Medication Use Therapeutic Pearls – Adult/Pediatric-Inpatient/Ambulatory/ED Clinical Practice Guideline

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Clinical Pearls [UW Health Specific]

Amphotericin B Liposomal (AMBISOME)

- Amphotericin B causes hypokalemia, hypomagnesemia, renal tubular acidosis, and azotemia. Normal saline boluses (1000 mL) pre- and post-infusion may prevent or slow renal toxicity.[1,2] *(UWHealth Weak/Conditional Recommendation, Low - Moderate Quality of Evidence)*
- Avoid concurrent nephrotoxins.[3] *(UWHealth Strong Recommendation, Low - Moderate Quality of Evidence)*
- Incompatible with normal saline (NS). Flush administration lines with D5W before and after amphotericin administration.[4]
- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

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[1]Heidemann HT, Gerkens JF, Spickard WAm Jackson EK, Branch RA. Amphotericin B nephrotoxicity in humans decreased by salt repletion. *Am J Med.* 1983;75(3):476-481.
[2]Karimzdadeh I, Farsaei S, Khalili H, Dashti-Khavidaki S. Are salt loading and prolonging infusion period effective in prevention of amphotericin B-induced nephrotoxicity? *Expert Opin Drug Saf.* 2012;11(6):969-983.
[3]Harbarth S, Pestotnik SL, Lloyd JG, Burke JP, Samroe, MH. The epidemiology of nephrotoxicity associated with conventional amphotericin B therapy. Am J Med. 2001;111(7):528.
[4]Lexicomp Online®, UW Health, Hudson, Ohio: Lexi-Comp, Inc.;December 16, 2016.

Acyclovir

- Maximum treatment dose is 500 mg/m^2.[1] *(UWHealth Strong Recommendation, Low Quality of Evidence)*
- The max intravenous dose for prophylactic indications is 200mg *(UWHealth Weak/Conditional Recommendation, Low Quality of Evidence)*
- Maintain adequate hydration to prevent renal toxicity and urine crystallization. Administration of normal saline (NS) boluses may be considered.[2] (*UWHealth Strong Recommendation, Moderate Quality of Evidence)*
- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

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[1]Bean B, Aeppli D, Balfour HH Jr. Acyclovir in shingles. *J Antimicrob Chemother.* 1983;12(Suppl B):123-127.
[2]Perazella MA. Crystal-induced acute renal failure. *American Journal of Medicine.* 1999;106(4):459-465.

Amikacin

- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

Amoxicillin/clavulanate

- The amount of clavulanate (125 mg) is the same in the 500 mg and the 875 mg tablets. Do not cut tablets to make half-doses, as this results in subtherapeutic amounts of clavulanate.[1] *(UWHealth Weak/Conditional Recommendation, Low Quality of Evidence)*

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[1]Amoxicillin clavulanate potassium [package insert]. Teva Pharmaceuticals, USA. https://dailymed.nlm.nih.gov/dailymed/archives/fdaDrugInfo.cfm?archiveid=3024. Accessed Dec 2, 2016.

Artemether and Lumefantrine

- Contact the ID service when considering use of this medication. *(UWHealth Strong Recommendation, Very Low Quality of Evidence)*
- Should be administered with food containing at least 1.6 g of fat.[1] *(UWHealth Weak/Conditional Recommendation, Low Quality of Evidence)*

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[1]Djimide A. Lefevre G. Understanding the pharmacokinetics of Coartem. *Malar J.* 2009;8(suppl 1:S4):1-8.

Atovaquone

- For *Pneumocystis jirovecii* (PCP) prophylaxis, the usual atovaquone dose is 1500 mg daily. In non-HIV and non-hematologic malignancy patients, a prophylaxis dose of 750 mg may be considered, although both prophylaxis success and prophylaxis failure have been observed with the lower dose atovaquone regimen.[1,2] *(UWHealth Weak/Conditional Recommendation, Low Quality of Evidence)*

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[1]Meyers B, Borrego F, Papanicolaou G. Pneumocystis carinii pneumonia prophylaxis with atovaquone in trimethoprim-sulfamethoxazole-intolerant orthotopic liver transplant patients: a preliminary study. *Liver Transpl.* Aug 2001;7(8):750-751.
[2]Rodriguez M, Sifri CD, Fishman JA. Failure of low-dose atovaquone prophylaxis against Pneumocystis jiroveci infection in transplant recipients. *Clin Infect Dis.* Apr 15 2004;38(8):e76-78.

Azithromycin

- May be used as an antiinflammatory in lung transplant recipients or cystic fibrosis patients.[1,2] *(UWHealth Weak/Conditional Recommendation, Moderate Quality of Evidence)*
- Macrolide antibiotics have been associated with increased digoxin concentration and digoxin toxicity.[3] Digoxin blood concentration monitoring may be considered with macrolide therapy. *(UWHealth Conditional Recommendation, Low Quality of Evidence)*
- Erythromycin is the preferred macrolide for gastric motility.[4,5] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*

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[1]Vos R, Vanaudenaerde BM, Verleden SE, et al. Anti-inflammatory and immunomodulatory properties of azithromycin involved in treatment and prevention of chronic lung allograft rejection. *Transplantation.* 2012; 94(2):101-109.
[2]Southern KW, Barker PM. Azithromycin for cystic fibrosis. *Eur Respir J.* 2004;24(5):834-838.
[3]Gomes T, Mamdani MM, Juurlink DN. Macrolide-induced digoxin toxicity: a population-based study. *Clin Pharmacol Ther.* 2009;86(4):383-386.
[4]Prather CM, Camilleri M, Thomforde GM, Forstrom LA, Zinsmeister AR. Gastric axial forces in experimentally delayed and accelerated gastric emptying. *Am J Physiol.* 1993;264(5 Pt 1):G928.
[5]Keshavarzian A, Isaac RM. Erythromycin accelerates gastric emptying of indigestible solids and transpyloric migration of the tip of an enteral feeding tube in fasting and fed states. *Am K Gastroenterol.* 1993;88(2):193.

Aztreonam

- Aztreonam has no anaerobic or Gram-positive coverage.[1] Many nosocomial Gram-negative organisms that are resistant to cephalosporins are also resistant to aztreonam, and the drug should not be used alone for nosocomial Gram-negative infection until it is known that the organisms are susceptible.[2] *(UWHealth Strong Recommendation, High Quality of Evidence)*
- Aztreonam and ceftazidime share the same side chain. Animal models suggest that aztreonam may be cross-allergenic with ceftazidime but not other beta-lactams, which have different side chains.[3] Treatment of Patients with Reported Allergies to Beta-Lactam Antibiotics – Adult – Inpatient *(UWHealth Strong Recommendation, Low-Moderate Quality of Evidence)*

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[1]Sykes RB, Bonner DP, Bush K, Georgopapapdakou NH. Aztreonam (SQ 26,776), a synthetic monobactam specifically active against aerobic gram-negative bacteria. *Anitmicrob Agents Chemother.* 1982;21(1):85-92.
[2]Thomson KS. Extended-spectrum-beta-lactamase, AmpC, and Carbapenemase issues. *J Clin Microbiol.* 2010;48(4):1019-1025.

Cefepime

- Cefepime can often be used to treat infections caused by Gram-negative bacteria possessing ESBL and AmpC resistance mechanisms if the MIC is interpreted as susceptible (currently < 8mcg/ml). *(UWHealth Weak/conditional Recommendation, Low - Moderate Quality of Evidence)*

Table 1. Considerations for selecting broad-spectrum beta-lactam antibiotics based on clinical indication for patients with MDR or HCAP risk factors (see Table 2 for risk factors)

Cefepime	Piperacillin/tazobactam	Meropenem
• Meningitis • Pneumonia • Aspiration pneumonia (add metronidazole) • SSTI, cellulitis • Intraabdomnial infection involving the small instestine (add metronidazole)	• Pneumonia • Aspiration pneumonia with HCAP risk factors • Diabetic foot infection • Intraabdominal infection involving the colon • Cholangitis • Positive culture for ampicillin-sensitive *Enterococcus*AND ongoing need for broad-spectrum coverage	• Patients unable to tolerate cefepime AND piperacillin-tazobactam • Empiric coverage for septic shock and history of ESBL pathogens (requires ID Approval beyond 72 hours)

Table 2. MDR and HCAP Risk Factors

MDR Pathogen Risk Factors	HCAP-specific Risk Factors
• Antimicrobial therapy in past 90 days • Current hospitalization with antibiotic exposure of greater than 5 days • Immunosuppressive disease and/or therapy	• Hospitalized 2 or more days in the preceding 90 days • Resident of skilled nursing facility or

• Currently on hospital unit or service with a high rate of resistance -- see UWHC Antibiograms	extended care facility • Receiving home infusion therapy • Receiving chronic hemodialysis in preceding 30 days • Receiving home wound care

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[1]Dudley MN, Ambrose PG, Bhavnani SM, Craig WA, Ferraro MJ, Jones RN. Background and rationales for revised clinical and laboratory standards institute interpretive criteria (breakpoints) for Enterobacteriaceae and Psuedomonas aeruginosa: I. cephalosporins and aztreo

Ceftaroline

For adult MRSA pneumonia[1] or adult cystic fibrosis exacerbations[2], consider alternative dosing (*UWHealth Strong Recommendation, Moderate Quality of Evidence*) as detailed here:

- CRCL ≥ 50 mL/min: 600 mg IV every 8 hours
- CRCL 30-50 mL/min: 400 mg IV every 8 hours
- CRCL 15-30 mL/min: 300 mg IV every 8 hours
- CRCL <15 mL/min: 200 mg IV every 8 hours

References

[1] Forest Laboratories. Safety and Efficacy Study of Ceftaroline in Subjects With Staphylococcus Aureus Bacteremia or With Persistent Methicillin-Resistant Staphylococcus Aureus Bacteremia. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [2016 June 30]. Available from: https://clinicaltrials.gov/ct2/show/NCT01701219 Identifier: NCT01701219.

[2] Autry EB, Rybak JM, Leung NR, Gardner BM, Burgess DR, Anstead MI, Kuhn RJ. Pharmacokinetic and Pharmacodynamic Analyses of Ceftaroline in Adults with Cystic Fibrosis. Pharmacotherapy. 2016 Jan;36(1):13-8.

Ceftriaxone

- Ceftriaxone can cause biliary sludging, especially in neonates and children. Ceftriaxone is contraindicated in neonates requiring calcium containing intravenous solutions due to risk of precipitation.[1] *(UWHealth Strong Recommendation, Low - Moderate Quality of Evidence)*

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[1]Rocephin [package insert]. Genentech USA, Inc., South San Francisco, CA. https://www.gene.com/download/pdf/rocephin_prescribing.pdf . Accessed December 16, 2016.

Cidofovir

- May cause renal toxicity. Creatinine and urine protein should be monitored prior to each dose. If creatinine increases greater than 0.5 above baseline or 3+ proteinuria occurs, cidofovir should be discontinued.[1] *(UWHealth Strong Recommendation, Low - Moderate Quality of Evidence)*
- Concomitant probenecid (2 g PO 3 hours prior to infusion, then 1 g PO 1 hour after infusion and 8 hours after infusion, for a total of 4 g) and aggressive saline diuresis (a minimum of 500 mL before and 500 mL after treatment) have been shown to reduce the incidence of nephrotoxicity.[2] *(UWHealth Strong Recommendation, Low - Moderate Quality of Evidence)*

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[1]Vistide [package insert]. Gilead Sciences, Inc. Foster City, CA. http://www.gilead.com/~/media/Files/pdfs/medicines/other/vistide/vistide.pdf. Accessed December 9, 2016.
[2]Lexicomp Online®, UW Health, Hudson, Ohio: Lexi-Comp, Inc.;December 16, 2016.

Ciprofloxacin

- Contraindicated with tizanidine. Interaction can be life threatening.[1,2] *(UWHealth Strong Recommendation, Low Quality of Evidence)*
- Like other fluoroquinolones, ciprofloxacin may result in false positive opiate screen.[1] *(UWHealth Weak/conditional Recommendation, Low - Moderate Quality of Evidence)*
- Minimize use of fluoroquinolones based on recent FDA warnings.[2] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*

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[1]Lexicomp Online®, UW Health, Hudson, Ohio: Lexi-Comp, Inc.;December 16, 2016.
[2]Elsayed A, Elsharkawy H, Sakr W. A severe interaction between tizanidine and ciprofloxacin. *J Clin Anesth.* 2015;27(8):698.
[3]Food and Drug Administration (FDA), "Fluoroquinolone Antimicrobial Drugs Information." Available at http://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm346750.htm

Clarithromycin

Macrolide antibiotics have been associated with increased digoxin concentration and digoxin toxicity.[1] Digoxin blood concentration monitoring may be considered with macrolide therapy. *(UWHealth Conditional Recommendation, Low Quality of Evidence)*

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[1]Gomes T, Mamdani MM, Juurlink DN. Macrolide-induced digoxin toxicity: a population-based study. *Clin Pharmacol Ther.* 2009;86(4):383-386.

Clindamycin

- Clindamycin oral suspension is poorly accepted due to unpleasant taste.[1] *(UWHealth Weak/Conditional Recommendation, Moderate Quality of Evidence)*
- High doses of oral clindamycin (>450 mg Q6H) may cause esophagitis.[2] *(UWHealth Weak/Conditional Recommendation, Low Quality of Evidence)*
- Sometimes used in combination with other antibiotics for toxic shock syndrome or necrotizing fasciitis to suppress toxin production.[3] *(UWHealth Conditional Recommendation, Moderate Quality of Evidence)*
- Intravenous to oral conversion is not equivalent.

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[1]Steele RW, Russo TM, Thomas MP. Adherence issues related to the selection of antistaphylococcal or antifungal antibiotic suspensions for children. *Clin Pediatr (Phila).* 2006;45(3):245-250.
[2]Jaspersen D. Drug-induced oesophageal disorders: pathogenesis, incidence, prevention and management. *Drug Saf.* 2000;22(3):327-249.
[3]Lappin E, Ferguson AJ. Gram-positive toxic shock syndromes. *Lancet Infect Dis.* 2009;9(5):281-290.

Colistin

- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

Daptomycin

- Do not use for lung infection due to drug inactivation by lung surfactant.[1] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

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[1]Silverman JA, Mortin LI, Vanpraagh AD, et al. Inhibition of daptomycin by pulmonary surfactant: in vitro modeling and clinical impact. *J Infect Dis.* 2005;191(12):2149-2152.

Doripenem

- Carbapenems may decrease the serum concentration of valproate products. Management: concurrent use of carbapenem antibiotics with valproic acid is generally not recommended. Alternative antimicrobial agents should be considered, but if a concurrent carbapenem is necessary, consider additional seizure medication. Risk D: Consider therapy modification.[1]

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[1]Lexicomp Online®, UW Health, Hudson, Ohio: Lexi-Comp, Inc.;December 16, 2016.

Ertapenem

- Carbapenems may decrease the serum concentration of valproate products. Management: concurrent use of carbapenem antibiotics with valproic acid is generally not recommended. Alternative antimicrobial agents should be considered, but if a concurrent carbapenem is necessary, consider additional seizure medication. Risk D: Consider therapy modification.[1]

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[1]Lexicomp Online®, UW Health, Hudson, Ohio: Lexi-Comp, Inc.;December 16, 2016.

Erythromycin

- When given orally, use the minimally effective dose because as many as 30% of patients experience severe gastrointestinal intolerance which can limit erythromycin's use.[1] *(UWHealth Conditional Recommendation, Low Quality of Evidence)*
- Erythromycin is the preferred to azithromycin for gastric motility.[2,3] *(UWHealth Conditional Recommendation, Moderate Quality of Evidence)*
- Macrolide antibiotics have been associated with increased digoxin concentration and digoxin toxicity.[4] Digoxin blood concentration monitoring may be considered with macrolide therapy. *(UWHealth Weak/Conditional Recommendation, Low Quality of Evidence)*

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[1]Catnach SM, Fairclough PD. Erythromycin and the gut. *Gut.* 1992;33(3):397-401.
[2]Prather CM, Camilleri M, Thomforde GM, Forstrom LA, Zinsmeister AR. Gastric axial forces in experimentally delayed and accelerated gastric emptying. *Am J Physiol.* 1993;264(5 Pt 1):G928.
[3]Keshavarzian A, Isaac RM. Erythromycin accelerates gastric emptying of indigestible solids and transpyloric migration of the tip of an enteral feeding tube in fasting and fed states. *Am K Gastroenterol.* 1993;88(2):193.
[4]Gomes T, Mamdani MM, Juurlink DN. Macrolide-induced digoxin toxicity: a population-based study. *Clin Pharmacol Ther.* 2009;86(4):383-386.

Ethambutol

- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

Flucytosine

- To avoid toxicity in patients with impaired renal function, the peak concentration should be monitored and maintained at <100 mg/L. Draw peak concentrations two hours following dose before the next dose.[1,2]
- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

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[1]Lexicomp Online®, UW Health, Hudson, Ohio: Lexi-Comp, Inc.;December 16, 2016.

Foscarnet

- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

Ganciclovir

- Infertility and fetal harm possible. This applies during treatment and up to 90 days post therapy.[1] *(UWHealth Strong Recommendation, Low Quality of Evidence)*
- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

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[1]Valcyte [package insert]. Genentech, Inc. South San Francisco, CA. https://www.gene.com/download/pdf/valcyte_prescribing.pdf. Accessed December 10, 2016.

Gentamicin

- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

Imipenem/Cilastatin

- Carbapenems may decrease the serum concentration of valproate products. Management: concurrent use of carbapenem antibiotics with valproic acid is generally not recommended. Alternative antimicrobial agents should be considered, but if a concurrent carbapenem is necessary, consider additional seizure medication. Risk D: Consider therapy modification.[1]

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[1]Lexicomp Online®, UW Health, Hudson, Ohio: Lexi-Comp, Inc.;December 16, 2016.

Itraconazole

- Itraconazole solution provides higher blood levels than the tablet formulation and is preferred for initial itraconazole therapy. Solution should be taken on an empty stomach.[1] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
- Concentration monitoring is not routinely performed when using for prophylactic indications unless there is suspected treatment failure or poor absorption. If concentration monitoring performed, concentrations should be evaluated during the second week of therapy as a level 2-4 hours following a dose or as a trough level before the next dose. Itraconazole and hydroxyitraconazole concentrations *combined* should not exceed 10 mcg/mL.[2] UWHC Itraconazole Lab Test Directory *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*

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[1] Stevens DA. Itraconazole in cyclodextrin solution. *Pharmacotherapy.* 1999;19(5):603-611.
[2] Lexicomp Online®, UW Health, Hudson, Ohio: Lexi-Comp, Inc.;December 16, 2016.

Ketorolac

- An analgesic therapeutic ceiling dose for ketorolac has been described. Studies have shown that there is no greater pain relief associated with doses > 10mg[1-5] and that higher doses of ketorolac increase risk of adverse events[6]. (*UW Health Weak/Conditional Recommendation, Moderate Quality of Evidence)*

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[1] Motov S, Yasavolian M, Likourezos A, et al. Comparison of Intravenous Ketorolac at Three Single-Dose Regimens for Treating Acute Pain in the Emergency Department: A Randomized Controlled Trial. *Ann Emerg Med.* 2017;70(2):177-184.
[2] Reuben SS, Connelly NR, Lurie S, Klatt M, Gibson CS. Dose-Response of Ketorolac as an Adjunct to Patient-Controlled Analgesia Morphine in Patients After Spinal Fusion Surgery. *Anesth Analg.* 1998;87(1):98-102.
[3] Minotti V, Betti M, Ciccarese G, Fumi G, Tonato M, Del Favero A. A double-blind study comparing two single-dose regimens of ketorolac with diclofenac in pain due to cancer. *Pharmacotherapy.* 1998;18(3):504-508.
[4] Staquet MJ. A Double-Blind Study with Placebo Control of Intramuscular Ketorolac Tromethamine in the Treatment of Cancer Pain. *J Clin Pharmacol.* 1989;29(11):1031-1036.
[5] Brown CR, Moodie JE, Wild VM, Bynum LJ. Comparison of Intravenous Ketorolac Tromethamine and Morphine Sulfate in the Treatment of Postoperative Pain. *Pharmacotherapy.* 1990;10(6P2):116S-121S.
[6] Hernández-Díaz S, García-Rodríguez LA. Epidemiologic assessment of the safety of conventional nonsteroidal anti-inflammatory drugs. *Am J Med.* 2001;110(3, Supplement 1):20-27.

Levofloxacin

- Like other fluoroquinolones, ciprofloxacin may result in false positive opiate screen.[1] *(UWHealth Weak/conditional Recommendation, Low - Moderate Quality of Evidence)*
- Minimize use of fluoroquinolones based on recent FDA warnings.[2] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*

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[1]Lexicomp Online®, UW Health, Hudson, Ohio: Lexi-Comp, Inc.;December 16, 2016.
[2]Food and Drug Administration (FDA), "Fluoroquinolone Antimicrobial Drugs Information." Available at http://www.fda.gov/drugs/drugsafety/informationbydrugclass/ucm346750.htm

Mefloquine

- Any live vaccines should be completed at least 3 days before initiation of therapy.[1] *(UWHealth Strong Recommendation, Low Quality of Evidence)*

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[1]Lariam [package insert]. Roche Laboratories Inc. Nutley, New Jersey. http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/019591s026s028lbl.pdf. Accessed December 10, 2016.

Meropenem

- Carbapenems may decrease the serum concentration of valproate products. Management: concurrent use of carbapenem antibiotics with valproic acid is generally not recommended. Alternative antimicrobial agents should be considered, but if a concurrent carbapenem is necessary, consider additional seizure medication. Risk D: Consider therapy modification.[1]

Table 1. Considerations for selecting broad-spectrum beta-lactam antibiotics based on clinical indication for patients with MDR or HCAP risk factors (see Table 2 for risk factors)

Cefepime	Piperacillin/tazobactam	Meropenem
• Meningitis • Pneumonia • Aspiration pneumonia (add	• Pneumonia • Aspiration pneumonia with HCAP risk factors • Diabetic foot infection	• Patients unable to tolerate cefepime AND piperacillin-tazobactam • Empiric coverage for septic shock and

metronidazole) • SSTI, cellulitis • Intraabdominal infection involving the small intestine (add metronidazole)	• Intraabdominal infection involving the colon • Cholangitis • Positive culture for ampicillin-sensitive *Enterococcus* AND ongoing need for broad-spectrum coverage	history of ESBL pathogens (requires ID Approval beyond 72 hours)

Table 2. MDR and HCAP Risk Factors

MDR Pathogen Risk Factors	**HCAP-specific Risk Factors**
• Antimicrobial therapy in past 90 days • Current hospitalization with antibiotic exposure of greater than 5 days • Immunosuppressive disease and/or therapy • Currently on hospital unit or service with a high rate of resistance -- see UWHC Antibiograms	• Hospitalized 2 or more days in the preceding 90 days • Resident of skilled nursing facility or extended care facility • Receiving home infusion therapy • Receiving chronic hemodialysis in preceding 30 days • Receiving home wound care

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[1]Lexicomp Online®, UW Health, Hudson, Ohio: Lexi-Comp, Inc.;December 16, 2016.

Metronidazole

- 500mg PO/IV every 8 hours is sufficient for most infections. Every 6 hour dosing should be considered for treatment of a patient in active septic shock from *Clostridium difficile* infection OR in patients receiving therapy for treatment of anaerobic meningitis or CNS abscess.[1] *(UWHealth Weak/Conditional Recommendation, Low Quality of Evidence)*

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[1] Solomkin JS, Mazuski JE, Bradley JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: Guidelines by the Surgical Infection Society and the Infectious Diseases Society of America *Clin Infect Dis* 2010; 50:133-64

Minocycline

- IV minocycline is available for the treatment of multi-drug resistant *Acinetobacter* and should be used with the guidance of the Infectious Diseases service.[1]*(UWHealth Strong Recommendation, Low - Moderate Quality of Evidence)*

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[1]Ritchie DJ, Garavaglia-Wilson A. A review of intravenous minocycline for treatment of multidrug-resistant Acinetobacter infections. *Clin Infec Dis.* 2014;59(Suppl 6):S374-380.

Nitrofurantoin

- For patients with CrCL ≥60 mL/min, nitrofurantoin is recommended as one of the first-line therapies for treatment of uncomplicated cystitis.[1]*(UWHealth Strong Recommendation, High Quality of Evidence*)
- Patients with Stage III kidney disease (CrCL 31-59 mL/min), nitrofurantoin may be considered, but patients should be monitored closely for resolution of infection. [2,3] (*UWHealth Strong Recommendation, Moderate Quality of Evidence*)
- Patients with Stage IV or V kidney disease (CrCL <30 mL/min) should not receive nitrofurantoin due to concerns of lack of efficacy.[4] (*UWHealth Strong Recommendation, Moderate Quality of Evidence*)

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[1]Cunha BA, Schoch PE, Hage JR. Nitrofurantoin: preferred empiric therapy for community-acquired lower urinary tract infections. *Mayo Clinic proceedings. Mayo Clinic.* Dec 2011;86(12):1243-1244.
[2]Bains A, Buna D, Hoag NA. A retrospective review assessing the efficacy and safety of nitrofurantoin in renal impairment. *Can Param J*. 2009;142:248-252.
[3]Geerts AF, Eppenga WL, Heerdink R, et al. Ineffectiveness and adverse events of nitrofurantoin in women with urinary tract infection and renal impairment in primary care. *Eur. J. Clin. Pharmacol*. 2013;69(9):1701-1707.
[4]Gilbert DN. Urinary tract infections in patients with chronic renal insufficiency. *Clinical journal of the American Society of Nephrology : CJASN*. 2006;1(2):327-331.

Penicillin G

- Available as Na or K salt.[1]
- Penicillin G potassium contains 1.7 mEq potassium per million units.[2]
- Penicillin G sodium contains 1.68 mEq sodium per million units.[3]
- One million units of penicillin G equal 625 mg.[1]

- Long-acting injectable penicillin is available as penicillin G benzathine (Bicillin L-A®) and penicillin G benzathine/procaine (Bicillin C-R®).

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[1]Lexicomp Online®, UW Health, Hudson, Ohio: Lexi-Comp, Inc.; February 21, 2017.
[2]Penicillin G Potassium [package insert], Baxter Healthcare. Deerfield, IL. http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/050638s016lbl.pdf. Accessed February 21, 2017.
[3]Penicillin G Sodium [package insert], Sandoz. Princeton, New Jersey. http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/065068s013lbl.pdf. Accessed February 21, 2017.

Pentamidine

- To increase patient tolerance and efficacy of the aerosolized treatment, consider administering two puffs of an inhaled bronchodilator (e.g., albuterol) prior to pentamidine doses. Aerosolized Respiratory Drugs - Adult/Pediatric - Inpatient/Ambulatory *(UWHealth Weak/Conditional Recommendation, Low - Moderate Quality of Evidence)*
- Patients receiving pentamidine IV should have glucose monitored frequently and creatinine monitored daily. Hypoglycemia most commonly seen after 5-7 days but can occur at any time, including after therapy have been stopped.[1] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*

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[1]Waskin H, Stehr-Green JK, Helmick CG, Sattler FR. Risk factors for hypoglycemia associated with pentamidine therapy for Pneumocystis pneumonia. *JAMA.* 1988;260(3):345-347.

Piperacillin/tazobactam

- Galactomannan antigen assay when used in patient receiving piperacillin/tazobactam may result in false-positive results, although this is less so with current, refined formulations of the drug.[1,2] *(UWHealth Weak/Conditional Recommendation, Low-Moderate Quality of Evidence)*
- Piperacillin/tazobactam should not be relied upon for serious oxacillin-sensitive *S. aureus* infections as anti-staphylococcal penicillins are preferred[3] *(UWHealth Weak/Conditional Recommendation, Moderate Quality of Evidence)*
- Piperacillin/tazobactam contains 2.35 mEq (54 mg) of sodium per gram of piperacillin.[4] *(UWHealth Weak/Conditional Recommendation, Low - Moderate Quality of Evidence)*

Table 1. Considerations for selecting broad-spectrum beta-lactam antibiotics based on clinical indication for patients with MDR or HCAP risk factors (see Table 2 for risk factors)

Cefepime	Piperacillin/tazobactam	Meropenem
• Meningitis • Pneumonia • Aspiration pneumonia (add metronidazole) • SSTI, cellulitis • Intraabdominal infection involving the small intestine (add metronidazole)	• Pneumonia • Aspiration pneumonia with HCAP risk factors • Diabetic foot infection • Intraabdominal infection involving the colon • Cholangitis • Positive culture for ampicillin-sensitive *Enterococcus* AND ongoing need for broad-spectrum coverage	• Patients unable to tolerate cefepime AND piperacillin-tazobactam • Empiric coverage for septic shock and history of ESBL pathogens (requires ID Approval beyond 72 hours)

Table 2. MDR and HCAP Risk Factors

MDR Pathogen Risk Factors	HCAP-specific Risk Factors
• Antimicrobial therapy in past 90 days • Current hospitalization with antibiotic exposure of greater than 5 days • Immunosuppressive disease and/or therapy • Currently on hospital unit or service with a high rate of resistance -- see UWHC Antibiograms	• Hospitalized 2 or more days in the preceding 90 days • Resident of skilled nursing facility or extended care facility • Receiving home infusion therapy • Receiving chronic hemodialysis in preceding 30 days • Receiving home wound care

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[1]Adam O, Auperin A, Wilguin F, Bourhis JH, Gachot B, Chachaty E. Treatment with piperacillin-tazobactam and false positive Aspergillus galactomannan antigen test results for patients with hematological malignancies. *Clin Infect Dis.* 2004;38(6):917-920.
[2]Penack O, Rempf P, Graf B, Thiel E, Blau IW. False-positive Aspergillus antigen testing due to application of piperacillin/tazobactam – is it still an issue? *Diagn Microbiol Infect Dis.* 2008;60(1):117-120.
[3]Schweizer ML, Furona JP, Harris AD, et al. Comparative effectiveness of nafcillin or cefazolin versus vancomycin in methicillin-susceptible Staphylococcus aureus bacteremia. *BMC Infect Dis.* 2011;19(11):279.

[4]Piperacillin and tazobactam [package insert]. Sagent Pharmaceuticals, Schaumburg, IL. http://www.sagentpharma.com/wp-content/uploads/2014/11/PiperacillinTazobactam_PI.pdf Accessed December 10, 2016.

Polyethylene Glycol

Polyethylene glycol 3350 (MIRALAX) Conversion and Reconstitution (*UWHealth Weak/Conditional Recommendation, Low Quality of Evidence*)

Number of dry powder teaspoonfuls	Equivalent mL of dry powder	Equivalent grams of dry powder	Equivalent capfuls of dry powder	Recommended volume of juice or water to add to dry powder before administration
0.5	2.5	1.7	1/10	1 oz
1	5	3.4	1/5	1-2 oz
1.5	7.5	5.1	3/10	2-4 oz
2	10	6.8	2/5	
2.5	12.5	8.5	1/2	
3	15	10.2	3/5	4-8 oz
3.5	17.5	11.9	7/10	
4	20	13.6	4/5	
4.5	22.5	15.3	9/10	
5	25	17	1	

* Dry Powder: 1 teaspoonful = 5 mL = 1/5 capful = 3.4 g
1 oz = 1/8 cup = 30 mL
2 oz = 1/4 cup = 60 mL
4 oz = 1/2 cup = 120 mL
8 oz = 1 cup = 240 mL

Posaconazole

- Posaconazole tablets provide higher blood levels than the suspension formulation and are preferred for initial posaconazole therapy. Tablets should be taken with food.[1] *(UWHealth Weak/Conditional Recommendation, Moderate Quality of Evidence)*
- Suspension: food and/or acid is required for the absorption. 15 grams of fat are necessary for maximal absorption of a dose. PPI acid suppressants should be avoided, or another class (e.g. histamine H2-blockers) should be substituted to maximize absorption.[2,3] For examples of 15 grams of fat follow: UW-Health 'Health facts for you' Food Drug interactions: Posaconazole *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*

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[1]Lexicomp Online®, UW Health, Hudson, Ohio: Lexi-Comp, Inc.;December 16, 2016.
[2]Courtney R, Wexler D, Radwankski E, Lim J, Laughlin M. Effect of food on the relative bioavailability of two oral formulations of posaconazole in healthy adults. *Br J Clin Pharmacol.* 2004;57(2):218-222.
[3]Krishna G, Moton A, Ma L, Medlock MM, McLeod J. Pharmacokinetics and absorption of posaconazole oral suspension under various gastric conditions in health volunteers. *Antimicrob Agents Chemother.* 2009;53(3):958-966.

Pyrazinamide

- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

Quinupristin/dalfopristin

- After completing infusion of the dose, flush with D5W. Heparin or saline flushes should not be used.[1] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*

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[1]Synercid [package insert]. Pfizer Inc. New York, NY. http://labeling.pfizer.com/ShowLabeling.aspx?id=712 Accessed December 10, 2016.

Ribavirin

- Oral ribavirin is the preferred agent as inhaled has been shown to have poorer outcomes.[1,2] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
- Enteral ribavirin use for treatment of *Paramyxoviridae* family viruses (including RSV, parainfluenza virus, and human metapneumovirus) has been described. In adult patients with normal renal function, the usual recommended dose for this indication is 1200 to 1600 mg daily enterally divided twice or three times daily.[3,4] Pediatric dosing is 15 mg/kg orally twice daily (800 mg maximum). Doses should be adjusted based on renal function. (*UW Health Weak/Conditional Recommendation, Low Quality of Evidence*)

CrCL	Adult Ribavirin Dosing
≥ 50 mL/min	Normal dose (example: 800 mg BID)
30-50 mL/min	50% dose reduction (example: 400 mg BID)
< 30 mL/min	75% dose reduction (example: 200 mg BID)

- Because of concerns regarding environmental exposure to aerosolized ribavirin, refer to the Respiratory Therapy Ribavirin Policy and Procedure #2.29. The drug must be administered via a Small Particle Aerosol Generator (SPAG-2). Aerosolized Respiratory Drugs - Adult/Pediatric - Inpatient/Ambulatory *(UWHealth Weak/Conditional Recommendation, Low Quality of Evidence)*

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[1]Gross AE, Bryson ML. Oral ribavirin for the treatment of noninfluenza respiratory viral infections: a systematic review. *Ann Pharmacother.* 2015;49(10)1125-1135.
[2]Marcelin JR, Wilson JW, Razonable RR. Oral ribavirin therapy for respiratory syncytial virus infections in moderately to severely immunocompromised patients. *Transpl Infect Dis.* 2014;16(2):242-250.
[3]Fuehner T, Dierich M, Duesberg C, et al. Single-centre experience with oral ribavirin in lung transplant recipients with paramyxovirus infections. *Antivir Ther.* 2011;16(5):733-740.
[4]Pelaez A, Lyon GM, Force SD, et al. Efficacy of oral ribavirin in lung transplant patients with respiratory syncytial virus lower respiratory tract infection. *J Heart Lung Transplant.* Jan 2009;28(1):67-71.

Rifabutin

- Use in combination with other antibiotics due to concern of resistance development.[1] *(UWHealth Strong Recommendation, Moderate Quality of Evidence*

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[1]Mandell GL, Moorman DR. Treatment of experimental staphylococcal infections: effect of rifampin alone and in combination on development of rifampin resistance. *Antimicrob Agents Chemother.* 1980;17(14):658-662.

Rifapentin

- Use in combination with other antibiotics due to concern of resistance development.[1] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*

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[1]Mandell GL, Moorman DR. Treatment of experimental staphylococcal infections: effect of rifampin alone and in combination on development of rifampin resistance. *Antimicrob Agents Chemother.* 1980;17(14):658-662.

Rifampin

- Use in combination with other antibiotics due to concern of resistance development.[1] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*

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[1]Mandell GL, Moorman DR. Treatment of experimental staphylococcal infections: effect of rifampin alone and in combination on development of rifampin resistance. *Antimicrob Agents Chemother.* 1980;17(14):658-662.

Rifaxamin

- Consider oral metronidazole therapy in patients who cannot afford rifaximin as outpatients.[1] *(UWHealth Weak/Conditional Recommendation, Very Low Quality of Evidence)*

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[1] Shah SC, Day LW, Somsouk M, Sewell JL. Meta-analysis: antibiotic therapy for small intestinal bacterial overgrowth. Aliment Pharmacol Ther. 2013;38(8):925-34.

Sulfadiazine

- Monitor for crystalluria by UA. Crystalluria may be prevented by adequate hydration (daily urinary output >1500 mL) and alkalinizing urine to pH >7.15.[1] *(UWHealth Conditional Recommendation, Moderate Quality of Evidence)*

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[1]Dong BJ, Rodriquez RA, Goldschmidt RH. Sulfadiazine-induced crystalluria and renal failure in a patient with AIDS. *J Am Board Fam Pract.* 1999:12(3):243-248.

Tobramycin

- Tobramycin is the preferred aminoglycoside for the empiric treatment of Gram negative sepsis since MIC values of pathogens are usually 10 fold less than gentamicin. UWHC Inpatient Antibiogram *(UWHealth Weak/Conditional Recommendation, Low Quality of Evidence)*
- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

Trimethoprim-sulfamethoxazole

- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

Valacyclovir

- Patient should maintain adequate hydration during drug therapy to prevent precipitation of acyclovir (active drug) in the renal tubules.[1] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
- Acyclovir 10 mg/kg Q8H = Valacyclovir 2 gm PO Q6H. *(UWHealth Weak Recommendation, Very low Quality of Evidence)*

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[1]Perazella MA. Crystal-induced acute renal failure. *American Journal of Medicine.* 1999;106(4):459-465.

Valgancyclovir

- Patient should maintain adequate hydration to avoid renal toxicity.[1] *(UWHealth Strong Recommendation, Low Quality of Evidence)*
- Infertility and fetal harm possible. This applies during treatment and up to 90 days post therapy.[1] *(UWHealth Strong Recommendation, Low Quality of Evidence)*
- Valganciclovir tablets should not be crushed; may use suspension.[1] *(UWHealth Strong Recommendation, Low Quality of Evidence)*

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[1]Valcyte [package insert]. Genentech, Inc. South San Francisco, CA. https://www.gene.com/download/pdf/valcyte_prescribing.pdf. Accessed December 10, 2016.

Vancomycin

- Oral vancomycin is only effective *C difficile* colitis and will not treat systemic infection.[1] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
- Limit parenteral co-administration with nephrotoxic agents due to higher incidence of nephrotoxicity.[2] *(UWHealth Strong Recommendation, Moderate Quality of Evidence)*
- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

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[1]Rao S, Kupfer Y, Pagala M, Chapnick E, Tessler S. Systemic absorption of oral vancomycin in patients with Clostridium difficile infection. *Scand J Infect Dis.* 2011;43(5):386-388.
[2]Elyasi S, Khalili H, Dashti-Khavidake S, Mohommadpour A. Vancomycin-induced nephrotoxicity: mechanism, incidence, risk factors and special populations. A literature review. *Eur J Clin Pharmacol.* 2012;68(9):1253-1255.

Voriconazole

- The IV formulation is not recommended for patients with moderate-to-severe renal dysfunction (creatinine clearance <50 mL/min) because the intravenous vehicle is excreted renally and will accumulate in these patients.[1] *(UWHealth Weak/Conditional Recommendation, Low - Moderate Quality of Evidence)*
- Administer oral formulation on an empty stomach *(UWHealth Weak/Conditional Recommendation, Low - Moderate Quality of Evidence)* Medication Dosing for Enteral Feeding - Inpatient/ Ambulatory - Adult/ Pediatric/ Neonate
- Guidance for selection of which weight to use for dosing may be found in Renal Function-Based Dose Adjustments – Adult – Inpatient/Ambulatory – Clinical Practice Guideline Appendix B. Selecting Appropriate Dosing Weight for Antimicrobial Medications

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[1]Lexicomp Online®, UW Health, Hudson, Ohio: Lexi-Comp, Inc.;December 16, 2016.