

Will Avilamycin Convert Zircine into Zerocine?

To the Editor: Avilamycin and evernimicin (Zircine), which belong to the everninomicin class of drugs, are oligosaccharide antibiotics active against numerous gram-positive bacteria, including emerging pathogens such as glycopeptide-resistant enterococci, methicillin-resistant staphylococci, and penicillin-resistant pneumococci (1,2). The two drugs share the same mode of action—inhibition of translation—by binding to the same target in the large 50S ribosomal subunit (3). As a result, they also display cross-resistance: bacteria resistant to avilamycin are resistant to evernimicin (and vice versa), but not to other classes of drugs (4). Two mechanisms of resistance to this class of drugs are amino-acid substitution in ribosomal protein L16 (5) and mutations in the peptidyltransferase domain of 23S ribosomal RNA (6).

Avilamycin has been used in Europe for several years as a growth promoter for food animals, particularly pigs. Enterococci resistant to everninomycins have been isolated from animals receiving avilamycin as a food additive (4). Evernimicin is being evaluated as a human therapeutic agent. Indirect evidence indicates that the use as growth promoters of antibiotics that display cross-resistance with those used in human therapy contributes to antibiotic resistance in bacteria responsible for human infections (7). As early as 1969, a recommendation was published in the United Kingdom that antibiotics used to treat infections in humans not be used as animal food additives (8). In 1999, four antibiotics were banned as food additives in the European community.

Antibiotic resistance in human pathogens has become a major health issue, complicated by the fact that no new class of drugs has been introduced for human therapy in the last 25 years. Since the use of avilamycin in animals has favored selection of enterococcal strains that are cross-resistant to evernimicin (4), these bacteria can colonize the human gut or form a pool of resistance genes that can spread to human commensals or pathogens (9). The continued use of avilamycin as a growth promoter is likely to diminish the effectiveness of

evernimicin if Zircine or any member of the class is used for human therapy. Since everninomycins will be prescribed mainly for infections due to multiresistant gram-positive cocci, avilamycin should be prospectively banned as an animal growth promoter.

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References

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