalmic use. Concomitant topical acne therapy should be used with caution because a possible cumulative irritancy effect may occur, especially with the use of peeling, desquamating, or abrasive agents.

The use of antibiotic agents may be associated with the overgrowth of nonsusceptible organisms including fungi. If this occurs, discontinue use of this medication and take appropriate measures.

Avoid contact with eyes and mucous membranes.

Clindamycin and erythromycin containing products should not be used in combination. *In vitro* studies have shown antagonism between these two antimicrobials. The clinical significance of this *in vitro* antagonism is not known.

**Information for Patients:** Patients using **BenzaClin Topical Gel** should receive the following information and instructions:

- BenzaClin Topical Gel** is to be used as directed by the physician. It is for external use only. Avoid contact with eyes, and inside the nose, mouth, and all mucous membranes, as this product may be irritating.
- This medication should not be used for any disorder other than that for which it was prescribed.
- Patients should not use any other topical acne preparation unless otherwise directed by physician.
- Patients should minimize or avoid exposure to natural or artificial sunlight (tanning beds or UVA/B treatment) while using **BenzaClin Topical Gel**. To minimize exposure to sunlight, a wide-brimmed hat or other protective clothing should be worn, and a sunscreen with SPF 15 rating or higher should be used.
- Patients should report any signs of local adverse reactions to their physician.
- BenzaClin Topical Gel** may bleach hair or colored fabric.
- BenzaClin Topical Gel** can be stored at room temperature up to 25°C (77°F) for 3 months. Do not freeze. Discard any unused product after 3 months.
- Before applying **BenzaClin Topical Gel** to affected areas wash the skin gently, then rinse with warm water and pat dry.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Benzoyl peroxide has been shown to be a tumor promoter and progression agent in a number of animal studies. The clinical significance of this is unknown.

Benzoyl peroxide in acetone at doses of 5 and 10 mg administered twice per week induced skin tumors in transgenic Tg.AC mice in a study using 20 weeks of topical treatment.

In a 52 week dermal photocarcinogenicity study in hairless mice, the median time to onset of skin tumor formation was decreased and the number of tumors per mouse increased following chronic concurrent topical administration of **BenzaClin Topical Gel** with exposure to ultraviolet radiation (40 weeks of treatment followed by 12 weeks of observation).

Genotoxicity studies were not conducted with **BenzaClin Topical Gel**. Clindamycin phosphate was not genotoxic in *Salmonella typhimurium* or in a rat micronucleus test. Clindamycin phosphate sulfoxide, an oxidative degradation product of clindamycin phosphate and benzoyl peroxide, was not clastogenic in a mouse micronucleus test. Benzoyl peroxide has been found to cause DNA strand breaks in a variety of mammalian cell types, to be mutagenic in *S. typhimurium* tests by some but not all investigators, and to cause sister chromatid exchanges in Chinese hamster ovary cells. Studies have not been performed with **BenzaClin Topical Gel** or benzoyl peroxide to evaluate the effect on fertility. Fertility studies in rats treated orally with up to 300 mg/kg/day of clindamycin (approximately 120 times the amount of clindamycin in the highest recommended adult human dose of 2.5 g **BenzaClin Topical Gel**, based on mg/m<sup>2</sup>) revealed no effects on fertility or mating ability.

#### Pregnancy: Teratogenic Effects: Pregnancy Category C:

Animal reproductive/developmental toxicity studies have not been conducted with **BenzaClin Topical Gel** or benzoyl peroxide. Developmental toxicity studies performed in rats and mice using oral doses of clindamycin up to 600 mg/kg/day (240 and 120 times amount of clindamycin in the highest recommended adult human dose based on mg/m<sup>2</sup>, respectively) or subcutaneous doses of clindamycin up to 250 mg/kg/day (100 and 50 times the amount of clindamycin in the highest recommended adult human dose based on mg/m<sup>2</sup>, respectively) revealed no evidence of teratogenicity.

There are no well-controlled trials in pregnant women treated with **BenzaClin Topical Gel**. It also is not known whether **BenzaClin Topical Gel** can cause fetal harm when administered to a pregnant woman.

**Nursing Women:** It is not known whether **BenzaClin Topical Gel** is excreted in human milk after topical application. 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.

**Pediatric Use:** Safety and effectiveness of this product in pediatric patients below the age of 12 have not been established.

#### ADVERSE REACTIONS

During clinical trials, the most frequently reported adverse event in the **BenzaClin** treatment group was dry skin (12%). The Table below lists local adverse events reported by at least 1% of patients in the **BenzaClin** and vehicle groups.

Local Adverse Events - all causalities in >= 1% of patients		
	BenzaClin n = 420	Vehicle n = 168
Application site reaction	13 (3%)	1 (<1%)
Dry skin	50 (12%)	10 (6%)
Pruritus	8 (2%)	1 (<1%)
Peeling	9 (2%)	-
Erythema	6 (1%)	1 (<1%)
Sunburn	5 (1%)	-

The actual incidence of dry skin might have been greater were it not for the use of a moisturizer in these studies.

#### DOSAGE AND ADMINISTRATION

**BenzaClin Topical Gel** should be applied twice daily, morning and evening, or as directed by a physician, to affected areas after the skin is gently washed, rinsed with warm water and patted dry.

#### HOW SUPPLIED AND COMPOUNDING INSTRUCTIONS

Size (Net Weight)	NDC 0066-	Benzoyl Peroxide Gel	Active Clindamycin Powder (In plastic vial)	Purified Water To Be Added to each vial
25 grams	0494-25	19.7g	0.3g	5 mL
50 grams	0494-50	41.4g	0.6 g	10 mL
50 grams (pump)	0494-55	41.4g	0.6 g	10 mL

**Prior to dispensing, tap the vial until powder flows freely. Add indicated amount of purified water to the vial (to the mark) and immediately shake to completely dissolve clindamycin. If needed, add additional purified water to bring level up to the mark.** Add the solution in the vial to the gel and stir until homogenous in appearance (1 to 1½ minutes). For the 50 gram pump only, reassemble jar with pump dispenser. **BenzaClin Topical Gel** (as reconstituted) can be stored at room temperature up to 25°C (77°F) for 3 months. Place a 3 month expiration date on the label immediately following mixing.

Store at room temperature up to 25°C (77°F) (See USP).

**Do not freeze. Keep tightly closed. Keep out of the reach of children.**

US Patents 5,446,028; 5,767,098; 6,013,637

Brief Summary of Prescribing Information as of February 2006.

#### Rx Only

#### Dermik Laboratories

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