

Medical Schools Take Stand Against Industry Gifts

BY CATHY DOMBROWSKI AND
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"The Pink Sheet"

Medical schools and teaching hospitals should prohibit their physicians, faculty, residents, and students from taking gifts and services from drug companies, according to the Association of American Medical Colleges.

Industry support for continuing medical education (CME) activities also should be

limited, according to a report unanimously adopted by the AAMC executive council.

The association is urging member institutions to adopt policies consistent with the report by July 1, 2009.

Many Schools Are Studying Gifts Issue

The recommendations might be particularly influential because of their timeliness. The AAMC notes that many academic institutions are in the midst of developing

policies on interactions with drug and device manufacturers, though some have not yet taken up the issue.

The AAMC cites the medical schools at the University of Pittsburgh; the University of Pennsylvania; Stanford University; the University of California, Davis; University of California, Los Angeles; and Yale University as among the institutions that have implemented policies in the past few years.

The association represents 129 U.S. and

17 Canadian medical schools, about 400 teaching hospitals and health systems, and a number of scientific societies.

The AAMC's strong stance against industry gifts to physicians comes as drug and device makers are signing on to federal legislation that would bring transparency to their financial interactions with doctors by requiring public disclosure of gifts.

But the "sunshine" approach might prove to be temporary. In addition to the AAMC's call for a ban, the Massachusetts Senate adopted a bill in April that would ban pharmaceutical industry gifts of any value to physicians, their office staffs, or their families.

The Institute of Medicine also is assessing the effectiveness of transparency in preventing conflicts of interest arising from such interactions, with a report due in July 2009.

The medical schools report, titled "Report of the AAMC Task Force on Industry Funding of Medical Education to the AAMC Executive Council," calls on members to take the following actions:

- ▶ Ban acceptance of industry gifts by doctors, faculty, students, and residents, whether given on- or off-site.
- ▶ Either end acceptance of drug samples, or manage their distribution through a centralized process.
- ▶ Restrict visits to individual doctors by industry representatives to nonpatient areas and by appointment only.
- ▶ Create a central office to receive and coordinate distribution of industry support for CME.
- ▶ Strongly discourage faculty participation in industry-sponsored speakers bureaus.
- ▶ Bar physicians, residents, and students from using presentations ghostwritten by industry members.

Lessons on the Nature of the Industry

The group also notes that medical students often take their cue from faculty and medical residents, suggesting that those in a mentoring role must lead by example in industry interactions. At the same time, most medical students have "limited understanding" of such issues as the process of drug development, nature of the pharmaceutical industry, product marketing, "meaning and limitation" of FDA product approval, and physician role in adverse event reporting, the report notes. Medical curricula should include information on these topics.

The report also emphasizes that while academic institutions are not responsible for policing activities outside their facilities, faculty and students should be advised that prohibited activities are also barred off-site. For example, they should not accept meals from industry (outside of officially sanctioned CME), whether at the medical school or across the street.

The report affirms that "substantive, appropriate, and well-managed interactions between industry and academic medicine are vital to the public health," saying that industry and the medical community should work together "to develop new paradigms" for scientific information transfer.

The Accreditation Council for Continuing Medical Education

Continued on following page

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 CLOSTRIDIUM 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:

1. 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.
2. This medication should not be used for any disorder other than that for which it was prescribed.
3. Patients should not use any other topical acne preparation unless otherwise directed by physician.
4. 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.
5. Patients should report any signs of local adverse reactions to their physician.
6. BenzaClin Topical Gel may bleach hair or colored fabric.
7. 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.
8. 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).

In a 2-year dermal carcinogenicity study in rats, treatment with BenzaClin Topical Gel at doses of 100, 500 and 2000 mg/kg/day caused a dose-dependent increase in the incidence of keratoacanthoma at the treated skin site of male rats. The incidence of keratoacanthoma at the treated site of males treated with 2000 mg/kg/day (8 times the highest recommended adult human dose of 2.5 g BenzaClin Topical Gel, based on mg/m²) was statistically significantly higher than that in the sham- and vehicle-controls.

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/m²) 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/m², 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/m², 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.

DOSE 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 May 2007.

Rx Only

Dermik Laboratories

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Bridgewater, NJ 08807

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Pediatric Hospitalists Cut Costs, Length of Stay

BY ROBERT FINN
San Francisco Bureau

HONOLULU — Patients on a pediatric hospitalist service spent a mean 38% fewer days in the hospital and had 29% lower direct costs, on average, than did patients on traditional house staff services, according to a 1-year study of more than 900 patients.

Dr. Arpi Bekmezian of the University of California, Los Angeles, and colleagues retrospectively compared 816 pediatric cases assigned to GI and hematology/oncology subspecialty services with 109 cases assigned to a pediatric hospitalist service between July 1, 2005, and June 30, 2006.

Patients were admitted to the hospitalist service when the faculty/house staff services reached their maximum capacity. The assignments were made solely on the basis of the hospital census, not on diagnosis, acuity, or complexity.

The study was conducted at the UCLA

Hospital and Medical Center, a nonprofit tertiary care teaching hospital with 70 pediatric beds. The patients' mean age was 8 years, and there were no statistically significant differences on the all-patient refined diagnostic-related group severity scale.

Neither were there any statistically significant differences in the proportion of patients with private insurance, Medicaid, or other insurance, Dr. Bekmezian reported in a poster presentation at the

annual meeting of the Pediatric Academic Societies.

The mean length of stay was 10 days in the subspecialty services vs. 7 days in the hospitalist service.

The average variable of direct cost of stay excluding physician fees was \$16,500 in the subspecialty services vs. \$11,000 in the hospitalist service.

Both differences were statistically significant.

Rates of readmission also were signif-

icantly different: a mean 4% for patients in the subspecialty services, compared with 0% for patients in the hospitalist service.

There were no statistically significant differences in mortality: a mean 2% in the subspecialty services, compared with a mean 1% in the hospitalist service, Dr. Bekmezian said.

Dr. Bekmezian declared that he had no conflicts of interest related to his presentation. ■

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using Medical Education is seeking comments on such a paradigm with regard to industry support for CME.

AMA Awaits Federal Legislation

The American Medical Association also has been reviewing industry funding and gifts at its annual House of Delegates meeting but declined to take a clear-cut position. Its Council on Ethical and Judicial Affairs drafted a report recommending that individual physicians and institutions of medicine not accept industry funding for education.

But during their June 14-18 session, the AMA delegates referred the report for further review at the recommendation of the group's Committee on Amendments to the Constitution and Bylaws.

The panel said testimony on the report noted a lack of clarity with regard to certified CME and uncertified promotional education, and concern for unintended consequences.

The delegates also declined to get embroiled in the debate over reporting of industry gifts. Pending was a resolution for the AMA to back annual reporting by drug and medical device firms of all physician payments with a value of more than \$100.

An AMA committee advised delegates that testimony on the measure generally was unfavorable, with concerns raised about the logistics and how and to whom the information would be disclosed.

Noting that legislation on the issue "is pending and may serve to answer many of these questions," the committee recommended that the resolution not be adopted and the delegates concurred.

On the question of conflicts of interest in CME, the delegates accepted the recommendation of the AMA's Council on Medical Education to monitor implementation of ACCME standards. ■

This newspaper and "The Pink Sheet" are both published by Elsevier.



Powerful relief

to help patients face their allergies

POTENT

- Potent inhibition of histamine-induced wheal and flare
- The clinical relevance of histamine wheal skin testing is unknown

CONSISTENT EFFICACY

- Consistent efficacy across 8 placebo-controlled clinical trials
- Six clinical trials in allergic rhinitis (seasonal and perennial) and 2 in chronic idiopathic urticaria

FAST AND LONG-LASTING EFFECT

- Onset of efficacy was seen at 60 minutes and efficacy was demonstrated at the end of the 24-hour dosing interval (Environmental Exposure Unit study)

CONVENIENT ONCE-DAILY PM DOSING



IMPORTANT SAFETY INFORMATION

XYZAL is indicated for the relief of symptoms associated with allergic rhinitis (seasonal and perennial), and the treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 years of age and older.

The use of XYZAL is contraindicated in: patients with a known hypersensitivity to levocetirizine or any of the ingredients of XYZAL or to cetirizine (observed reactions range from urticaria to anaphylaxis); and pediatric patients aged 6 to 11 years with impaired renal function.

Patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness and motor coordination, such as operating machinery or driving a motor vehicle, after ingestion of XYZAL. Concurrent use of XYZAL with alcohol or other central nervous system (CNS) depressants should be avoided because additional reductions in alertness and additional impairment of CNS performance may occur.

In clinical trials, the most common adverse reactions in $\geq 2\%$ of adult and adolescent patients (12 years of age and older) taking XYZAL 2.5 mg, XYZAL 5 mg, or placebo were somnolence (5%, 6%, 2%), nasopharyngitis (6%, 4%, 3%), fatigue (1%, 4%, 2%), dry mouth (3%, 2%, 1%), and pharyngitis (2%, 1%, 1%), respectively. In clinical trials, the most common adverse reactions in $\geq 2\%$ of pediatric patients (6-12 years of age) taking XYZAL 5 mg included pyrexia (4% vs 2% placebo), cough (3% vs <1% placebo), somnolence (3% vs <1% placebo), and epistaxis (2% vs <1% placebo).

XYZAL[®]
(levocetirizine dihydrochloride)
Powerful relief

For more information, visit www.XYZAL.com
Please see adjacent brief summary of Prescribing Information.

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