



BY WILLIAM G. WILKOFF, M.D.

## LETTERS FROM MAINE

# Battle Tested—and Better for It

The good news is that the flow of sick patients into the office has begun to slow. The viral gastroenteritis and the influenza-like illnesses that have plagued our community seem to be abating. We are

now back to a more comfortable mix of slow-gaining breast-feeders, runny-nosed toddlers, and limping teenaged athletes.

Physicians and staff are getting home in time to tuck their own children in for the night and sometimes even arriving before dinner is served. There are empty seats in the waiting room from time to time, and I no longer feel that I must begin each visit with an apology for running behind.

The rest of the good news is that weath-

ering this 8-week siege of illness has forced everyone in the office to improve their efficiency so that now we are purring along like a well-oiled machine. Exam rooms are well supplied with otoscope pieces, tongue depressors, and ear cures when the day begins because the nurses realize that once the patients start arriving, the window of opportunity to restock the drawers may not open again.

All the patients with vomiting or diar-

rhea are weighed before they see the physician. Children with urine complaints have already been coaxed into peeing and the results of their urinalyses are already on the chart before they are readied for an exam, and those with headaches or head bumps have had their blood pressures taken. The nurses who float over from the internist's pod from time to time are no longer wasting their time and irritating the patients by taking "routine" and meaningless temperatures.

The receptionists are asking more and better questions before they make appointments. After seeing a big influx of sicker-than-usual patients, they have witnessed multiple examples that support our office philosophy: Seeing the sicker patients early in the day helps things run more smoothly. Children with injuries that might require an x-ray are scheduled to come in when our in-house x-ray is staffed. Nearly all of the phone messages that arrive on the counter above the chart rack include sufficient information for the physician to give the correct advice without having to ask time-consuming follow-up questions.

The physicians are arriving in time to make their callbacks and are ready to sit down for our scheduled and promised call-in times. For some, this punctuality is a new habit spawned by the realization that when double-booking is the norm, there is no time to compensate for a late arrival.

The bad news is that 30 years of watching the ebb and flow of patient volume has taught me that after a few weeks of relative quiet, some old habits and inefficiencies will creep back into the routine. It's only natural. No one enjoys churning away at top speed, seeing patients in less time than they deserve.

For some staff members, this double-barreled outbreak was their first opportunity to see how busy a pediatric office can get. Of course, it also gave some of us old-timers the chance to tell a few "If you think this is busy ..." stories. And I have grown to enjoy answering those, "Did you really see 85 patients in one day?" questions.

But there is even more good news. None of our permanent employees quit during the siege, and I think that most of our new employees now understand how some of our apparently trivial office policies came to be. When things are relatively quiet, it may not seem terribly important that each exam room always has an extra roll of paper towel under the sink. However, when a physician who is running 40 minutes behind finds herself out in the hall with wet hands instead of beginning her exam of a fussy and feverish 3-month-old, it isn't a pretty picture.

Office pediatrics will always be an unpredictable mix of chaos and calm. No one can write a practice manual that will make every day a stroll in the park. But, a well-run office can create commonsense policies that may help preserve the lessons that were so painfully learned in the heat of battle. ■

### 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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