

Clinicians Echoed 2006 FDA Approval of RotaTeq

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More than 80% of pediatricians surveyed in January and February 2006 said they would recommend the rotavirus vaccine, reported Dr. Allison Kempe from the University of Colorado, Denver, and colleagues in the January 2007 issue of Pediatrics.

The vaccine in question is RotaTeq (Merck & Co.) and was approved by the

Food and Drug Administration on Feb. 3, 2006—in the middle of the survey period. It is not clear what percentage of the survey's 305 mail and Internet respondents answered before or after the approval (Pediatrics 2007;119:1-10).

The FDA approval subsequently was followed by a recommendation from the Centers for Disease Control's Advisory Committee on Immunization Practices (ACIP) for routine use of the vaccine in infants in August 2006 (dose one at 12

weeks of age and all three vaccinations by 32 weeks of age, with at least a 4- to 10-week interval between doses), and a similar recommendation from the American Academy of Pediatrics shortly afterward, in November.

"The findings of this nationally representative survey demonstrate that pediatricians recognize the burden of rotavirus disease and the value of a rotavirus vaccine for children in this country," wrote the authors. Of the respondents, 51%

strongly agreed that the burden of rotavirus disease was sufficient in the United States to justify the need for a vaccine, while 83% agreed the burden in developing countries was sufficient to justify a global need.

When asked what they would recommend in the event that ACIP recommended routine use of the vaccine, 50% of the respondents said they would strongly recommend the vaccine and 34% said they would recommend it but not strongly.

Additionally, 52% said they would begin using the vaccine within 6 months of the recommendation, 27% from 6 months to 1 year, 7% from 1 to 2 years, and 1% more than 2 years after the recommendation. A total of 0.3% said they would never use the

vaccine, and 13% were unsure. The most common reasons given for delaying for more than 6 months from the recommendation were as follows: determining that insurers would cover the vaccine; waiting to see if there

Of the survey respondents, 51% strongly agreed that the burden of rotavirus disease was sufficient in the United States to justify the need for a vaccine.

were adverse effects reported; and ensuring that vaccine supplies were adequate.

Respondents indicated that the three most commonly perceived barriers to implementing rotavirus vaccine recommendations were their concerns about uneven coverage by insurers, concerns about lack of adequate reimbursement, and parents' safety concerns in light of the withdrawal of the previous RotaShield (Wyeth Laboratories) vaccine from the market in 1999 because of its association with intussusception, wrote the authors.

"Implementation in this country will be greatly facilitated if lessons learned from the implementation of other recent new vaccines such as PCV7 [the heptavalent pneumococcal conjugate] vaccine are heeded," Dr. Kempe and her associates suggested.

"Some of the problems faced by pediatricians in the initial stages of implementation, including substantial delays in being able to bill for vaccines to insurers who have not yet changed their billing procedures to accommodate a new vaccine and unsynchronized timing of coverage between the public and private sectors, might well be ameliorated by an increased coordination between ACIP, vaccine manufacturers, and health plans before recommendation of a new vaccine," they concluded.

The surveyed physicians are representative of pediatricians in the AAP nationally in regards to practice characteristics, demographics, and location throughout the United States, they said. The response rate to the survey was high.

Dr. Kempe and associates indicated they have no conflicts of interest to disclose. The study was funded by a CDC grant. ■

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

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