

Establishment of Quality Control Ranges for Testing the Susceptibility of Target Organisms to Solithromycin (CEM-101) by Disk Diffusion

Abstract D-689

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Background:

Solithromycin is a novel fluoroketolide undergoing Phase 2 trials for the treatment of community-acquired pneumonia. With any new agent, it is important to have available reliable and reproducible methods of evaluating *in vitro* activity during development and post-approval. Solithromycin disks zones correlate well with broth microdilution MICs demonstrating the feasibility of disk diffusion testing of solithromycin. This study establishes quality control ranges to be used for disk diffusion susceptibility testing of solithromycin during development and post-approval.

Methods:

Quality control ranges for the disk diffusion testing of solithromycin disks (15 micrograms) were determined per CLSI guidelines (M23-A3). 9 separate laboratories each tested 10 independent replicates of each relevant ATCC QC organism (*S. aureus* ATCC 25923, *S. pneumoniae* ATCC 49619, and *H. influenzae* ATCC 49247) across three lots of media from different manufacturers against two disk lots of solithromycin (one from MAST and one from BioRad). One disk lot of telithromycin was tested as an in class control. Statistical methods (Gavin statistic and Rangefinder) were used to evaluate the data and generate ranges suitable for quality control testing.

Results: Proposed QC ranges for the disk diffusion testing of solithromycin and their overall performance are shown in the table below:

Organism	QC Range (mm)	# mm	Total Results (N)	N (%) in Range
<i>S. aureus</i> ATCC 29213 ^a	22-30	9	540	522 (96.7)
			536 ^b	520 (97.0)
<i>S. pneumoniae</i> ATCC 49619	24-32	9	540	528 (97.8)
			532 ^b	520 (97.7)
<i>H. influenzae</i> ATCC 49247	16-23	8	540	527 (97.6)

^ain the instance of double zones, diameter of inner zones were reported

^bsolithromycin results for replicates where telithromycin control was out of QC removed from analysis

The above ranges take into account intra-laboratory, intra-media lot, and intra-disk lot variation.

Conclusions:

The proposed ranges are suitable for quality control testing of solithromycin disks at the indicated disk mass. The performance of these ranges should be continually monitored during disk testing that takes place as part of the clinical development of solithromycin going forward.