

Lactamide-MEA Gel Looks Good for Cradle Cap

BY SHARON WORCESTER
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RHODES, GREECE — Lactamide monoethanolamine, a lactic acid-derived humectant commonly found in over-the-counter lotions and bath gels, appears to be beneficial for the treatment of cradle cap, Virginie Ribet, Ph.D., said at the 15th Congress of the European Academy of Dermatology and Venereology.

A lactamide monoethanolamine-based

gel was safe, effective, and well tolerated in a randomized, controlled, open-label phase III study of 124 infants with mild to moderate seborrheic dermatitis of the scalp, Dr. Ribet of Pierre Fabre Research Institute in Ramonville Saint Agne, France, reported in a poster presentation.

Lesional scores, which were based on the area of involvement and intensity of scaling on four zones of the scalp, decreased significantly more in the 63 infants in the treatment group, compared with

the 61 infants in the control group, at day 7 (55% vs. 42%), day 21 (81% vs. 70%), and day 42 (96% vs. 86%).

A lesional score of 0 was noted in 73% of infants in the treatment group at the end of the study, compared with 50% of those in the control group, said Dr. Ribet who did not disclose interest in the gel.

Parents of the 63 infants in the treatment group were asked to apply the gel, followed by a soft shampoo, daily for the first week, then two to three times per

week thereafter for the course of the study. Only soft shampoo was applied to the 61 infants in the control group.

The gel was safe and well tolerated in both groups. Erythema was significantly improved from baseline to study end in both groups.

Both the investigators and the parents reported satisfaction on overall assessment; the product led to recovery or definite improvement in all treated infants, she noted. ■

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).

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.

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

a business of sanofi-aventis U.S. LLC
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Country of Origin Canada

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Experimental Drug Thwarts Toenail Fungus

PARIS — An experimental antifungal drug appears to significantly reduce toenail fungal infection and encourage clear nail growth, according to a poster presented at the annual meeting of the European Society for Dermatological Research.

AN2690, under development by Anacor Pharmaceuticals Inc., is thought to work by penetrating the nail plate and blocking fungal protein synthesis, wrote Dr. Karl Beutner, chief medical officer of Anacor.

He and his associates recruited 60 patients with distal, subungual onychomycosis of at least one great toenail (20%-60% involvement).

The patients were sequentially assigned to be treated with 5% AN2690 or 7.5% AN2690.

Patients underwent a screening evaluation and evaluations at baseline (day 1) and at days 14, 30, 60, and 90. Potassium hydroxide (KOH) wet mounts and fungal cultures were performed on the treatment-targeted great toenail at each visit. Clear nail growth—determined by measuring nondiseased nail in sequential digital photos—was measured only for the targeted great toenails (days 1, 30, and 90).

At day 90, there was a 63% reduction in septate hyphae observed in the 5% AN2690 group and a 60% reduction in the 7.5% AN2690 group, compared with baseline, based on KOH staining of nail bed samples. Likewise, positive culture rates dropped by 97% and 94%, vs. baseline, for the 5% and 7.5% groups, respectively.

For the 5% group, the average clear nail growth was 1.8 mm at day 30 and 2.6 mm at day 90. For the 7.5% group, the average clear nail growth was 1.2 mm at day 30 and 2.0 mm at day 90. Overall, 67% of patients were considered to be responders (defined as at least 1 mm of nail growth by day 90).

Local skin reactions were observed in 10 patients (6 in the 5% group and 4 in the 7.5% group). Resolution occurred between days 12 and 35.

—Kerri Wachter