# Stanford De-escalation Guide for Gram-negative Bacteremia

## Antibiotic Selection

<table>
<tr><th>Pathogens</th><th>Preferred therapeutic options IF SUSCEPTIBLE<br>Switch to PO when clinically stable, able to take orals, no concern for absorption issues</th></tr>
<tr><td rowspan="2">E.coli, Klebsiella spp., Proteus spp, Citrobacter koseri</td><td>Ceftriaxone 2g IV q24h<br>Ciprofloxacin 500mg PO BID<br>Levofloxacin 500-750mg* PO daily<br>Cefazolin 2g IV q8h – please call micro lab to add on susceptibility testing<br>2nd line oral alternatives: Case by case basis. Consult ASP or ID if unsure. May consider if ALL conditions met†:
<table>
<tr><td>• source-controlled<br>• uncomplicated<br>• received ≥ 3 days of active IV therapy<br>• data strongest in urinary and biliary sources</td><td>• TMP-SMX† 2DS PO BID or 8-10mg TMP/kg/day PO divided in 2 or 3 doses if TMP/SMX MIC ≤ 20 (TMP MIC ≤1)<br>• Amoxicillin† 1g PO q8h if MIC ≤ 2<br>• Amoxicillin/clavulanate† 875/125mg PO q8h or 2g XR BID (if covered by insurance) if MIC ≤ 2<br>• Call ASP or ID if cephalosporins are needed</td></tr>
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†In recent published data, stepdown to oral β-lactams and TMP/SMX appeared to result in similar clinical outcomes vs FQ after ~3 days of effective IV therapy.[1,4] However, a meta-analysis found a higher recurrence of infection with non-FQs.[13] Limited clinical data with use of oral β-lactams</td></tr>
<tr><td><u>ESBL-producers (often ceftriaxone resistant, cefoxitin susceptible. See Micro comments)</u><br>Ertapenem 1g IV q24h<br>Ciprofloxacin 500-750mg* PO BID<br>Levofloxacin 500-750mg* PO daily<br>TMP-SMX 8-10mg/kg/day PO divided in 2 or 3 doses if TMP/SMX MIC ≤ 20 (TMP MIC ≤1)<br>Note: Avoid most beta-lactams (including piperacillin-tazobactam and amoxicillin-clavulanate). May report as susceptible, but treatment failure may occur. MERINO trial: higher mortality in those treated with piperacillin-tazobactam vs meropenem.</td></tr>
<tr><td>Enterobacter cloaecae complex, Enterbacter aerogenes, Hafnia alvei and Citrobacter freundii spp, Serratia marcescens, Morganella morganii, Providencia spp.[18,19**]</td><td>Cefepime 2g IV q12-8h* extended infusion if ceftriaxone and ceftazidime susceptible. Otherwise call lab to add on cefepime testing.<br>Ertapenem 1g IV q24h<br>Ciprofloxacin 500-750mg* PO BID<br>Levofloxacin 500-750mg* PO daily<br>TMP-SMX 8-10mg/kg/day PO divided in 2 or 3 doses if TMP/SMX MIC ≤ 20 (TMP MIC ≤1)<br>Piperacillin-tazobactam: ongoing investigation (MERINO-2 trial). Consider alternatives or monitor closely if used<br>Caution with ceftriaxone, ceftazidime, even if reported as susceptible. Prolonged use may select for derepressed AmpC mutants (often ceftriaxone resistant + cefoxitin resistant).</td></tr>
<tr><td>Pseudomonas aeruginosa</td><td>Consider ID consult<br>Cefepime 2g IV q8h extended infusion<br>Ceftazidime 2g IV q8h<br>Piperacillin-tazobactam 4.5g* IV q8h extended infusion<br>Meropenem 1g IV q8h extended infusion<br>Ciprofloxacin 750mg PO BID<br>Levofloxacin 750mg PO daily</td></tr>
<tr><td>Stenotrophomonas</td><td>ID consult recommended<br>TMP-SMX 10-15mg/kg/day IV/PO divided in 2 or 3 doses<br>If severe TMP-SMX allergy or intolerance/contraindication: levofloxacin 750mg IV/PO daily</td></tr>
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|---|---|
| *Acinetobacter baumanii* | ID consult recommended. Commonly resistant to many antibiotics. Ampicillin-sulbactam is usually active. |

* Lower doses listed are for typical 70kg, normal renal function, tailored for the organism causing bacteremia. Higher dose may be considered for deep seated infections, obese (BMI ≥ 30), high CrCl > 100 ml/min. Use clinical judgement.
**Clinical reports of emergence of resistance has been reported mainly in *Enterobacter spp*; few reports in *C.freundii*, *Serratia spp*.[19] Higher mutation rates reported in experimental model of *Enterobacter cloacae complex, E, aerogenes, C. freundii, H. alvei* than *Providencia spp, Serratia spp. M. morganii*.[18]
Abbreviations: TMP-SMX= trimethoprim/sulfamethoxazole, DS = double strength, FQ= fluoroquinolone, PK/PD = pharmacokinetic/pharmacodynamic, MIC= minimum inhibitory concentration

**Duration (excludes neutropenia-** see FN pathway**)**

| **Source of bacteremia** | **Duration of therapy** | **Notes** |
|---|---|---|
| General: urine, biliary, intraabdominal, skin/soft tissue, respiratory, surgical site, ENT | 7 days[2, 7, 8]<br>Consider 10-14 days in high risk circumstances (*e.g.* significant immunocompromise) or some cases of *P.aeruginosa*[3;] consider ID consult | • Must have clinically improved rapidly<br>• Must have source control for intra-abdominal infections<br>• Excludes neutropenic patients: see FN pathway; consider ID consult<br>• Rule out infections involving long term catheters, ports, or hardware: longer treatment may be warranted if prosthesis/foreign materials are infected. Consider ID or ASP consult.<br>• Day 1 = 1st day of active antibiotic if source controlled and clinically improved (no need for clearance on repeat blood cultures. See below)† |
| Line (CVC, PICC, port, etc) | 7 days[2]<br>Uncomplicated + line removed (no abscess, endovascular, or metastatic infection)<br>10-14 days in some circumstances | • Day 1 = 1st negative blood culture<br>• Remove infected catheters if possible. Consider pathogen, clinical status, clearance of blood culture, metastatic infection – see IDSA guidelines. If unable to remove infected line or port, some cases may require longer treatment, e.g. ≥10-14 days, ± antibiotic lock therapy. Consult ID.<br>• If no clinical response, repeat blood culture and consult ID |
| Endovascular (e.g. infective endocarditis, VAD ICD/pacemaker)<br>Osteomyelitis<br>Complicated abdominal<br>Meningitis/ventriculitis | Varies depending on source control and other co-morbid conditions | Consult ID |
| †Repeat blood cultures are generally not necessary to confirm clearance of uncomplicated gram negative bacteremias and are not necessary to determine day 1 of treatment.[10, 12] For clinically improved patients with source control, count day 1 from the 1st day of active therapy. Consult ID or ASP if unsure. | | |

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