ABSTRACT

Background: Retapamulin (RE, SB-275833) is a novel pleuromutilin with a unique mode of action and a broad spectrum, being developed for the topical treatment of uncontrolled skin infections. As a new agent, it is critical to establish performance of the commonly used, dried susceptibility panel to determine its accuracy and reproducibility compared with reference methods. An evaluation was undertaken to assess performance of the Sensititre 18–24 h dried susceptibility plate (TREK Diagnostics Systems, Cleveland, OH) for RE.

METHODS: Two hundred isolates (20 Coagulase Negative Staphylococci spp., 60 S. aureus, 60 Beta Hemolytic streptococci spp., 20 Enterococcus spp., 20 Enterobacteriaceae, and 20 Non-Enterobacteriaceae) were tested with RE (0.015–256 μg/ml) and 10 comparator drugs (Erythromycin, Tetracycline, Amoxicillin, Gentamicin, Cefotaxime, Vancomycin, Linezolid, Tazobactam, Amoxicillin/Clavulanic acid, and Cefotaxime) as per the Sensititre 18–24 h dried susceptibility plate. The Sensititre 18–24 h dried susceptibility plate demonstrated an equivalent level of performance 100% using the manual method.

RESULTS: The overall essential agreement for Retapamulin was 100% (+/- one log 2 dilution range) was 100% using the manual method.

SUSCEPTIBILITY TESTING METHODS

- Each isolate was tested using a Sensititre 18–24 h susceptibility plate containing Retapamulin and comparator antimicrobials. The plates were set-up and tested according to the manufacturer’s instructions.
- The reference broth microdilution plates were prepared and tested according to the Clinical Laboratory Standards Institute (CLSI, M7-A6).
- Repeat testing was performed for any organism/antimicrobial combination that resulted in a greater than +/- one log 2 dilution error. These were repeated in triplicate on both the dried test plate and reference plate.

CONCLUSIONS: This evaluation indicates that the performance of the Sensititre 18–24 h dried susceptibility plate is RE is equivalent to the CLSI (M7) reference broth microdilution method and is an acceptable method for susceptibility testing of RE.*

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PURPOSE OF THE STUDY

To evaluate the performance of Retapamulin, (SB-275833) a novel pleuromutilin, on the dried Susceptibility 18–24 hour susceptibility plate compared to the CLSI reference broth microdilution method (M7 – A6).

MATERIALS & METHODS

Organisms Tested

- 200 Clinical and Challenge isolates consisting of:
  - Coagulase negative staphylococci
  - S. aureus
  - Beta-hemolytic streptococci
  - Enterococcus spp.
  - Enterobacteriaceae
  - Non-Enterobacteriaceae

- 10 Reproducibility isolates with on-scale endpoints

Organisms Tested

- Methicillin Resistant Staphylococcus aureus
- Methicillin Sensitive Staphylococcus aureus
- Enterococcus faecalis
- Enterococcus faecium
- Escherichia coli
- K. pneumoniae
- Pseudomonas aeruginosa

CLSI quality control strains (20 replicates of each tested)

- E. coli ATCC 25922
- K. pneumoniae ATCC 700603
- H. influenzae ATCC 49247
- S. aureus ATCC 29213
- S. pneumoniae ATCC 49247
- E. faecalis ATCC 29212

RESULTS

Essential agreement for the 200 isolates were calculated using the +/- one log 2 dilution standard reference broth microdilution method and all comparator drugs.

Conclusions: The agreement rates for the 200 isolates were as follows:

- Retapamulin (% Essential Agreement of Total = 100%)
- Comparator antimicrobials within +/- one log 2 dilution of the CLSI reference broth microdilution method (% Essential Agreement of Total = 100%)

REPRODUCIBILITY RESULTS FOR RETAPAMULIN

- The overall essential agreement for Retapamulin, within +/- one log 2 dilution range, was 100% using the manual method.
- The overall essential agreement for all comparators, within +/- one log 2 dilution range, was 100% using the manual method.
- Interlaboratory reproducibility was 100% for Retapamulin and all comparator drugs.

REFERENCES


Table: Results of susceptibility testing for Retapamulin and comparator antimicrobials within +/- one log 2 dilution of the CLSI reference broth microdilution method (% Essential Agreement of Total = 100%).

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>% Essential Agreement of Total</th>
<th>Comparator Antimicrobials</th>
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</thead>
<tbody>
<tr>
<td>Retapamulin</td>
<td>100%</td>
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<tr>
<td>Comparator</td>
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<tr>
<td>Erythromycin</td>
<td>100%</td>
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<tr>
<td>Gentamicin</td>
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<td>Tetracycline</td>
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<td>Amoxicillin</td>
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<tr>
<td>Clindamycin</td>
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<tr>
<td>Amoxicillin/Clavulanic acid</td>
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<tr>
<td>Erythromycin</td>
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