

# HIV-Positive Patients Struggle With Weight Gain

BY DOUG BRUNK  
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SAN DIEGO — In the 1980s, patients with HIV/AIDS commonly lost an excessive amount of weight, a process known as wasting.

But today, these patients are becoming just as overweight and obese as the general population of the U.S., Dr. Nancy F. Crum-Cianflone reported at the annual meeting of the Infectious Diseases Society of

America. A study of 663 HIV-positive patients treated at two U.S. Navy clinics revealed that 63% were overweight or obese.

According to the Centers for Disease Control and Prevention, 66% of the general population in the U.S. is overweight or obese.

In 2005, she and her associates collected data from 663 HIV patients at Naval Medical Center in San Diego and National Naval Medical Center in Bethesda, Md., including duration of HIV infection, CD4

count, viral load, antiretroviral therapy, diabetes, and hypertension. They defined wasting as a body mass index of less than 20 kg/m<sup>2</sup>, overweight as a BMI of 25-29.9, and obesity as a BMI of 30 or greater, said lead author Dr. Crum-Cianflone, an HIV research physician with the TriService AIDS Clinical Consortium in San Diego.

The mean age of patients was 41 years, and 50% were white, 26% had hypertension, and 8% had diabetes. Some had been followed in the clinics since 1986.

Of the 663 patients, 46% were overweight, 17% were obese, and 3% met the definition of wasting. None of the study participants met the strictest criteria for wasting, which is a BMI of 18.5 or less.

At the time of diagnosis, 46% were overweight or obese. Over the course of their infection, 72% gained weight.

Multivariate analysis revealed two significant predictors of increasing BMI: younger age at HIV diagnosis and longer duration of HIV infection. "We also learned that people who gained weight were more likely to have high blood pressure," Dr. Crum-Cianflone said during a press briefing.

Patients with high CD4 counts also were more likely to be overweight than were those with lower CD4 counts.

No association was observed between the use of highly active antiretroviral treatment (HAART) and weight gain.

Specific reasons for the rise in obesity among HIV patients are unclear. Dr. Crum-Cianflone said it may partly have to do with

## 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:

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/m<sup>2</sup>) 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/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.

### DOSEAGE 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  
a business of sanofi-aventis U.S. LLC  
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DR. CRUM-CIANFLONE

the fact that with improved HAART, HIV has essentially become a chronic condition with a longer expected life span.

In another study presented at the meeting, researchers at Washington University in St. Louis found that HIV-positive patients aged 50 and older were no more likely to have heart disease or diabetes than a group of age-matched HIV-negative controls from the general population.

"Although our study was small, we can probably begin to reassure people living with HIV who are over the age of 50 and clinicians looking after them that comorbidities and toxicities to medications, such as dyslipidemia, diabetes mellitus, and osteoporosis, may not be increased compared to the general U. S. population as it ages," lead study author Dr. Nur Onen said in an interview at the meeting.

She and her associates compared the incidence of heart disease, diabetes, high blood pressure, osteoporosis, and other conditions between a group of 70 HIV-positive patients aged 50 and older on HAART and a group of HIV-negative controls from the National Health and Nutrition Examination Survey matched by age, gender, race, smoking status, and BMI. The mean age of patients was 56 years, 86% were male, and 66% were white. Their mean BMI was 25, and 90% were on HAART (a mean duration of 7 years, 91% with full viral suppression).

Dr. Onen, an infectious diseases fellow at the university, reported that while hypertension was significantly more prevalent in HIV-positive patients than in controls (51% vs. 31%, respectively), there were no differences in the prevalence of heart disease (10% vs. 14%), diabetes (13% vs. 11%), or osteoporosis (2% in each group).