

A Pharmacovigilance Analysis of Daptomycin Use Based on CLSI Susceptible Dose-Dependent Category – Supplementary Material

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Supplemental Figure 1. Time to Event Curves for Primary Composite Outcome, Elevated Liver Function Tests, and Peripheral Eosinophilia

- Abbreviations: LFT: liver function test

Supplemental Table 1. Clinical and Laboratory Standards Institute Guidance for Daptomycin Breakpoints for *Enterococcus* Species

| CLSI Guidance | Dates During Which Institution Reported CLSI Guidance | Organism Group | Minimal inhibitory concentration (mg/L) | | | |
|---------------|---|--|---|----------------------------|--------------|-----------|
| | | | Susceptible | Susceptible Dose-Dependent | Intermediate | Resistant |
| 2018 | Prior to Sept 2018 | <i>Enterococcus</i> spp. | ≤4 | - | - | - |
| 2019 | Sept 2018 ^a – Sept 2020 | <i>Enterococcus</i> spp. | ≤1 | 2-4 | - | ≥8 |
| 2020 | Sept 2020 – Present | <i>Enterococcus faecium</i> only | - | ≤4 | - | ≥8 |
| | | Non- <i>faecium</i> <i>Enterococcus</i> spp. | ≤2 | - | 4 | ≥8 |

- a. CLSI 2019 recommendations were implemented prior to formal release of the CLSI M100 2019 document, based on meeting minutes from the CLSI annual meeting
- Abbreviations: CLSI: Clinical and Laboratory Standards Institute; Sept: September; spp: species

Supplemental Table 2. Breakdown of Antihistaminergic Agents in Patients with Concomitant Antihistamine Usage

| Antihistaminergic medication | Number of patients taking medication |
|-------------------------------------|---|
| Cetirizine | 2 |
| Diphenhydramine | 5 |
| Doxepin | 1 |
| Hydroxyzine | 4 |
| Loratadine | 2 |
| Meclizine | 1 |
| Mirtazapine | 8 |

Supplemental Table 3. Concomitant Antimicrobials During Infectious Course

| | Standard-dose (N=76) | High-dose (N=43) | Total (N=119) | p value |
|--------------------------------|-----------------------------|-------------------------|----------------------|----------------|
| Ampicillin, n (%) | 1 (1.3%) | 2 (4.7%) | 3 (2.5%) | 0.26 |
| Piperacillin-tazobactam, n (%) | 32 (42.1%) | 21 (48.8%) | 53 (44.5%) | 0.48 |
| Cefazolin, n (%) | 3 (3.9%) | 1 (2.3%) | 4 (3.4%) | 0.64 |
| Ceftriaxone, n (%) | 16 (21.1%) | 5 (11.6%) | 21 (17.6%) | 0.20 |
| Cefepime, n (%) | 23 (30.3%) | 15 (34.9%) | 38 (31.9%) | 0.60 |
| Ceftazidime-avibactam, n (%) | 3 (3.9%) | 0 (0.0%) | 3 (2.5%) | 0.19 |
| Ceftolozane-tazobactam, n (%) | 2 (2.6%) | 0 (0.0%) | 2 (1.7%) | 0.28 |
| Ertapenem, n (%) | 20 (26.3%) | 13 (30.2%) | 33 (27.7%) | 0.65 |
| Meropenem, n (%) | 16 (21.1%) | 9 (20.9%) | 25 (21.0%) | 0.99 |
| Ciprofloxacin, n (%) | 6 (7.9%) | 2 (4.7%) | 8 (6.7%) | 0.50 |
| Levofloxacin, n (%) | 5 (6.6%) | 0 (0.0%) | 5 (4.2%) | 0.086 |
| Vancomycin, n (%) | 52 (68.4%) | 22 (51.2%) | 74 (62.2%) | 0.062 |
| Linezolid, n (%) | 8 (10.5%) | 5 (11.6%) | 13 (10.9%) | 0.85 |
| Gentamicin, (%) | 0 (0.0%) | 2 (4.7%) | 2 (1.7%) | 0.058 |
| Metronidazole, n (%) | 24 (31.6%) | 14 (32.6%) | 38 (31.9%) | 0.91 |
| Other antibiotic, n (%) | 8 (10.5%) | 3 (7.0%) | 11 (9.2%) | 0.52 |