Proposed susceptibility testing criteria for AZD2563, a novel long-acting oxazolidinone

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Introduction

- During the last several decades, there has been an increase in the number of Gram-positive pathogens responsible for clinical infections and consequently has led to a rise in the number of types of antimicrobial resistances found among those pathogens.
- Depending on the geographical location, it is not uncommon to see oxacillin-resistant or glycopeptide-intermediate staphylococci, vancomycin-resistant enterococci, and penicillin- and macrolide-resistant pneumococci clinical isolates.4 With the continuing increase in multi-drug resistances there has been a push to develop new and novel antimicrobial agents such as the oxazolidinones.
- The oxazolidinones, which include the already licensed linezolid, work by inhibiting bacterial protein synthesis by stopping the formation of the 70S ribosome.5

Results

- For the broth microdilution panels, the 0.5% McFarland was diluted in either Mueller-Hinton broth for staphylococci, enterococci, and Bacillus spp. or Mueller-Hinton broth supplemented with 3-5% defibrinated horse blood for staphylococcal and other rare Gram-positive species. The dilution was then plated onto a semi-automatic inoculator into the dry-form microdilution panel prepared by TREK Diagnostics (Westlake, OH).
- Zone diameters for the disk diffusion tests were read with digital calipers and recorded to the nearest whole millimeter while the broth microdilution panels were read at 80% inhibition of the antibiotic in the panel.

Susceptibility test methods

- MIC and disk diffusion test methods followed the guidelines in the NCCLS.6 A 0.5% McFarland was made for each organism tested and was plated on Mueller-Hilton agar for staphylococci, enterococci and Bacillus spp. or Mueller-Hilton agar supplemented with 3.5% sheep blood for staphylococcal and other rare Gram-positive species.
- For the broth microdilution panels, the 0.5% McFarland was diluted in either Mueller-Hilton broth for staphylococci, enterococci, and Bacillus spp. or Mueller-Hilton broth supplemented with 3-5% defibrinated horse blood for staphylococcal and other rare Gram-positive species.
- Depending on the geographical location, it is not uncommon to see oxacillin-resistant or glycopeptide-intermediate staphylococci, vancomycin-resistant enterococci, and penicillin- and macrolide-resistant pneumococci clinical isolates.4 With the continuing increase in multi-drug resistances there has been a push to develop new and novel antimicrobial agents such as the oxazolidinones.
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Methods

Bacterial isolates

- A total of 3722 Gram-positive bacterial isolates were tested from a collection of recent clinical and surveillance isolates.
- The staphylococci isolates included 169 oxacillin-susceptible and 144 oxacillin-resistant S. aureus and 69 oxacillin-susceptible and 230 oxacillin-resistant coagulase-negative staphylococci (CNS; represents 14 different species).
- The streptococci isolates consisted of 355 Streptococcus pneumoniae (about 65% were penicillin-resistant or -intermediate), 51 streptococci viridans group and 150 Rhophilic streptococci (includes 50 group A, 49 group B, 8 group C, 1 group F, 8 group G).
- A total of 70 rare Gram-positive species (11 Bacillus spp., 12 Listeria spp., 13 Corynebacterium spp., 10 Micrococcus spp., 3 Drococcus spp., and 1 Actinomyces spp.) were also tested. QC strains obtained from the American Type Culture and Collection (ATCC, Manassas, VA) included 5 pneumococci ATCC 6919, 6 staphylococci ATCC 29213 and 29215, and 6 Enterococcus ATCC 29212.

Results of testing 1572 Gram-positive pathogens against AZD2563 by MIC and disk diffusion comparisons. This collection included linezolid-resistant strains that might support once-daily dosing.4

Conclusions

- The overall interpretative error rates were:
  - very major - 0.0% (0.2%) of organisms.

References