

# Opposition Growing Against Azithromycin for Infections

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NEW YORK CITY — Treatment guidelines increasingly recommend that certain antibiotics, particularly the macrolide azithromycin, no longer be used to treat many common infections. Inappropriate use has led to widespread antibiotic resistance and is contributing to the emergence of super bugs.

At least one prominent emergency medicine expert suggests that the drug not be used at all.

"If we don't stop, we're not going to have good antibiotics in the future," warned Joseph Lex, MD, from Temple University in Philadelphia, here at the American Academy of Emergency Medicine (AAEM) 20th Annual Scientific Assembly. "Every country that has recommended the use of narrow-spectrum antibiotics instead has seen a fall in their resistance rates. We just have to get to the point where we do the same thing."

Dr. Lex is hardly a lone voice in this call to move away from the abuse of broad-spectrum antibiotics. Current guidelines present a chorus of similar opinions.

Azithromycin was developed in 1980 and has been marketed in the United States since 1991. As of 2011, it is the most commonly prescribed antibiotic. The current indications for azithromycin are acute bacterial exacerbations of chronic pulmonary disease, acute bacterial sinusitis, community-acquired pneumonia, pharyngitis, tonsillitis, uncomplicated skin and skin structure infection, urethritis and cervicitis, and genital ulcer disease.

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However, just last year, the Canadian Pediatric Society strongly recommended that azithromycin not be used to treat acute pharyngitis, otitis media, or community-acquired pneumonia ( *Paediatr Child Health*. 2013;18:311-313).

That guidance did not recommend that clinicians consider not using it — it's recommendation is "do not use," stressed Dr. Lex. The only exceptions for azithromycin use are life-threatening beta-lactam allergy and pneumonia caused by an atypical bacteria.

"The long half-life of azithromycin contributes to the development of resistance," he explained. The way the drug is being used, "you're likely to get a subinhibitory nasal pharyngeal concentration, so these kids actually become carriers of azithromycin-resistant pneumococci."

## **Alternatives**

The data show that macrolides have limited efficacy against 2 of the most common bacterial pathogens associated with acute otitis media — *Haemophilus influenzae* and *Streptococcus pneumoniae*.

Macrolide resistance is not a potential, it is a reality, and rates are increasing. "There is a better drug than azithromycin for every one of the indications," Dr. Lex pointed out.

The rhinosinusitis guidelines issued in 2012 by the Infectious Disease Society of America (IDSA) recommend considering antibiotics if symptoms persist beyond 10 days, are severe or worsening, or if there is high fever

and nasal discharge for at least 3 days ( *Clin Infect Dis.* 2012;54:1041-1045). Macrolides are not recommended at all. "Roughly 30% of these cases will be resistant to azithromycin," said Dr. Lex.

The acute bacterial sinusitis clinical practice guidelines from the American Academy of Pediatrics recommend amoxicillin with or without clavulanate for patients 1 to 18 years of age ( *Pediatrics.* 2013;132:e262-e280). There is no recommendation for macrolides.

For group A streptococcal pharyngitis, the 2012 IDSA guidelines recommend first-line treatment with penicillin, and macrolides only for patients allergic to penicillin. "In the United States, 5% to 8% of pharyngeal isolates of group A strep are resistant to a macrolide," Dr. Lex reported.

For children older than 2 years of age with bacterial pediatric pneumonia, the 2011 IDSA clinical practice guidelines recommend first-line treatment with amoxicillin with or without clavulanate ( *Clin Infect Dis.* 2011;53:e25-e76). Second-line choices do not include macrolides. "We know that 80% of pediatric pneumonia under the age of 2 is viral," said Dr. Lex, adding that azithromycin has no activity against a virus.

In the 2007 consensus guidelines on the management of community-acquired pneumonia in adults, macrolides in combination with doxycycline can be considered in previously healthy adults who have not recently taken an antibiotic ( *Clin Infect Dis.* 2007;44[Suppl 2]:S27-S72). "This is before our concern about widespread macrolide overuse, and they're still not recommending using a macrolide alone," Dr. Lex noted.

Recently, "there has been a spate of new treatment recommendations that have demoted the use of azithromycin, especially in pediatrics," said Dr. Lex.

"Unfortunately, physicians get into a groove — a habit of prescribing a particular antibiotic for a particular condition. Right now, there's at least a year or 2 of lag time before these recommendations are adopted."

### **Patient Education**

"Part of the reason for the overuse of azithromycin is pressure from the patients," Michael Epter, DO, emergency medicine physician in Las Vegas and education chair for the AAEM, told *Medscape Medical News*. "Patients come in with the symptomatology of a respiratory tract infection — which is commonly due to virus — yet they will insist on receiving an antibiotic."

When this happens, azithromycin is usually the agent prescribed. "With the once-a-day, 5-day regimen, patient compliance is high. Doctors like that." Even newer-generation macrolides are not as easy to use.

This time of year, "patients come in with your basic winter cold. In the majority of cases, it's a viral-related illness and antibiotics are only effective for their placebo effect," said Dr. Epter.

Azithromycin is also overused in sinusitis, which has repeatedly been shown to be the result of a viral infection. In fact, "94 of 100 patients will show no change in their symptoms when treated with an antibiotic, yet the use of azithromycin in sinusitis is rampant."

But no matter what the data say, it is a hard sell to convince patients to settle for over-the-counter symptom relief. "I try to explain it to them," Dr. Epter lamented, "but it's an uphill battle."

He said he first tries to explain the consequences of antibacterial resistance, and how treatment for a cold can complicate treatment for a more serious subsequent problem, such as pneumonia. Unfortunately, he said, more often than not, patients aren't happy until they get a prescription.

The easiest solution is point-of-care rapid testing to properly identify and narrowly treat the offending bug. However, "that technology is not yet being aggressively adopted in hospitals," said Dr. Epter. "We're still a couple of years away from getting to that point."

*Dr. Lex and Dr. Epter have disclosed no relevant financial relationships.*

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