



Evaluation of Gepotidacin Activity when Combined with Select Antimicrobial Agents and Tested Against Bacterial Isolates Using Checkerboard Methodology

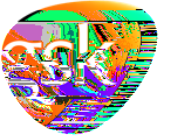
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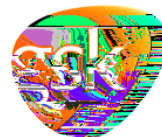
Introduction and Methods



- Gepotidacin (GSK2140944) is a novel triazaacenaphthylene bacterial type II topoisomerase inhibitor in clinical development for the treatment of uncomplicated UTI (acute cystitis) and urogenital gonorrhoea. This study evaluated combinations of gepotidacin and other antimicrobial agents for synergistic or antagonistic activity.

Study Design

- 5 isolates from each of the following species were evaluated:
 - *S. saprophyticus*, *E. faecalis*, *E. coli*, *C. freundii*, *E. cloacae* species complex, *K. aerogenes*, *K. pneumoniae*, *P. mirabilis*, and *P. rettgeri*
- Interactions between gepotidacin and 10 marketed antibiotics were studied by checkerboard broth microdilution method.
 - azithromycin, ceftazidime, levofloxacin, nitrofurantoin, tetracycline, trimethoprim/sulfamethoxazole, aztreonam, meropenem, linezolid, and vancomycin
- Minimum and maximum fractional inhibitory concentration (FIC) values were calculated for each combination.
 - FICs ≤ 0.5 : Synergy
 - FICs $0.5 - 4$: Indifference
 - FICs > 4 : Antagonism
 - Indeterminate was assigned when combination effects could not be determined.



Codrug										
5	4	5	4	5	5	5	Indifference ^a	5	5	
0	1	0	1	0	0	0	Synergy	0	0	
4	5	5	Indifference	4	3	5	5	5	4	
5	5	4	5	5	5	5	Indifference	5	5	
4	5	5	Indifference	5	5	5	Indifference	5	5	
5	5	5	5	5	5	5	5	5	5	
0	5	5	5	5	5	5	5	4	5	Tetracycline
0	Synergy	0	0	0	0	0	0	0	1	Indifference
5	Indifference	5	5	5	5	5	3	5	5	5
0	0	0	0	0	Synergy	0	0	0	0	2
5	4				Aztreonam					5
0	1				Indifference	4	3	5	5	5
0	0				Synergy	4	3	0	2	0
1	1	0	0	1				Synergy	1	1
5	Indifference									5
0	0	0	Synergy							
4	Synergy									0