

NMH Beta-lactam Therapeutic Drug Monitoring Protocol

CLINICAL PROTOCOL:

- A. Clinical pharmacist to identify patients who require antibiotic TDM. Only pharmacists can order and interpret levels.
 1. The patient's primary team must also agree to monitoring.
- B. Recommended patients include those with impaired organ function, altered beta-lactam PK/PD, and/or pathogens with minimum inhibitory concentration (MIC) near breakpoint.

For patients with serious infections, consider the following:

1. Concern for altered PK (e.g., immunocompromised, risk for augmented clearance, obesity, low or high rate CRRT, renal replacement with residual urine output, or requires ECMO).
 2. Likelihood of having a difficult-to-treat pathogen (e.g., MIC near breakpoint).
 3. Clinical response to current treatment or difficult-to-penetrate site of infection.
 4. Risk factors for antibiotic toxicity (e.g., history of neurotoxicity, > 65 years of age with concurrent renal dysfunction, worsening mental status).
 5. BAL or [Blood Biofire](#) with *Pseudomonas*, *Enterobacter cloacae*, *Klebsiella aerogenes*, Enterobacterales, *Acinetobacter baumannii*
 6. Planned prolonged surgical prophylaxis post-procedure (e.g. lung transplant)
- C. Clinical pharmacist to order corresponding antibiotic levels in EPIC for cefepime, meropenem, piperacillin, or tazobactam (typically will order piperacillin, tazobactam infrequently)
 1. A post-distribution peak level and trough level should be ordered:
 - a. For dedicated collection instructions, refer to [lab handbook](#)
 2. Beta-Lactam plasma concentrations can be ordered after a single dose with Bayesian analysis (Table 1.)
 - a. Additional doses, creatinine trend, or levels will increase model accuracy of prediction for individual patients.
 - b. For beta-lactams other than those listed below, there may be a send out option depending on the drug and timing, reach out to ADSP pharmacist on a case-by-case basis
 3. Use of a two-point PK assessment is recommended for TDM:
 - a. Post-dose peak drawn after end of infusion (refer to **Table 1**).
 - b. Pre-dose trough (drawn 30 mins prior to dose).

Table 1. Orderable Beta-Lactam Antibiotics and Corresponding Desired Peak Sample Times at NMH

Antibiotic	Infusion time	Desired peak sample time	Lab Range
Cefepime	30 mins	2 hrs post-dose	1-200 mcg/mL
Cefepime (if extended infusion)	3 hrs	3 hrs post-dose (end of infusion)	1-200 mcg/mL
Piperacillin-tazobactam	4 hrs	4 hrs post-dose (end of infusion)	1-200 mcg/mL pip 1-100 mcg/mL tazo
Meropenem	3 hrs	3 hrs post-dose (end of infusion)	1-200 mcg/mL

- D. Clinical pharmacist to interpret drug levels, communicate any required dose changes to team, and document in Beta-lactam monitoring note in EPIC using the dotphrase (.BLMONITORING)
- i. General recommendations for PK/PD targets for TDM (Table 2):

PK/PD Index	Population	Target*	Pathogens	Drug class
$fT_{>MIC}$	ICU	100% >1x to 4x MIC**	All	All
$fT_{>MIC}$	SOT/SCT	100% >1x to 4x MIC	All	All
$fT_{>MIC}$	Floor/Ward	100% > 1x MIC	All	All

Abbreviations: ICU, intensive care unit; MIC, minimum inhibitory concentration; SCT, stem cell transplantation; SOT, solid organ transplant

* The choice of the PK/PD target should be selected based on the clinical status of the patient

**For seriously ill patients and those with deep seated infections or immunocompromised status consider selecting a more aggressive PK/PD target in the context of the patient's status and response to therapy

E. Interpretation of TDM results:

1. Once PK analysis is complete, $T_{>MIC}$ can be assessed
2. If **floor patient** and $T_{>MIC}$ is < 100%, increase dose or prolong infusion time to target 100% $T_{>MIC}$
3. If **ICU patient** and $T_{>1-4x MIC}$ is < 100%, increase dose or prolong infusion time to target 100% $T_{>1-4x MIC}$
4. If calculated/optimized beta-lactam dosing is greater than that recommended in the [NM Renal Dose Adjustment Guidance](#) or FDA label, if challenging interpretation, or if unexpected PK/PD, consult with ID pharmacist on call (pager 55955)
 - a. ID pharmacy consult to assess model accuracy in the context of the patient
 - b. May consider changing agent or optimizing dosing depending on clinical scenario
5. General considerations for toxicity:
 - a. **Consider dose reduction in populations who are at increased risk for toxicity:**
 - i. Increased risk for toxicity documented among older patients, those with renal dysfunction, and patients who have trough >5x breakpoint
 - b. Examples of potentially elevated plasma trough concentrations:
 - i. The following are suggested upper bounds for plasma. These may not account for target site concentrations. Consider risk vs. benefit for plasma trough-based dose adjustment for deep-seated infections.
 1. Piperacillin: trough >160 mg/L
 2. Meropenem: trough >20 mg/L
 3. Cefepime: trough >40 mg/L
 - c. If a patient has signs of neurotoxicity and an elevated trough, consider holding dose for 2 half-lives and restarting a half-life adjusted dose or changing agents.
 - d. Of note, these are suggested upper bounds and have not been well validated, use clinical judgement.
6. Clinical pharmacist to document as a note in Epic using the dotphrase **(.BLMONITORING)**