INTRODUCTION

Isavuconazole is a novel broad-spectrum triazole agent with activity against a variety of opportunistic and pathogenic yeasts and moulds. Isavuconazole can be administered either orally or intravenously as a water soluble prodrug, isavuconazonium sulfate (Cresemba®), which then is rapidly cleaved by esterases into active component and an inactive prodrug cleavage product (Figure). As with other members of the triazole class of antifungal drugs, isavuconazole inhibits ergosterol synthesis in the fungal membrane. Previous in vitro studies have shown good activity against all Candida spp and species of Aspergillus and Mucorales. Potent activity against Cryptococcus spp and other emerging yeast infections has been demonstrated as well.

TEST PROCEDURE

Before using MIC Test Strip Isavuconazole from an unopened package, visually inspect to ensure the package is intact. Do not use the strips if the package has been damaged. When removed from the refrigerator, allow the package or storage container to reach room temperature for about 30 minutes. Moisture condensing on the outer surface must evaporate completely before opening the package.

Materials required but not provided:
- RPMI Agar plates (ref. 11509)
- Sterile saline (0.85% NaCl) (ref. 20095)
- Sterile loops, swabs (not too tightly spun), test tubes, pipettes and scissors
- Forceps
- 0.5 McFarland turbidity standard (ref. 80400)
- Incubator (35 ± 2°C)
- Quality control organisms
- Additional technical information from www.liofilchem.net

Inoculum preparation

Suspend well-isolated colonies from an overnight agar plate into saline to achieve a 0.5 McFarland standard turbidity. A confluent or almost confluent lawn of growth will be obtained after incubation, if the inoculum is correct. In order to verify that your procedure gives the correct inoculum density in terms of CFU/mL, performing regular colony counts is recommended.

Inoculation

Dip a sterile swab in the adjusted microbial suspension and squeeze it on the wall of the test tube to eliminate excess liquid. Alternatively, use a rotation plater to efficiently streak the inoculum over the agar surface. Streaking has to be done twice with the swab dipped into the inoculum before each streaking. Allow excess moisture to be absorbed so that the surface is completely dry before applying MIC Test Strip.

Incubation

Incubate the agar plates in an inverted position at 35 ± 2°C for 24-48 hours in ambient atmosphere. Extend the incubation for up to 72 hours in case of slow growing organisms.

EVALUATING THE RESULTS

Reading

Observe where the relevant inhibition ellipse intersects the strip and read the MIC at 80% inhibition. Growth along the entire gradient i.e. no inhibition ellipse indicates that the value is greater than or equal to (≥) the highest value on the scale. An inhibition ellipse that intersects below the lower end of the scale is read as less than (<) the lowest value.

See page 2 for example of results. Also consult the MIC Test Strip Photographic Guide.

Interpretation

EUCAST breakpoints for Aspergillus spp are shown below. Always round up MIC Test Strip half dilution values to the next upper two-fold value before categorization.

QUALITY CONTROL

The following quality control strains are used as outlined under TEST PROCEDURE:
C. krusei ATCC® 6258, C. parapsilosis ATCC® 22019, C. albicans ATCC® 90028.

<table>
<thead>
<tr>
<th>Organism group</th>
<th>Breakpoint (μg/mL)</th>
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<tbody>
<tr>
<td></td>
<td>S ≤</td>
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<tr>
<td>Aspergillus fumigatus</td>
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</tr>
<tr>
<td>Aspergillus nidulans</td>
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<tr>
<td>Aspergillus terreus</td>
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</tbody>
</table>
MIC Test Strip Isavuconazole Reading Guide

Fig. 1

Ignore lawn of microcolonies and read at 80% inhibition. MIC 0.004 μg/mL.

Fig. 2

Ignore lawn of microcolonies and read at 80% inhibition. MIC 0.003 μg/mL.

Fig. 3

MIC 0.38 μg/mL.

Fig. 4

Read at 80% inhibition. MIC 0.25 μg/mL.

REFERENCES

- EUCAST Definitive Document (2012) Method for the determination of broth dilution minimum inhibitory concentrations of antifungal agents for yeasts. EDef. 7.2 Revision.

PRESENTATION

<table>
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<tr>
<th>µg/mL</th>
<th>Code</th>
<th>Packaging</th>
<th>Ref.</th>
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<tr>
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MIC Test Strip, Patent No. 1395483

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