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Public Citizen

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Joan Claybrook, President

August 3, 1999

Donna Shalala
Secretary
Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC

Dear Secretary Shalala:

We are writing to make you aware of an apparent effort by Pfizer, Inc. to counter the CDC guidelines for the treatment of ear infections in children and cause millions of dollars of unnecessary spending on antibiotics. According to an internal company document that we have obtained (see attached), Pfizer appears to have launched a campaign to convince doctors to ignore Centers for Disease Control and Prevention (CDC) recommendations favoring the effective and inexpensive antibiotic amoxicillin (full course for 10 kg child = $18.98, retail, CVS) over Pfizer's drug azithromycin (full course for 10 kg child = $34.69, retail). The Pfizer document explicitly states the purpose of the campaign: "The focus is to counter the CDC guidelines." We urge you to inform the nation's pediatricians, family practitioners and nurse practitioners of this campaign so they are not duped into draining the Medicaid program of needed resources and of wasting large amounts of money on treating other patients with this needlessly expensive and second rate drug for ear infections.

At issue are CDC recommendations developed after consultation with a working group of national experts and published in the *Pediatric Infectious Disease Journal* in January 1999.[1] The recommendations address treatment options at a time of increasing antibiotic resistance to the most important cause of ear infections, the bacteria pneumococcus. The CDC concluded that:

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[1] Dowell S, et al. Acute otitis media: management and surveillance in an era of pneumococcal resistance. *Pediatric Infect Disease Journal* 1999;18(1):1-9.

* Amoxicillin, the most commonly used and least expensive of antibiotics considered, remains the first choice for the treatment of uncomplicated ear infections. The experts recommended increasing the dosage of amoxicillin for some children to overcome drug-resistant pneumococcus, saying "no oral antimicrobial agent currently available would be expected to consistently eradicate penicillin nonsusceptible pneumococcus better than amoxicillin."

* When amoxicillin fails, appropriate treatment options are drugs that treat both resistant pneumococcus and other possible causes of ear infections. These include certain other drugs in the penicillin and cephalosporin families. One of these drugs is given as an injection and can achieve higher levels of drug in the middle ear than amoxicillin.

* Drugs in the family of macrolides (such as azithromycin), however, offer no advantage over amoxicillin in initial treatment of ear infections and are unproven for treatment failures.

In the months since publication of the CDC-sponsored recommendations, no new research or significant opposition from experts have undermined these conclusions.

Yet we have become aware of an apparent national campaign by Pfizer, the maker of the macrolide drug azithromycin (known as Zithromax) to counter the CDC guidelines, evidently by encouraging physicians and other primary caregivers of children to listen to inaccurate presentations by teleconference.

Pfizer's financial motive to counter the CDC guidelines is as massive as it is obvious. Ear infections are responsible for about 25 million office visits in the United States--more than for any other diagnosis in pediatrics.[2] Over the past several years, Pfizer has aggressively marketed azithromycin to pediatricians, distributing the drug's mascot (a zebra) as dolls and attachments to stethoscopes and using wrap-around advertisements that arrive covering major pediatric publications such as *American Academy of Pediatric News*. Pfizer is well known as a company that sponsors countless promotional events and lunches for physicians. At least one of these events violated the drug manufacturers code of marketing ethics.[3]

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[2] Otitis Media. Behrman: Nelson Textbook of Pediatrics, 15th ed., W. B. Saunders Company, 1996, p. 1814.

[3] Sharfstein J. Pfizer Night at Boston Billiards. *New England Journal of Medicine* 1997; 337(2):134.

The overall zithromax campaign has paid off handsomely for Pfizer--to the tune of about $1 billion each year worldwide (including its use for conditions besides ear infections).[4] So what to do when a consensus panel of experts says your drug doesn't work consistently enough to be recommended for the most common condition of childhood?

According to information we've obtained, the answer is to fight back--hire your own experts and encourage practitioners to listen to Pfizer-sponsored presentations that illegitimately criticize the CDC recommendations (see attached document).

We tuned in to one such presentation that ran for over one month to the beginning of July to hear Dr. Russell Steele, a pediatric infectious disease specialist at the Louisiana State University School of Medicine claim:

1. *"If we increase the amoxicillin resistance to what we are seeing today, that is to between 50 and 60 percent, then the failure rate [for amoxicillin] anticipated would be 1 in 4 to 1 in 3."*

Dr. Steele cites no evidence to support his claim that 25 to 33 percent of all children with ear infections will not respond to amoxicillin. That's because there have not been any such data published or presented.

Looking only at cases of the most highly resistant pneumococcus, if amoxicillin fails in a significant proportion of cases, other oral antimicrobial drugs (such as macrolides) will also fail. That's because, as the CDC noted, amoxicillin is the best available oral antibiotic for resistant pneumococcus.

Indeed, the most recent available evidence suggests that Pfizer's drug azithromycin may have a microbiological failure rate of as high as 60 percent. Data presented from an international multicenter trial in May 1999 at the European Society for Pediatric Infectious Diseases conference showed that azithromycin killed the bacteria in just 39 percent of ear infections in children.[5]

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[4] Galewitz P. SmithKline's Augmentin beats Pfizer's Zithromax in antibiotic battle. AP business wire, May 4, 1999.

[5] Leibovitz E, Dagan R, Jacobs MR, et al. Bacteriological and clinical response in acute otitis media: amoxicillin/clavulanic acid vs. azithromycin. Paper presented at the 17th annual meeting of the European Society for Pediatric Infectious Diseases in Greece, May 19-21, 1999.

2. *"If the failure rate [of amoxicillin] is unacceptable, then macrolides and cephalosporins would be considered."*

This suggestion to use macrolides for resistant pneumococcus is unjustifiable. As the consensus panel makes clear, macrolides do not have proven efficacy against resistant pneumococcus and are not recommended when amoxicillin fails. In fact, the potential for increasing resistance to macrolides is a very serious concern. A recent study of pneumococcus in the noses of healthy Italian children found a rate of macrolide resistance of 40 percent, compared to a rate of penicillin (or amoxicillin) resistance of just 5 percent.[6]

3. *"Another option is starting with a macrolide or cephalosporin as first line therapy."*

This is an indefensible and expensive proposition. Indefensible, because azithromycin and other macrolides have poor proven efficacy against resistant pneumococcus. Expensive, because only about 5 percent of initial ear infections are now treated with azithromycin--compared to about 65 percent with amoxicillin.[7] Because azithromycin is at least 50 to 100 percent more expensive than amoxicillin (depending on the dosing), using azithromycin as a first line therapy would add millions of dollars of needless expense to the health care system.

4. *"Most children will respond to macrolides even if the laboratory tells you [the bacteria] is resistant."*

Since most ear infections clinically resolve on their own, with or without antibiotic therapy,[8] it is true that most children taking azithromycin will also feel better. This isn't saying very much about the drug, however. From a microbiologic point of view, as noted above, the most recent evidence suggests that azithromycin frequently fails to successfully eradicate the organisms that cause ear infections.

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[6] Principi N, et al. Risk factors for the carriage of respiratory pathogens in the nasopharynx of healthy children. *Pediatric Infectious Disease Journal* 1999;18: 517-23.

[7] Thompson D, et al. Management of otitis media among children in a large health insurance plan. *Pediatric Infectious Disease Journal* 1999;8: 239-44.

[8] Berman S. Otitis Media in Children. *New England Journal of Medicine* 1995;332:1560-5.

Moreover, the CDC recommendations state: "Unlike the graded resistance to [penicillin and cephalosporin antibiotics], which may be overcome by increasing the dose, when macrolide resistance is present these agents should not be used."

5. *"With the way things are going, I think we'll have to probably abandon even the high dosage [of amoxicillin]."*

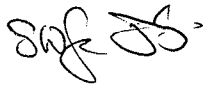
Less than six months after the CDC concluded that "amoxicillin is the best oral antimicrobial agent in clinical use for treating [resistant pneumococcus]," a Pfizer sponsored presenter is predicting, without presenting any evidence, that the drug will have to be abandoned! Of course, the use of high-dose amoxicillin may eventually lead to the development and spread of significant pneumococcal resistance. (The use of any antibiotic carries the risk of resistance.)

But the CDC, after reviewing the recommendations of experts from around the country, has concluded that amoxicillin remains the best oral treatment for ear infections in children, with azithromycin offering no additional advantage.

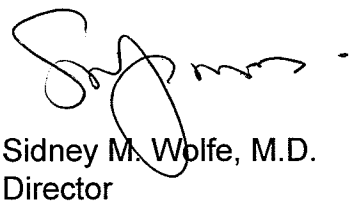
In summary, Pfizer appears to have launched an unprecedented campaign to counter the CDC recommendations for treatment of ear infections, a campaign that if successful, would leave children no better off but would cost the health care system millions of dollars. We urge you to defend these recommendations and protect the Medicaid budget and total health expenditures by informing primary care providers of children of this inappropriate marketing campaign.

cc: David Satcher, M.D., Ph.D.
Surgeon General of the United States

Sincerely,



Joshua Sharfstein, M.D.
Fellow in General Pediatrics
Boston Medical Center



Sidney M. Wolfe, M.D.
Director
Public Citizen's Health Research Group

MID-ATLANTIC STEERE
TELENET SCHEDULE
MAY-JULY 1999

May 6
Zithromax O/S

1:15PM EST
Otitis Media: Antibiotic Resistance and Treatment Alternatives
Stanford Shulman, MD
Chief of Infectious Diseases
Children's Memorial Hospital, Chicago
Professor of Pediatrics
Northwestern University

Day of: (800) 779-9311 Password: Shulman
96 Hour Playback: (800) 841-4034
Playback Password: 4848

Target Audience: Pediatricians or PCP's who treat pediatric patients.
The focus is to counter the CDC guidelines

May 12
Viagra
Cardura

12:15PM EST
Men's Health Issues Entering the New Millennium
Dominick Carbone, MD
Asst. Professor of Urology/Surgery
Bowman Gray School of Medicine
Wake Forest University

Day of: 800-946-0705 Password: Carbone
7 Day Playback: 888-707-8783 Conf. Code: 635527

Target Audience: Primary Care Physicians

Three July 99

May 18
Zithromax O/S

12:15PM EST
Otitis Media: What's Common is not Always Easy
Russell Steele, MD
Professor and Vice Chairman of Pediatrics
Division Head of Infectious Diseases
LSU School of Medicine and Children's Hospital

Day of: 888-567-7962 Password: Dr. Steele
1 Month Playback: 888-567-0844 Conf. Code: 685348

Target Audience: Pediatricians of PCP's who treat pediatric patients.
The focus is to counter the CDC guidelines.

Three July 99

May 25
Glucotrol XL

12:15PM EST
Type 2 Diabetes Management after the U.K P.D.S. Study