

Ceftriaxone Alone Can't Treat Mastoiditis

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SAN FRANCISCO — Ceftriaxone by itself is not sufficient for acute or chronic pediatric mastoiditis, according to a group of emergency physicians who compared cases treated before and after adoption of the pneumococcal conjugate vaccine.

The proportion of *Streptococcus pneumoniae* isolates that were resistant to ceftriaxone increased from 7% in the pre-PCV

era to 30% afterward, Dr. Dewesh Agrawal reported in a poster at the annual meeting of the Pediatric Academic Societies.

Although *S. pneumoniae* remained the most frequent cause of acute mastoiditis, *Pseudomonas aeruginosa* was found in five of seven chronic cases in which children had ear disease for more than 3 weeks before coming to the emergency department. In addition, *P. aeruginosa* was the second most common cause of acute mastoiditis.

"That's a really bad bug, and ceftriaxone

isn't good enough for that," Dr. Agrawal, of the Children's National Medical Center in Washington, said in an interview.

The study compared 68 cases seen from January 1995 through December 2000 with 54 cases seen from January 2005 through April 2005. Patients ranged in age from 30 days to 18.2 years with a median age of 5.4 years. Over half (54%) were female.

All told, 93 patients (76%) had acute mastoiditis, and 29 patients (24%) had chronic mastoiditis. In all, 75 children

(61%) went on to have surgery; among these, myringotomy tubes were placed in ears (57 children) and/or mastoidectomy was performed (56 children).

The investigators were able to determine the etiologic agents causing mastoiditis in 60 children (49%). The other pathogens identified in the study were *Staphylococcus aureus*, *Staphylococcus pyogenes*, and *Haemophilus influenzae* (acute only).

Dr. Agrawal said the investigators were surprised to find that the proportion of mastoiditis cases caused by *S. pneumoniae* did not decrease in the PCV era. *S. pneumoniae* accounted for 21% (14 of 68) of the

*Vusion™ Ointment is indicated for the adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast) in immunocompetent pediatric patients 4 weeks and older. A positive fungal culture for *C. albicans* is not adequate evidence of candidal infection since colonization with *C. albicans* can result in a positive culture. The presence of candidal infection should be established by microscopic evaluation prior to initiating treatment.

Vusion™ Ointment should be used as part of a treatment regimen that includes measures directed at the underlying diaper dermatitis, including gentle cleansing of the diaper area and frequent diaper changes.



Vusion™ Ointment should not be used as a substitute for frequent diaper changes. Vusion™ Ointment should not be used to prevent the occurrence of diaper dermatitis, since preventative use may result in the development of drug resistance.

The safety of Vusion™ Ointment when used for longer than 7 days is not known.

Vusion™ Ointment should not be used in cases of known hypersensitivity to any of its components, in which case treatment should be discontinued.

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Ointment

BRIEF SUMMARY

Rx only.
FOR TOPICAL USE ONLY.
NOT FOR OPHTHALMIC, ORAL, OR INTRAVAGINAL USE.

INDICATIONS AND USAGE

VUSION Ointment is indicated for the adjunctive treatment of diaper dermatitis only when complicated by documented candidiasis (microscopic evidence of pseudohyphae and/or budding yeast), in immunocompetent pediatric patients 4 weeks and older. A positive fungal culture for *Candida albicans* is not adequate evidence of candidal infection since colonization with *C. albicans* can result in a positive culture. The presence of candidal infection should be established by microscopic evaluation prior to initiating treatment.

VUSION Ointment should be used as part of a treatment regimen that includes measures directed at the underlying diaper dermatitis, including gentle cleansing of the diaper area and frequent diaper changes. **VUSION Ointment should not be used as a substitute for frequent diaper changes. VUSION Ointment should not be used to prevent the occurrence of diaper dermatitis, since preventative use may result in the development of drug resistance.**

CONTRAINDICATIONS

VUSION Ointment is contraindicated in those patients with a history of sensitivity reactions to any of its components. It should be discontinued if hypersensitivity is noted.

GENERAL USE

General: If irritation occurs or if the disease worsens, use of the medication should be discontinued, and the health care provider should be contacted. For external use only. VUSION Ointment is for topical use only, and not for ophthalmic, oral or intravaginal use.

The safety and efficacy of VUSION Ointment has not been demonstrated in immunocompromised patients, or in infants less than 4 weeks of age (premature or term).

The safety and efficacy of VUSION Ointment have not been evaluated in incontinent adult patients. **VUSION Ointment should not be used to prevent the occurrence of diaper dermatitis, such as in an adult institutional setting, since preventative use may result in the development of drug resistance.**

Information for Patients: Patients using VUSION Ointment should receive the following information and instructions: (See Patient Package Insert)

1. VUSION Ointment is to be used only for diaper dermatitis that is complicated by documented candidiasis (i.e. documented by microscopic testing).
2. VUSION Ointment should not be used as a substitute for frequent diaper changes.
3. VUSION Ointment should not be used to prevent diaper dermatitis.
4. VUSION Ointment should not be used long term.
5. VUSION Ointment is to be used only as directed by the health care provider.
6. VUSION Ointment is for external use only. It is not to be used orally, intravaginally, or for the eyes.
7. Gently cleanse the diaper area with lukewarm water or a very mild soap and pat the area dry with a soft towel before applying VUSION Ointment.
8. Gently apply VUSION Ointment to the diaper area with the fingertips after each diaper change. Do not rub VUSION Ointment into the skin as this may cause additional irritation.
9. Thoroughly wash hands after applying VUSION Ointment.
10. Treatment should be continued for 7 days, even if there is improvement. Do not use VUSION Ointment for longer than 7 days. If symptoms have not improved by day 7, see your health care provider.
11. VUSION Ointment should not be used on children for whom it is not prescribed.

Drug Interactions: Drug-drug interaction studies were not conducted. Although women who take a warfarin anticoagulant and use a miconazole intravaginal cream or suppository may be at risk for developing an increased prothrombin time, international normalized ratio (INR) and bleeding, the potential for this interaction to occur between warfarin and VUSION Ointment is unknown.

Carcinogenesis, Mutagenesis, Impairment of fertility: Studies to evaluate the carcinogenic potential of VUSION Ointment in animals have not been performed.

Miconazole nitrate was negative in a bacterial reverse mutation test, a chromosome aberration test in mice, and micronucleus assays in mice and rats.

Miconazole nitrate had no adverse effect on fertility in a study in rats at oral doses of up to 320 mg/kg/day, which is 89 times the maximum possible topical exposure of caregivers, assuming 100% absorption.

Pregnancy Category C:

There are no adequate and well-controlled studies of VUSION Ointment in pregnant women. Miconazole nitrate administration has been shown to result in prolonged gestation and decreased numbers of live young in rats and in increased number of resorptions and decreased number of live young in rabbits at oral doses of 100 mg/kg/day and 80 mg/kg/day, which are 28 and 45 times the maximum possible topical exposure of caregivers, respectively, assuming 100% absorption.

Pregnant women should exercise appropriate precautions when administering the product.

Nursing Mothers: Safety and efficacy of the product have not been established in nursing mothers. It is not known if the active components of VUSION Ointment may be present in milk. Nursing mothers should exercise appropriate precautions when administering the product.

Pediatric Use: Efficacy was not demonstrated in infants less than 4 weeks of age. Use in infants below the age of 4 weeks is not recommended. Safety and efficacy have not been established in very-low-birth-weight infants.

VUSION Ointment should not be used to prevent diaper dermatitis.

The safety of VUSION Ointment when used for longer than 7 days is not known.

Geriatric Use: Clinical studies of VUSION Ointment did not include any subjects aged 65 and over. Safety and effectiveness in a geriatric population have not been evaluated.

ADVERSE REACTIONS

A total of 835 infants and young children were evaluated in the clinical development program. Of 418 subjects in the VUSION Ointment group, 58 (14%) reported one or more adverse events. Of 417 subjects in the zinc oxide/white petrolatum control group, 85 (20%) reported one or more adverse events. Adverse events that occurred at a rate of $\geq 1\%$ for subjects who were treated with VUSION were approximately the same in type and frequency as for subjects who were treated with zinc oxide/white petrolatum ointment.

The potential for dermal toxicity of VUSION Ointment formulation was investigated in healthy adult volunteers in four topical safety studies. These studies were conducted to assess the potential for contact phototoxicity, photoallergy, sensitization, and cumulative irritation potential. Phototesting was conducted with UV-A only. Results indicated that VUSION Ointment did not induce a contact dermal phototoxic response, contact dermal photoallergic response, or contact dermal sensitization in adult subjects. In addition, VUSION Ointment did not show any evidence of cumulative irritation potential in adult subjects.

OVERDOSAGE

VUSION Ointment is intended for topical use only. Young children are at risk for accidentally ingesting VUSION Ointment. A health care provider or poison control center should be contacted in the event of accidental ingestion.

Keep out of reach of children.
For additional information, please call toll free 1-866-440-5508.

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DSM Pharmaceuticals, Inc.
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'That's a really bad bug [*Pseudomonas aeruginosa*], and ceftriaxone isn't good enough for that.'

DR. AGRAWAL

early cases and 19% (10 of 54) of the later cases. He speculated that the study may have been done "too soon" in that many of the older children in the post-PCV-era cohort turned out not to have been given the vaccine.

Physicians were much more likely to choose empirical parenteral combination therapy with ceftriaxone when treating acute mastoiditis: It was used in 49% of acute cases vs. 10% of chronic cases.

Empirical parenteral combination therapy with ceftriaxone was used more often in the post-PCV era as well (57% of the later cases vs. 24% in the earlier cohort). Clindamycin use, either alone or in combination, also increased from 12% of the early cases to 22% of later cases.

Even so, Dr. Agrawal and his colleagues reported that, based on the etiologic findings and antibiotic sensitivities, only 43% of the first-choice antibiotics were appropriate in the vaccine era. "In the post-PCV era, or in chronic mastoiditis, empirical antimicrobial therapy with ceftriaxone alone is not appropriate," they concluded.

"With acute ear disease, you've got to add on other antibiotics," Dr. Agrawal said.

