



BY WILLIAM G. WILKOFF, M.D.

LETTERS FROM MAINE

This Shot Won't Hurt

If there is one quality that predominates among new parents, it is self-doubt. Fortunes have been made, (although not by me) in the publishing industry by tapping into the large and predictable market of

confidence-deficient neo-parents. I suspect that to some extent it's always been this way. While familiarity may breed contempt, unfamiliarity has always bred trepidation.

The drive to make babies is a powerful force we are comfortable with because Mother Nature does the driving. But we often feel she has abandoned us the moment she hands us that wet, wail-

ing, and totally dependent newborn.

While I am sure that back in the 1700's new parents worried, I suspect they suffered far less from self-doubt than new millennium parents. Several generations ago, new parents were surrounded by their families and grandparents who had been there, done that a dozen times. They grew up in large families and were familiar with what babies and children do.

Contrast this to the parents we see today. They are often geographically divorced from their own families. They come from small families, and may not have participated in raising their siblings, if they had them. They have delayed having children, and it may have been decades since they had any close contact with babies. Their only experience that is anywhere close to parenting has been raising a Labrador retriever. Although they may have been initially deluded that there will be some carryover, it takes only a few minutes to realize that parenting is a whole new ball game.

New parents are older and, to some extent, wiser. They have seen more and read more and know that the world presents much more to worry about than they imagined as teenagers. Of course, the media compounds this with horror stories about how even the most everyday events can go awry. We physicians unwittingly compound the situation with well-meaning suggestions about things like how long to breastfeed.

The bottom line is that new parents seriously need reassurance. Too few of them articulate this by asking, "Am I doing this right?" And too few of us answer the unasked question by unambiguously stating, "You're doing a great job!"

In a recent issue of AAP News (October 2009), Dr. Martin Stein and Dr. J. Lane Tanner reported on some findings from their study of 20 parent focus groups and 31 pediatric clinician focus groups. Among other things, they asked how an ideal pediatric practice would look. They observed, "Parents spoke to an issue that many doctors may be less aware of—how much they value the reassurance that the pediatrician or PNP can give, not only that their child is healthy, but also that they are doing a good job as parents."

Sometimes we feel that saying, "That's a good weight gain" or complimenting parents on their child's cuteness is sufficient. But I've found that it's not. Parents hear those platitudes from their family and even strangers in the grocery store checkout line all the time. There is nothing more powerful than a respected child health provider saying, "I just want to tell you that you're doing a nice job!"

It's even more important when things aren't going well. Be reassuring during those first few weight checks in the office for the mother who's struggling with a marginal milk supply or who has terribly sore nipples. One doesn't have to be specific. "I know you're worried about how the breastfeeding is going, but you are doing a very good job of parenting."

There are so few overconfident new parents that it is easy to recommend a shot of confidence at every well-child visit. I promise it won't hurt. ■

DR. WILKOFF practices general pediatrics in a multispecialty group practice in Brunswick, Maine. To comment, e-mail him at pdnews@elsevier.com.

BRIEF SUMMARY

ALTABAX™ (retapamulin ointment), 1%

The following is a brief summary only; see full prescribing information for complete product information.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Local Irritation

In the event of sensitization or severe local irritation from ALTABAX, usage should be discontinued, the ointment wiped off, and appropriate alternative therapy for the infection instituted [See Patient Counseling Information (17)].

5.2 Not for Systemic or Mucosal Use

ALTABAX is not intended for ingestion or for oral, intranasal, ophthalmic, or intravaginal use. ALTABAX has not been evaluated for use on mucosal surfaces [See Patient Counseling Information (17)].

5.3 Potential for Microbial Overgrowth

The use of antibiotics may promote the selection of nonsusceptible organisms. Should superinfection occur during therapy, appropriate measures should be taken.

Prescribing ALTABAX in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

The safety profile of ALTABAX was assessed in 2,115 adult and pediatric patients ≥9 months who used at least one dose from a 5-day, twice a day regimen of retapamulin ointment. Control groups included 819 adult and pediatric patients who used at least one dose of the active control (oral cephalixin), 172 patients who used an active topical comparator (not available in the US), and 71 patients who used placebo.

Adverse events rated by investigators as drug-related occurred in 5.5% (116/2,115) of patients treated with retapamulin ointment, 6.6% (54/819) of patients receiving cephalixin, and 2.8% (2/71) of patients receiving placebo. The most common drug-related adverse events (≥1% of patients) were application site irritation (1.4%) in the retapamulin group, diarrhea (1.7%) in the cephalixin group, and application site pruritus (1.4%) and application site paresthesia (1.4%) in the placebo group.

Because clinical studies are conducted under varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice. The adverse reaction information from the clinical studies does, however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating rates.

Adults: The adverse events, regardless of attribution, reported in at least 1% of adults (18 years of age and older) who received

ALTABAX are listed in Table 1.

Table 1. Adverse Events Reported by ≥1% of Adult Patients Treated With ALTABAX in Phase 3 Clinical Studies

Adverse Event	ALTABAX N=1527 %	Cephalexin N=698 %
Headache	2.0	2.0
Application site irritation	1.6	<1.0
Diarrhea	1.4	2.3
Nausea	1.2	1.9
Nasopharyngitis	1.2	<1.0
Creatinine phosphokinase increased	<1.0	1.0

Pediatrics: The adverse events, regardless of attribution, reported in at least 1% of pediatric patients aged 9 months to 17 years who received ALTABAX are listed in Table 2.

Table 2. Adverse Events Reported by ≥1% in Pediatric Patients Aged 9 Months to 17 Years Treated With ALTABAX in Phase 3 Clinical Studies

Adverse Event	ALTABAX N=588 %	Cephalexin N=121 %	Placebo N=64 %
Application site pruritus	1.9	0	0
Diarrhea	1.7	5.0	0
Nasopharyngitis	1.5	1.7	0
Pruritus	1.5	1.0	1.6
Eczema	1.0	0	0
Headache	1.2	1.7	0
Pyrexia	1.2	<1.0	1.6

Other Adverse Events: Application site pain, erythema, and contact dermatitis were reported in less than 1% of patients in clinical studies.

7 DRUG INTERACTIONS

Co-administration of oral ketoconazole 200 mg twice daily increased retapamulin geometric mean AUC₍₀₋₂₄₎ and C_{max} by 81% after topical application of retapamulin ointment, 1% on the abraded skin of healthy adult males. Due to low systemic exposure to retapamulin following topical application in patients, dosage adjustments for retapamulin are unnecessary when co-administered with CYP3A4 inhibitors, such as ketoconazole. Based on in vitro P450 inhibition studies and the low systemic exposure observed following topical application of ALTABAX, retapamulin is unlikely to affect the metabolism of other P450 substrates.

The effect of concurrent application of ALTABAX and other topical products to the same area of skin has not been studied.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B. Effects on embryo-fetal development were assessed in

pregnant rats given 50, 150, or 450 mg/kg/day by oral gavage on days 6 to 17 postcoitus. Maternal toxicity (decreased body weight gain and food consumption) and developmental toxicity (decreased fetal body weight and delayed skeletal ossification) were evident at doses ≥150 mg/kg/day. There were no treatment-related malformations observed in fetal rats.

Retapamulin was given as a continuous intravenous infusion to pregnant rabbits at dosages of 2.4, 7.2, or 24 mg/kg/day from day 7 to 19 of gestation. Maternal toxicity (decreased body weight gain, food consumption, and abortions) was demonstrated at dosages ≥7.2 mg/kg/day (8-fold the estimated maximum achievable human exposure, based on AUC, at 7.2 mg/kg/day). There was no treatment-related effect on embryo-fetal development.

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, ALTABAX should be used in pregnancy only when the potential benefits outweigh the potential risk.

8.3 Nursing Mothers

It is not known whether retapamulin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ALTABAX is administered to a nursing woman. The safe use of retapamulin during breast-feeding has not been established.

8.4 Pediatric Use

The safety and effectiveness of ALTABAX in the treatment of impetigo have been established in pediatric patients 9 months to 17 years of age. Use of ALTABAX in pediatric patients is supported by evidence from adequate and well-controlled studies of ALTABAX in which 588 pediatric patients received at least one dose of retapamulin ointment, 1% [see Adverse Reactions (6), Clinical Studies (14)]. The magnitude of efficacy and the safety profile of ALTABAX in pediatric patients 9 months and older were similar to those in adults.

The safety and effectiveness of ALTABAX in pediatric patients younger than 9 months of age have not been established.

8.5 Geriatric Use

Of the total number of patients in the adequate and well-controlled studies of ALTABAX, 234 patients were 65 years of age and older, of whom 114 patients were 75 years of age and older. No overall differences in effectiveness or safety were observed between these patients and younger adult patients.

10 OVERDOSAGE

Overdosage with ALTABAX has not been reported. Any signs or symptoms of overdose, either topically or by accidental ingestion, should be treated symptomatically consistent with good clinical practice.

There is no known antidote for overdoses of ALTABAX.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential have not been conducted with retapamulin.

Retapamulin showed no genotoxicity when evaluated in vitro for gene mutation and/or chromosomal effects in the mouse lymphoma cell assay, in cultured human peripheral blood lymphocytes, or when evaluated in vivo in a rat micronucleus test.

No evidence of impaired fertility was found in male or female rats given retapamulin 50, 150, or 450 mg/kg/day orally.

17 PATIENT COUNSELING INFORMATION

Patients using ALTABAX and/or their guardians should receive the following information and instructions:

- Use ALTABAX as directed by the healthcare practitioner. As with any topical medication, patients and caregivers should wash their hands after application if the hands are not the area for treatment.
- ALTABAX is for external use only. Do not swallow ALTABAX or use it in the eyes, on the mouth or lips, inside the nose, or inside the female genital area.
- The treated area may be covered by a sterile bandage or gauze dressing, if desired. This may also be helpful for infants and young children who accidentally touch or lick the lesion site. A bandage will protect the treated area and avoid accidental transfer of ointment to the eyes or other areas.
- Use the medication for the full time recommended by the healthcare practitioner, even though symptoms may have improved.
- Notify the healthcare practitioner if there is no improvement in symptoms within 3 to 4 days after starting use of ALTABAX.
- ALTABAX may cause reactions at the site of application of the ointment. Inform the healthcare practitioner if the area of application worsens in irritation, redness, itching, burning, swelling, blistering, or oozing.

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