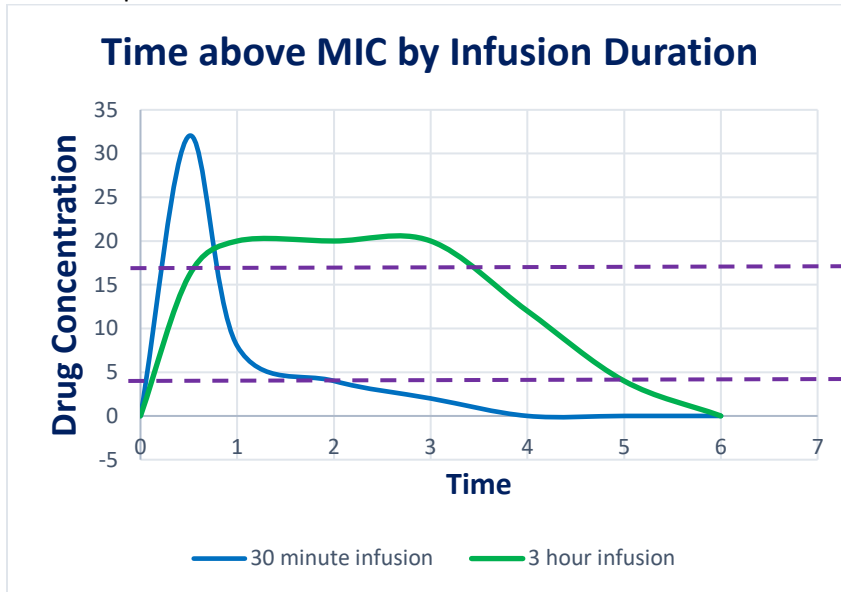


PRACTICE CHANGE: Meropenem and Piperacillin-Tazobactam Extended Infusion

Why is this important for our patients?

Time above the minimum inhibitory concentration (MIC) is the most important factor for effectiveness of beta-lactam antibiotics. The longer the drug concentration is above the MIC, the better bacterial killing effect. With rising antimicrobial resistance, optimizing the effectiveness of antibiotics we have available in Canada is critical. Extending the infusion time is one way we can overcome resistance, improve patient outcomes and reduce the need to escalate to broader-spectrum antibiotics.



The **green line (3-hour extended infusion)** keeps the drug level above the **MIC (purple lines)** longer than the **blue line (30-minute infusion)**. This improves bacterial killing and is particularly important for more resistant bacteria.

MIC of a more resistant bacteria

MIC of a less resistant bacteria

Green (3hr infusion): time > MIC = 3-5 hrs

Blue (30min infusion): time > MIC = 0.5-1 hrs

NEW DOSING APPROACH:

Meropenem

- 1) Initial dose: 1g x1 over 30 minutes
- 2) Subsequent doses: 1g IV Q8H over 3 hours, starting 4 hours after initial dose (interval adjusted for CrCl)

Piperacillin-Tazobactam

- 1) Initial dose: 4.5g x1 over 30 minutes
- 2) Subsequent doses: 4.5g IV Q6H over 3 hours, starting 3 hours after initial dose (interval adjusted for CrCl)

What is my role?

- ✓ **Check ED MAR for initial doses.** Omit initial dose/reschedule doses accordingly.
- ✓ **Usual renal dose adjustments apply.** Check interval between first and subsequent doses, see Table 1 on page 3.

When is it appropriate to reassess/change infusion duration?

Prescribers may consider shortening to 30 min infusions after 48-72hrs. Please see **"De-escalation Guide"** on page 2.

When verifying infusion duration shortening, please ensure:

1. Infuse over changed from 3hr to 30min
2. Check timing of last dose on eMAR to ensure subsequent doses are scheduled at proper interval
3. MD NOTES comments removed

Questions? Please contact:
Antimicrobial Stewardship Program at
antimicrobialstewardship@sinaihealth.ca

De-escalation Guide:

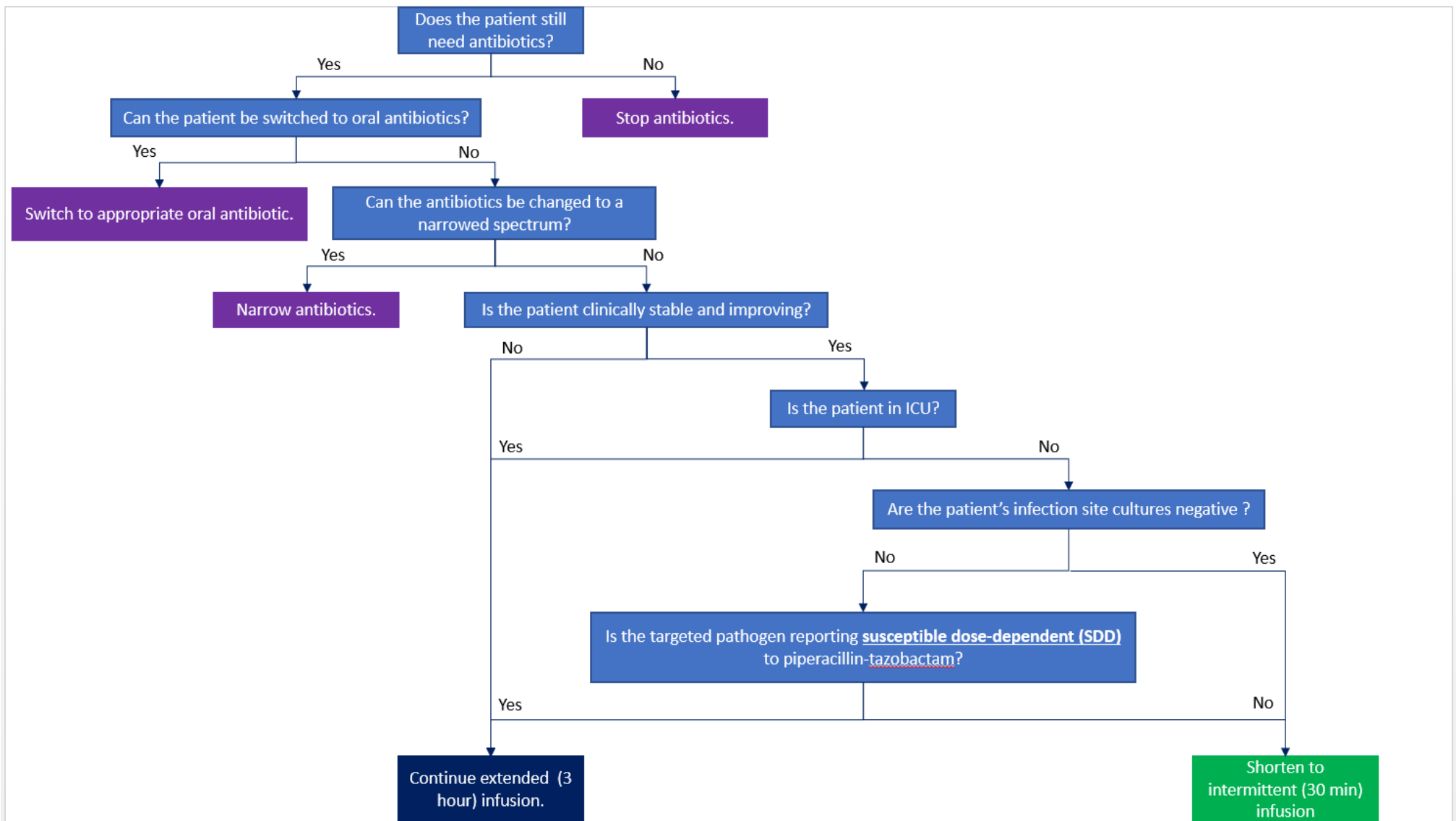


Table 1. Dosing and intervals for normal and impaired renal function for extended piperacillin/tazobactam and meropenem infusions

Drug	Dosing		Initial dose ^a	Subsequent Dose ^b
Piperacillin/ Tazobactam	CrCl≥40 CrCl 20-39 CrCl<20 IHD PD CRRT	4.5g q6h 4.5g q8h 4.5g q12h 4.5g q12h 4.5g q12h 4.5g q6h	Administered over 30 minutes	EI to start 3 hours after initial dose Exceptions – subsequent dose to start : • 6 hours after bolus for CrCl<20, IHD, or PD
Meropenem	CrCl≥50 CrCl 25-49 CrCl 10-24 CrCl<10 IHD PD CRRT	1g q8h 1g q12h 500mg q12h 500mg q24h 500mg q24h (AD) 500mg q24h 1g q8h	Administered over 30 minutes	EI to start 4 hours after initial dose Exceptions – subsequent dose to start : • 6 hours after bolus for CrCl 10-49 • 12 hours after bolus for CrCl<10, IHD, or PD
^a Initial dose should administered as a 30-minute infusion regardless of the drug dosage ordered (1g vs 500mg for meropenem) ^b Subsequent doses should be ordered according to renal function as specified under ‘dosing’ column and administered as 3-hour infusions. The interval from initial to the first subsequent dose is specified under ‘subsequent dose’ column (interval after this first subsequent dose should be based on the ‘dosing’ column) AD, after dialysis; CrCl, creatinine clearance; IHD, intermittent hemodialysis; PD, peritoneal dialysis; CRRT, continuous renal replacement therapy				