Pharmacy and Therapeutics Committee Approvals, September 2011

P&T Date: September 6, 2011

<table>
<tr><th>AGENDA ITEM</th><th>P&T COMMITTEE DECISION</th><th>COMMENTS</th></tr>
<tr><td>Fosphenytoin (Cerebyx®)</td><td>Add to formulary with use restricted to pediatric population</td><td>Indication: Status epilepticus; prevention and treatment of seizures occurring during neurosurgery

Mechanism of Action:
• Diphosphate ester salt of phenytoin which acts as a water soluble prodrug of phenytoin; after administration, plasma esterases convert fosphenytoin to phenytoin as the active moiety
• Phenytoin stabilizes neuronal membranes and decreases seizure activity by increasing efflux or decreasing influx of sodium ions across cell membranes in the motor cortex during generation of nerve impulses

Adverse effects (most common): Hypertension, injection site pain/reaction, nystagmus, somnolence

Precautions: Patients with hypotension and severe myocardial insufficiency, HLA-B*1502-positive (increases risk of Stevens-Johnson syndrome and toxic epidermal necrolysis), preexisting liver function impairment, phenytoin serum levels above optimal ranges

Dosing:
• Status epilepticus: Loading dose 15-20 mg PE/kg IV administered at 100-150 mg PE/minute
• Nonemergent: Loading dose 10-20 mg PE/kg IV or IM (maximum IV rate: 150 mg PE/minute); Initial daily maintenance dose 4-6 mg PE/kg/day IV or IM
• Fosphenytoin should always be prescribed and dispensed in phenytoin sodium equivalents (PE).
• Note: Fosphenytoin 1.5mg = Phenytoin 1mg = Fosphenytoin 1mg PE</td></tr>
<tr><td></td><td></td><td></td></tr>
<tr><td>ADDITIONS TO FORMULARY</td><td colspan="2">• Rivastigmine transdermal (Exelon® patch) 4.6 mg/24hr, 9.5 mg/24hr</td></tr>
<tr><td>REMOVALS FROM FORMULARY</td><td colspan="2">• Testosterone cypionate (Depo-testosterone®)</td></tr>
<tr><td>AUTOMATIC SUBSTITUTIONS</td><td colspan="2"><table><tr><th>Medication Ordered</th><th>Automatic Substitution</th></tr><tr><td>Testosterone cypionate (Depo-testosterone®)</td><td>Testosterone ethanate (Delatestryl®) at same dose and frequency</td></tr></table></td></tr>
<tr><td>ANTIBIOTIC USE REVIEW COMMITTEE</td><td colspan="2">• 2011 Adult Empiric Treatment Guidelines – The adult empiric treatment guideline was updated to specify cefepime as the preferred broad spectrum antibiotic.
Adult Antibiotic Empiric treatment_Ma
• 2011 Pediatrics Empiric Treatment Guidelines – The guideline was updated with regards to the treatment of neutropenic fever
Pediatric Empiric Antibiotics_AUR July.
• 2011 Antifungal Treatment Guidelines
2011 Antifungal treatment recs_Draft
• Antimicrobial Dosing Protocol – Dosing for Zosyn® (Piperacillin/Tazobactam) has been revised to the following: Piperacillin/Tazobactam (Zosyn®) 3.375 GM Q6H (4.5 GM Q6H for</td></tr>
</table>

	neutropenic fever, pneumonia, or severe sepsis)
OTHER TOPICS	• **Pioglitazone (Actos®)** o FDA alerts – Labeling changes  B2A. Actos FDA alert - labeling chang o Product update information for outpatients  B2B. Actos Letter for patients 08.11.do • **High-alert medications: Management of – MM.01.01.03**  B5B High-Alert Medications Managen • **Warfarin Patient Education by Pharmacists** – Pharmacists are currently providing warfarin education to hospitalized patients. The Warfarin PCER and Progress Note Sticker will be used for documentation in the patient's medical record. o Warfarin PCER #9994  9994 Warfarin PCER 08 11.pdf o Progress Note Sticker #10435  10435 Warfarin Education Sticker 08. • **Hypoglycemia Reactions: Adult/Pediatric/Newborn Treatment Protocol CCN00083 –** Based on new ADA recommendations, the policy was updated to use 4 glucose tablets (vs. 3 glucose tablets) in patients with hypoglycemia who tolerate PO. This change has already been implemented and communicated to staff.  B7C. Hypoglycemia Reactions - Adult Ped • **PRN Antiemetics – Clarification of Orders**: The Joint Commission and MERP (Medication Error Reporting and Prevention) have identified that ambiguous medication orders are a major issue. Oftentimes at CSMC, multiple orders for **PRN** antiemetics are ordered for patients. Currently, CSMC does not have an antiemetic visual analog scale developed, and therefore it is difficult to designate nausea/vomiting as mild, moderate, or severe. Hence, the following procedure was approved and will be implemented on Thursday, October 13. o If more than 1 PRN antiemetic is ordered without specific instructions for use then the following sequence of medications will be used: ondansetron, prochlorperazine, metoclopramide (**no clarification order needed**). o As an example, if all 3 antiemetics are ordered PRN, the pharmacist will enter the following into the administration instructions: ▪ Ondansetron: Try ondansetron first ▪ Prochlorperazine: Try prochlorperazine if inadequate response to ondansetron ▪ Metoclopramide: Try metoclopramide if inadequate response to both ondansetron and prochlorperazine • **Rituxan for Non-oncological Uses**  9165 Rituximab 07.11.pdf

Requests for full monographs or questions regarding this listing may be addressed to the Drug Information Center at **(310) 423-3784**

Rachel Ngo, PharmD — *Pharmacy Program Coordinator*
Hai Tran, PharmD — *Clinical Coordinator*
Rita Shane, PharmD, FASHP — *Director, Department of Pharmacy*

2011 "EMPIRIC" TREATMENT RECOMMENDATIONS FOR COMMON ADULT INFECTIONS

Approved by: The Medical Executive Committee

These recommendations are based on guidelines published by the Infectious Diseases Society of America and the CSMC 2010 antibiogram

Orders for piperacillin/tazobactam, cefepime, or imipenem expire after 5 days. With few exceptions, these antibiotics should be de-escalated to narrower-spectrum antibiotics by the 5th day of therapy if resistant organisms have not been isolated on culture results.

INFECTION SITE	SUSPECTED PATHOGENS	RECOMMENDED DRUGS ***Fluoroquinolones are discouraged at CSMC, 35% Pseudomonas aeruginosa and 32% E. coli are no longer susceptible	SPECIAL CONSIDERATIONS
LUNG COMMUNITY ACQUIRED	*S. pneumoniae* *H. influenzae* *M. catarrhalis* Atypical	• Cefotaxime + macrolide Recommend oral transition after 2-3 days of IV therapy where possible	**CRITICALLY ILL[1]:** cefotaxime + IV azithromycin **PCN ALLERGY:** consult Pharmacist **SUSPECT ASPIRATION:** add metronidazole **SUSPECT *PSEUDOMONAS*** – see footnote 5 **SUSPECT MRSA[10]:** add vancomycin (maintain trough at 15-20mg/L) +/- clindamycin
HEALTHCARE-ASSOCIATED PNEUMONIA[8]	*S. pneumoniae* *H. influenzae* Atypical	• Cefotaxime + macrolide	**SUSPECT MRSA:** add vancomycin **CRITICALLY ILL[1]:** imipenem[2] + tobramycin[3,4] **SUSPECT ASPIRATION**: add metronidazole if using cefepime or cefotaxime **SUSPECT MDR ACINETOBACTER[9]** : use colistin IV **CONSIDER STOPPING ANTIBIOTICS ON DAY 8 IF CULTURE NEGATIVE FOR *P. AERUGINOSA* OR *ACINETOBACTER SPP*. AND THE PATIENT HAS RESPONDED (IDSA GUIDELINES FOR VAP, HAP, HCAP 2005)CONSIDER EXTENDED INFUSION TIME OF 4 HOURS FOR PIPERACILLIN/TAZOBACTAM IN CRITICALLY ILL PATIENTS** • Maintain vancomycin trough at 15-20mg/L
	See hospital acquired section	**NONAMBULATORY-NURSING HOME, MULTIPLE COMORBIDITIES OR RECENT HOSPITALIZATION:** • See hospital acquired section	
HOSPITAL ACQUIRED	Enterobacteriaceae Resistant GNB *S. aureus* / MRSA Anaerobes	• Cefepime[2,] (preferred agent) + tobramycin[3,4] + vancomycin, **OR** • Piperacillin/tazobactam[2,11] + tobramycin[3,4] + vancomycin	
UROSEPSIS COMMUNITY ACQUIRED	Enterobacteriaceae *Enterococci*	• Cefotetan ± ampicillin Recommend oral transition after 2-3 days of IV therapy where possible	
HOSPITAL OR NURSING HOME ACQUIRED	Resistant GNB *Enterococci*	• Piperacillin/tazobactam[2,11] + tobramycin[3,4]	**CRITICALLY ILL[1]:** piperacillin/tazobactam[2,11] + amikacin[3,4]
ABDOMEN COMMUNITY ACQUIRED	Enterobacteriaceae *B. fragilis* *Enterococci* *Streptococcus spp.*	• Cefotaxime + metronidazole Recommend oral transition after 2-3 days of IV therapy where possible	**BILIARY TRACT INVOLVEMENT AND IMMUNOSUPPRESED**: add ampicillin for *E. faecalis* **CRITICALLY ILL:** IMIPENEM[2] ± TOBRAMYCIN
HOSPITAL OR NURSING HOME ACQUIRED OR POST-OPERATIVE INTRABDOMINAL OR PELVIC SURGERY	Enterobacteriaceae Resistant GNB *Enterococci* *B. fragilis*	• Piperacillin/tazobactam[2,11] + tobramycin[3,4]	**CRITICALLY ILL[1]:** imipenem[2] + tobramycin[3,4] SUSPECT *C. DIFFICILE*: see CSMC *C. Difficile* treatment guidelines[13]
FEVER WITH NEUTROPENIA[6] (SEE PATHWAY FOR COMPLETE ALGORITHM)	Enterobacteriaceae Resistant GNB *Staphylococci* *Enterococci*	• Cefepime[2,] (preferred agent)+ tobramycin[3,4] **OR** Piperacillin/tazobactam[2,11] + tobramycin[3,4] **MONOTHERAPY MAY BE CONSIDERED FOR UNCOMPLICATED PATIENTS:** cefepime[2] (preferred agent) or piperacillin/tazobactam[2,11]	**CRITICALLY ILL OR SUSPECT ESBL[1]:** imipenem[2] + amikacin[3,4] + vancomycin **ERYTHEMA & TENDERNESS AT EXIT SITE OR PENDING IDENTIFICATION OF GPC IN BLOOD CULTURE:** add vancomycin[14]
SEPSIS OF UNKNOWN SOURCE	Resistant GNB *S. aureus* /MRSA	• Cefepime[2,] (preferred agent) + tobramycin[3,4] ± metronidazole + vancomycin **OR** • Piperacillin/tazobactam[2,11] + tobramycin[3,4] + vancomycin,	**CRITICALLY ILL[1]:** imipenem[2] + tobramycin[3,4] + vancomycin **CONSIDER EXTENDED INFUSION TIME OF 4 HOURS FOR PIPERACILLIN/TAZOBACTAM IN CRITICALLY ILL PATIENTS**
SKIN COMMUNITY ACQUIRED	*Streptococci* (GpA) *S. aureus* (consider community onset MRSA)	• Cellulitis: cefazolin or oxacillin • Furunculosis or abscess, suspect community onset MRSA: vancomycin + incision and drainage when possible • Necrotizing fasciitis: Penicillin G + clindamycin • Suspected mixed infection: cefotaxime + clindamycin	• Severe cellulitis: consider adding clindamycin • Critically ill: consider vancomycin • FURUNCULOSIS OR ABSCESS-: DE-ESCALATION, IF SUSCEPTIBLE, TO TRIMETHOPRIM/SULFA, CLINDAMYCIN OR DOXYCYCLINE FOLLOWING IV vancomycin + incision/ drainage (if possible) • **ANIMAL BITE**: cefuroxime + clindamycin
HEALTHCARE -ASSOCIATED OR DIABETIC	*Streptococci* *Staphylococcci* Enterobacteriaceae Resistant GNB *B. fragilis*	**SUPERFICIAL OR NO ULCER:** see skin above **UNCOMPLICATED DIABETIC FOOT:** Cefotetan + vancomycin **HEALTH-CARE ASSOCIATED OR LIMB-THREATENING:** • Piperacillin/tazobactam[2,11] ± tobramycin[3,4] + vancomycin	**CRITICALLY ILL[1]:** imipenem[2] + tobramycin[3,4] + vancomycin
MENINGITIS COMMUNITY ACQUIRED	*S. pneumoniae* *N. meningitidis* *H. influenzae*	• Cefotaxime + vancomycin (maintain trough at 15-20mg/L)	**SUSPECT LISTERIA[12]:** add ampicillin ± gentamicin **SUSPECT S. PNEUMONIAE:** add dexamethasone[7] ***Use maximum antibiotic dose***
NEUROSURGERY OR HEAD TRAUMA	*S. aureus* Enterobacteriaceae Resistant GNB *S. pneumoniae*	• Cefepime[2,] + vancomycin (maintain trough at 15-20mg/L)	**HIGHLY SUSPECT *P. aeruginosa***: consider adding tobramycin[3,4] **CRITICALLY ILL[1]**: meropenem + vancomycin ***Use maximum antibiotic dose***

PSSP=penicillin sensitive resistant *S. pneumoniae*; PRSP=penicillin resistant *S. pneumoniae*; MRSA=methicillin-resistant *S. aureus*; GNB=gram negative bacilli; MDR=multidrug resistant; Enterobacteriaceae includes *E.coli, Klebsiella sp., Proteus sp., Enterobacter sp., Citrobacter sp., Serratia sp.*

1: Critically ill includes hemodynamic instability and in the ICU.
2: For patients with a history of serious penicillin allergy, substitute with aztreonam (nonformulary), ± vancomycin ± metronidazole as indicated.
3: Aminoglycosides should be dosed on a once daily basis or as per ICU protocol. In febrile neutropenic patients, consider discontinuing after 72 hours if cultures do not show *Pseudomonas aeruginosa*.
4: Nephrotoxicity typically occurs following several days of treatment (unlikely within 72 hours). Therefore aminoglycoside-containing regimens are recommended pending culture results. Substitution with fluoroquinolone is strongly discouraged.
5: Severe COPD, alcoholism; use cefepime plus tobramycin plus macrolides
6: These recommendations are intended for treatment of the first episode of neutropenia in the same hospitalization
7: Dexamethasone 10mg Q6H x 2-4 days with first dose administered 10-20 min before the first dose of antimicrobial therapy in adults with suspected or proven pneumococcal meningitis
8: Includes nursing home or long term care facility resident, recent hospitalization (within 30 days), received broad spectrum antibiotics or chemotherapy within 30 days of infection.
9. Suspect Acinetobacter in patients on vent or trach support failing broad spectrum antimicrobial therapy
10. Necrotizing or cavitary pneumonia or history of community acquired MRSA infection
11. May interfere with galactomannan measurement.
12. Age >50 years, immunocompromised, alcoholism, pregnant.
13. Discontinue inciting antimicrobials if possible
14. May be stopped after 2 days if there is no evidence for a gram-positive infection

References

1. Mandell LA, et al. Infectious diseases society of America/American thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. CID 2007;44:S27-72.
2. Lipsky BA, Berendt AR, Deery HG, et al. Diagnosis and Treatment of Diabetic Foot Infections. CID 2004;39:885-910.
3. Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice Guidelines for the Management of Bacterial Meningitis. CID 2004;39:1267-1284.
4. Hughes WT, Armstrong D, Bodey GP, et al. 2002 Guidelines for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer. CID 2002;34:730-751
5. Solomkin JS, Mazuski JE, 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. CID 2010:50;133-164
6. Chastre J, Wolff M, Fagon JY, et al. Comparison of 8 vs. 15 Days of Antibiotic Therapy for Ventilator-Associated Pneumonia in Adults. JAMA 2003;290(19):2588-2598.
7. Craven DE, Palladino R, McQuillen DP. Healthcare-associated Pneumonia in Adults: Management Principles to Improve Outcomes. Infectious Disease Clinics of North America 2004;18:939-962.
8. Nilederman MS, Craven DE, Boten MJ, et al. Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia. American Journal of Respiratory and Critical Care Medicine 2005;171:388-416.
9. E.J. Bow, et al. A Randomized, Open-Label, Multicenter Comparative Study of the Efficacy and Safety of Piperacillin-tazobactam and Cefepime for the Empirical treatment of Febrile Neutropenic Episodes in Patients with Hematologic Malignancies. CID 2006:43:447-459.
10. Jean-Damien R., et al. Levels of Vancomycin in Cerebral Fluid of Adults Patients Receiving Adjunctive Corticosteroids to Treat Pneumococcal Meningitis: A prospective Multicenter Observational Study. CID 200;44:250-5.
11. Moellering et al. Current Treatment Options for Community-Acquired Methicillin- Resistant *Staphylococcus aureus* CID April 2008;46:1032-7
12. Menendez, et. al. Treatment Failure in Community-acquired Pneumonia Chest October 2007;132:1348-55
13. Lodise et al. Piperacillin-tazobactam for *Pseudomonas aeruginosa* Infection: clinical implications of an extended-infusion dosing strategy CID 2007 44 :357-63.
14. National Comprehensive Cancer Network: www.NCCN.org
15. Talan D.A. et al. Emergency Department Management of Meningitis and Encephalitis. Infectious Diseases Clinics of North America 2008:33-52
16. 16. Cohen, SH, Dale DN, Johnson, S et al. Clinical practice guidelines for clostridium difficile infection in adults: 2010 update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA). *Infect Control Hosp Epidemiol.* 2010;31: 431-455.
17. Gupta K, Hooton, TM, Naber et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *CID.* 2011;52:e103-120.
18. Freifeld AG, Bow EJ, Sepkowitz KA et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Disease Society of America. *CID*. 2011;52:e56-e93.
19. Liu C, Bayer A, Coscgrove SE et al. Clinical practice guidelines by the infectious diseases society of America for the treatment of methicillin-resistant *Staphlococcus Aureus* infectious in adults and children. *CID*. 2011;52:1 – 38.

2011 EMPIRIC TREATMENT RECOMMENDATIONS FOR COMMON PEDIATRIC INFECTIONS

APPROVED BY: PEDIATRIC INFECTIOUS DISEASES, ANTIBIOTIC USE REVIEW COMMITTEE, PEDIATRIC P&T

BASED ON GUIDELINES FROM THE INFECTIOUS DISEASES SOCIETY OF AMERICA AND THE CSMC 2010 ANTIBIOGRAM

Antibiotic resistance is increasing in the Medical Center and is a direct result of wide-spread and prolonged use of broad-spectrum antibiotics. We strongly discourage use of these agents except when resistant pathogens are highly suspected and limited to the shortest acceptable duration.

INFECTION SITE	SUSPECTED PATHOGENS	RECOMMENDED INTRAVENOUS DRUGS	SPECIAL CONSIDERATIONS	ORAL TRANSITION[1]
LUNG (Community acquired)	*S. pneumoniae* *H. influenzae* *M. catarrhalis* *S. aureus* Atypical (>5 years)	cefotaxime ± macrolide	*If suspect parapneumonic process (abscess, empyema):* cefotaxime + clindamycin ± macrolide Suspect MRSA: add vancomycin (trough 15-20) +/- clindamycin	cefuroxime ± macrolide **OR** amox/clav ± macrolide
LUNG (Hospital acquired)	Enterobacteriaceae Resistant GNB *S. aureus* *H. influenzae* *S. pneumoniae*	Cefepime (preferred agent) + tobramycin, or piperacillin/tazobactam[3,4] + tobramycin	*Critically ill*[2]: imipenem[3]+ amikacin + vancomycin Suspect MRSA: add vancomycin (maintain trough 15-20)	Not recommended
URINARY TRACT & PYELONEPHRITIS (Community acquired) >3 months	Enterobacteriaceae *Enterococci*	cefotaxime + ampicillin	*Consider oral transition after 2-3 days of IV therapy*	TMP/SMX, **OR** cephalexin
ABDOMEN (Community acquired)	*Enterobacteriaceae* *B. fragilis* *Enterococci* *Streptococcus spp.*	cefotaxime + metronidazole	***PERITONITIS SECONDARY TO PERFORATED APPENDIX:*** piperacillin/tazobactam[3,4] ± tobramycin	amox/clav, **OR** metronidazole + cephalexin OR ciprofloxacin[7]
ABDOMEN (Hospital acquired)	Enterobacteriaceae Resistant GNB *Enterococci* *B. fragilis*	piperacillin/tazobactam[3] + tobramycin	*Critically ill*[2]*:* imipenem[3] + tobramycin Suspect *C. difficile:* metronidazole (see CSMC *C. difficile* treatment guidelines)[8] NEC : piperacillin/tazobactam[3] + tobramycin	Not recommended
FEVER WITH NEUTROPENIA (see pathway for complete algorithm)	Enterobacteriaceae Resistant GNB *Staphylococci*	Cefepime (preferred agent) + tobramycin or piperacillin/tazobactam[3,4] + tobramycin	*Critically ill*[2]*:* imipenem[3] + amikacin + vancomycin *Erythema and tenderness at line exit site:* add vancomycin[6] PCN allergy: see footnote[3] + tobramycin	Only if patient is low-risk, clinically stable and GI absorption is adequate
RULE OUT SEPSIS Age < 1 month	GBS *E. coli* *Listeria*	ampicillin + gentamicin	*Suspect HSV*: add acyclovir	Not recommended
RULE OUT SEPSIS Age ≥ 1 month	GBS *S. pneumoniae* *E. coli* *Listeria*	cefotaxime 1-3 months: add ampicillin for Listeria coverage	*Sickle cell disease:* - Critically ill: Add vancomycin (trough 15-20) *Use maximum antibiotic doses until CSF infection ruled out*	Not recommended
SKIN (Community-acquired)	*Streptococci* (GpA) *S. aureus* (consider community onset MRSA)	• Cellulitis: cefazolin or oxacillin • Furunculosis or abscess, suspect community onset MRSA: vancomycin + incision and drainage when possible • Necrotizing fasciitis: Penicillin G + clindamycin (if suspect mixed infection use cefotaxime + clindamycin)	• *Severe cellulitis:* consider adding clindamycin • *Critically ill:* consider vancomycin • *Human/Animal bite: cefuroxime + clindamycin* • *PCN allergy: TM*P/SMX or clindamycin or vancomycin	MSSA *or* GABHS[5]: dicloxacillin **OR** cephalexin Community onset MRSA: clindamycin OR TMP/SMX
SKIN (Peri-orbital)	*Streptococci* *H.influenzae* *S. aureus*	Cefotaxime + clindamycin	*Orbital involvement:* cefotaxime + clindamycin • Suspect MRSA: add vancomycin	amox/clav **OR** cephalexin **OR** clindamycin
BONE & JOINT INFECTIONS	*S. aureus* *S. pyogenes*	Oxacillin or cefazolin + clindamycin	*Foot puncture: requires debridment and anti-pseudomonal coverage* (cefepime or pip/tazo)	cephalexin, **OR** dicloxacillin, **OR** clindamycin
MENINGITIS (Community acquired) Age ≤3 mo	*GBS* *E. coli* *Listeria* *S. pneumoniae*	cefotaxime + ampicillin ± vancomycin (if bacterial highly suspected)	*Aseptic meningitis (<2 months):* consider HSV and empirically treat with acyclovir	Not recommended
MENINGITIS (Community acquired) Age > 3mo	*S. pneumoniae* *N. meningitidis* *H. influenzae*	cefotaxime + vancomycin (if bacterial highly suspected) (trough 15-20)	*Immunocompromised:* - Consider Listeria, add ampicillin ***Use maximum antibiotic dose***	Not recommended

MENINGITIS (Neurosurgery or head trauma or VP shunt)	*S. aureus/S. epi* Enterobacteriaceae Resistant GNR *S. pneumoniae*	cefepime + vancomycin (trough 15-20)	Externalization of shunt or hardware usually necessary for sterilization. *Critically ill*[2]: meropenem + vancomycin (trough 15-20) ***Use maximum antibiotic dose***	Not recommended

GNB=gram negative bacilli; GBS=group B streptococci; GABHS=Group A beta hemolytic streptococci; NEC=Necrotizing enterocolitis

1 Consider early transition to PO using well absorbed antibiotics (after 2-3 days of IV therapy) if the following criteria are met: (1) functioning GI tract, (2) fever < 100.5 for 24 hours, (3) hemodynamic stability, (4) clinical improvement.

2. Critically ill includes hemodynamic instability and in the ICU

3. For patients with a history of serious penicillin allergy, substitute with aztreonam (nonformulary), ± vancomycin ± metronidazole as indicated.

4. May interfere with galactomannan measurement

5. Consider for erysipelas, toxic shock syndrome, or scarlet fever

6. May be stopped after 2 days if there is no evidence for a gram-positive infection

7. For coverage for pseudomonas only

8. Discontinue inciting antimicrobials if possible

References:

1. Mandell LA, et al. Infectious diseases society of America/American thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. CID 2007;44:S27-72.
2. Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice Guidelines for the Management of Bacterial Meningitis. CID 2004;39:1267-1284.
3. Hughes WT, Armstrong D, Bodey GP, et al. 2002 Guidelines for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer. CID 2002;34:730-751
4. Solomkin JS, Mazuski JE, 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. CID 2010:50;133-164
5. Moellering et al. Current Treatment Options for Community-Acquired Methicillin- Resistant *Staphylococcus aureus* CID April 2008;46:1032-7
6. Gupta K, Hooton, TM, Naber et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *CID.* 2011;52:e103-120.
7. Freifeld AG, Bow EJ, Sepkowitz KA et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Disease Society of America. *CID*. 2011;52:e56-e93.
8. Liu C, Bayer A, Coscgrove SE et al. Clinical practice guidelines by the infectious diseases society of America for the treatment of methicillin-resistant *Staphlococcus Aureus* infectious in adults and children. *CID*. 2011;52:1 – 38.

2011 CSMC TREATMENT RECOMMENDATIONS FOR FUNGAL INFECTIONS

Approved by: The Antibiotic Use Review Committee, The Pharmacy and Therapeutics Committee

These recommendations are not intended to supercede clinical judgement

INDICATION	FLUCONAZOLE[1, 13] (FZ)	VORICONAZOLE[1,2,3] (VCZ)	CASPOFUNGIN[4,5]	AMPHOTERICIN B[6,7,8,9] (AMB)	ABLC[6,9]	OTHER CONSIDERATIONS
NEUTROPENIC FEVER-EMPIRIC Persistent fever of unknown origin despite 4-7 days of broad spectrum antibacterial therapy	CONSIDER IF **LOW RISK** FOR ASPERGILLOSIS ▪ no sinusitis ▪ no lung infection ▪ no CNS infection ▪ no recent use of FZ(within 30 days) **Dose:** **800 mg x1, then 400 mg daily**	CONSIDER FOR VERY **HIGH RISK** FOR INVASIVE ASPERGILLOSIS (IA) (BASED ON CHEST XRAY/CT ,H/O IA, **Dose:** **Loading:** **6 mg/kg IV/PO Q12H x 2** **Maintenance:** **4 mg/kg IV/PO Q12H**	PREFERRED AGENT **Dose:** **70 mg X1 then 50mg daily**	ALTERNATIVE TO ABLC FOR HIGH RISK OF RESISTANT MOLDS (ZYGOMYCETES) AND LIKELY TO TOELRATE[7] **Dose:0.7 mg/kg/day**	PREFERRED FOR PATIENTS WITH HIGH RISK FOR RESISTANT MOLDS (ZYGOMYCETES) **Dose:** **3-5 mg/kg/day** **(5 mg/kg/day: suspected Aspergillus or other molds)**	**CONSIDER OTHER CAUSES OF FEVER:** ▪ antibiotic resistance ▪ secondary or occult infection ▪ inadequate antibacterial dose or penetration ▪ drug fever
NON-NEUTROPENIC HOST-EMPIRIC (cultures pending) THERAPY SHOULD MAINLY BE LIMITED TO PATIENTS WITH **ALL** BELOW: ▪ Colonized with yeast (at ≥2 sites) ▪ Trial of antibiotics (broad spectrum) ▪ Full culture work up ▪ High Risk for fungal infection (TPN, central line, ICU stay >7 days, GI surgery, GI trauma or perforation,) ▪ If liver transplant patient: added risk if re-transplantation, or re-operation	PREFERRED IF: ▪ azole resistance **NOT** suspected* (see considerations) ▪ hemodynamically stable **Dose:** **800 mg x1 then 400 mg daily**	NO ADVANTAGE OVER FZ	PREFERRED WITH **ANY** BELOW: ▪ suspected azole resistance* ▪ persistent infection while on FZ ▪ hemodynamically unstable **Dose:** **70 mg X1 then 50mg daily**	ALTERNATIVE TO ABLC FOR DEEP ORGAN INFECTIONS IF LIKELY TO TOLERATE[7] AND • suspected azole resistance OR • hemodynamically unstable OR • failure of FZ or Caspofungin **Dose:** **0.7 mg/kg/day**	CONSIDER IF DEEP ORGAN INFECTION SUSPECTED AND • suspected azole resistance OR • hemodynamically unstable OR failure of FZ or Caspofungin • Suspected concomitant endocardial/CNS involvement **Dose:** **3-5 mg/kg/day**	***AZOLE RESISTANCE SUSPECTED:** ▪ recent history of *C. glabrata* or *C. krusei* ▪ recent use of FZ (within 30 days) **CONSIDER OTHER CAUSES OF FEVER:** ▪ antibiotic resistance ▪ secondary or occult infection ▪ inadequate antibacterial dose or penetration ▪ drug fever **Patients without risk factors of TPN, GI surgery, GI trauma or perforation are unlikely to benefit from antifungal therapy**

1 Use intravenous formulation ONLY if NPO
2 Dose based on total body weight. For voriconazole, total body weight greater than 130kg not studied
3 Avoid intravenous Voriconazole if CrCl <50 ml/min unless benefit outweighs risk (such as documented invasive aspergillosis and NPO)
4 Liver failure (Child-Pugh >7) use Caspofungin 70 mg load dose, then 35 mg daily
5 No Clinical Correlation with reported MIC values
6 Dose Obese patients (TBW > 140% IBW) on adjusted body weight: ABW = IBW + 0.4(TBW-IBW)
7 Likely to tolerate AmB: Receiving chronic hemodialysis; CrCl > 50ml/min and not on other nephrotoxins and no multi-organ failure
8 Consider test dose of AmB 1mg over 20 minutes to assess for infusion reactions
9 Bolus Hydrate with 500 ml normal saline pre and post infusion. Diligent potassium replacement required (consult pharmacist)
10 Renal adjustment necessary when CrCl ≤ 40 ml/min, standard dose is 100 mg/kg/day PO divided QID
11 Susceptible dose dependent refers to a Fluconazole MIC of 16 to 32 mg/L
12. Consider drug level monitoring in patients with suspected treatment failure, ADEs or prolonged treatment course
13. Higher doses may be required in obese patients (TBW >140% IBW). Consider 6 mg/kg based on corrected body weight: CBW= iBW + 0.3(TBW-IBW). Round final dose to nearest 200 mg.14. Includes fully susceptible and S-DDF (susceptible dosage dependant) fluconazole isolates. S-DDF indicates that success of therapy depends on achieving maximum possible blood levels; therefore, increase fluconazole dose to 800 mg daily.

2011 CSMC TREATMENT RECOMMENDATIONS FOR FUNGAL INFECTIONS

Approved by: The Antibiotic Use Review Committee, The Pharmacy and Therapeutics Committee

These recommendations are not intended to supercede clinical judgement

INDICATION	FLUCONAZOLE[1] (FZ)	VORICONAZOLE[1,2,3] (VCZ)	CASPOFUNGIN[4,5]	AMPHOTERICIN B[6,7,8,9] (AMB)	ABLC[6,9]	OTHER CONSIDERATIONS
SYSTEMIC CANDIDIASIS-A (RARELY AZOLE RESISTANT) *C. albicans* (or PNA FISH+) *C. tropicalis* *C. parapsilosis*	PREFERRED FOR MOST INFECTIONS **Dose: 800 mg x 1, then 400 mg daily**	NO ADVANTAGE OVER FLUCONAZOLE	NO ADVANTAGE OVER FLUCONAZOLE	ALTERNATIVE TO ABLC FOR DEEP ORGAN INFECTION IF LIKELY TO TOLERATE[7] **Dose: 0.7 mg/kg/day**	CONSIDER FOR DEEP ORGAN INFECTION **Dose: 3-5 mg/kg/day**	**THE MICROBIOLOGY LABORATORY ROUTINELY PERFORMS SUSCEPTIBILITY TESTING ON BLOODSTREAM ISOLATES** CATHETER OR "HARDWARE" RELATED INFECTIONS: REMOVE IF FEASIBLE CNS INFECTIONS: AMB OR ABLC + FLUCYTOSINE(5FC)[10] PREFERRED, THEN STEP-DOWN TO FZ
SYSTEMIC CANDIDIASIS-B (AZOLE RESISTANCE PREVALENT) *C. glabrata* *C. krusei* (rare at CSMC)	PREFERRED IF SUSCEPTIBILITY **CONFIRMED** **Dose:** • **800 mg x 1, then 400 mg daily** • **800 mg daily for susceptible dose dependent[11] *C. glabrata***	NO ADVANTAGE OVER FLUCONAZOLE CONSIDER FOR *C. KRUSEI* IF INTOLERANCE TO CASPOFUNGIN OR AS STEP DOWN ORAL THERAPY	PREFERRED AGENT FOR AZOLE-RESISTANT STRAINS **Dose: 70 mg X1 then 50 mg daily**	ALTERNATIVE TO CASPOFUNGIN FOR AZOLE RESISTANT STRAINS IF LIKELY TO TOLERATE[7] **Dose: 0.7 -** 1 **mg/kg/day**	CONSIDER FOR DEEP ORGAN INFECTION **Dose: 5 mg/kg/day**	THE MICROBIOLOGY LABORATORY ROUTINELY PERFORMS SUSCEPTIBILITY TESTING ON BLOODSTREAM ISOLATES CATHETER OR "HARDWARE" RELATED INFECTIONS: REMOVE IF FEASIBLE CNS INFECTIONS: AMB OR ABLC + 5FC[10] PREFERRED
ESOPHAGITIS	PREFERRED AGENT **Dose: 200 – 400 mg daily**	NO ADVANTAGE OVER FLUCONAZOLE	PREFERRED AGENT FOR AZOLE RESISTANT STRAINS **Dose: 70 mg X1 then 50 mg daily**	ALTERNATIVE TO CASPOFUNGIN FOR AZOLE RESISTANT STRAINS IF LIKELY TO TOLERATE[7] **Dose: 0.3-0.7 mg/kg/day**	NOT PREFERRED	▪ AVOID ITRACONAZOLE (NONFORMULARY)
URINARY TRACT INFECTION	PREFERRED AGENT **Dose: 200-400 mg daily (400mg for pyelonephritis)**	NO ROLE POOR PENETRATION	NO ROLE POOR PENETRATION (4%)	PREFERRED FOR FLUCONAZOLE RESISTANT CYSTITIS **Dose:** Cystitis: 0.3-0.6 mg/kg 1-7 days	NO ROLE	• PYELONEPHRITIS RESISTANT TO FZ: USE AMB (0.5-0.7MG/KG/DAY) WITH OR WITHOUT 5FC[10]. AVOID ABLC DUE TO TREATMENT FAILURES AND LOW TISSUE CONCENTRATION • FLUCONAZOLE RESISTANT CYSTITIS **AND** REFRACTORY: CONSIDER AMB BLADDER IRRIGATION **Dose:** 50 mg in 1 liter sterile water as continuous bladder irrigation via 3-way foley catheter X 5 days

1 Use intravenous formulation ONLY if NPO
2 Dose based on total body weight. For voriconazole, total body weight greater than 130kg not studied
3 Avoid intravenous Voriconazole if CrCl <50 ml/min unless benefit outweighs risk (such as documented invasive aspergillosis and NPO)
4 Liver failure (Child-Pugh >7) use Caspofungin 70 mg load dose, then 35 mg daily
5 No Clinical Correlation with reported MIC values
6 Dose Obese patients (TBW > 140% IBW) on adjusted body weight: ABW = IBW + 0.4(TBW-IBW)
7 Likely to tolerate AmB: Receiving chronic hemodialysis; CrCl > 50ml/min and not on other nephrotoxins and no multi-organ failure
8 Consider test dose of AmB 1mg over 20 minutes to assess for infusion reactions
9 Bolus Hydrate with 500 ml normal saline pre and post infusion. Diligent potassium replacement required (consult pharmacist)
10 Renal adjustment necessary when CrCl ≤ 40 ml/min, standard dose is 100 mg/kg/day PO divided QID
11 Susceptible dose dependent refers to a Fluconazole MIC of 16 to 32 mg/L
12. Consider drug level monitoring in patients with suspected treatment failure, ADEs or prolonged treatment course
13. Higher doses may be required in obese patients (TBW >140% IBW). Consider 6 mg/kg based on corrected body weight: CBW= iBW + 0.3(TBW-IBW). Round final dose to nearest 200 mg.14. Includes fully susceptible and S-DDF (susceptible dosage dependant) fluconazole isolates. S-DDF indicates that success of therapy depends on achieving maximum possible blood levels; therefore, increase fluconazole dose to 800 mg daily.

2011 CSMC TREATMENT RECOMMENDATIONS FOR FUNGAL INFECTIONS

Approved by: The Antibiotic Use Review Committee, The Pharmacy and Therapeutics Committee

These recommendations are not intended to supercede clinical judgement

INDICATION	FLUCONAZOLE[1] (FZ)	VORICONAZOLE[1,2,3,12] (VCZ)	CASPOFUNGIN[4,5]	AMPHOTERICIN B[6,7,8,9] (AMB)	ABLC[6,9]	OTHER CONSIDERATIONS
INVASIVE ASPERGILLOSIS	NO ROLE	PREFERRED AGENT **Dose:** **Loading:** **6 mg/kg IV / PO Q12H x 2** **Maintenance:** **4 mg/kg IV/PO Q12H**	MAY CONSIDER AS SALVAGE THERAPY IF VCZ AND ABLC ARE NOT AN OPTION (NOT TOLERATING OR CONTRAINDICATED) **Dose:** **70 mg X1 then 50 mg daily**	ALTERNATIVE TO ABLC IF ABLE TO TOLERATE[7]	PREFERRED IF VCZ IS NOT AN OPTION (NOT TOLERATING OR CONTRAINDICATED) **Dose:** **5 mg/kg/day**	COMBINATION ANTIFUNGAL THERAPY **HAS** NO ESTABLISHED CONSENSUS REGARDING USE GALACTOMANNAN ASSAY MAY AID IN THE DETECTION OF *ASPERGILLUS* SPECIES
CRYPTOCOCCUS: MENINGOENCEPHALITIS, SEVERE PULMONARY, OR CRYPTOCOCCEMIA	AFTER INITIAL AMB INDUCTION THERAPY, PREFERRED AZOLE **Dose:** **400 - 800 mg daily**	LIMITED ROLE DUE TO LACK OF CLINICAL DATA – MAY BE CONSIDERED IN REFRACTORY CASES	NO ROLE	PREFERRED AGENT WITH 5FC[10] FOR INDUCTION THERAPY **Dose:** **AmB:0.7-1 mg/kg/day** **5FC[10]: 100 mg/kg/day divided QID**	• ORGAN TRANSPLANT PATIENTS: PREFERRED AGENT WITH 5FC[9] FOR INDUCTION • ALTERNATIVE WITH 5FC[10] FOR NON-ORGAN TRANSPLANT PATIENTS AND INTOLERANT OF AMB **Dose:** **5 mg/kg/day** **5FC[10]: 100 mg/kg/day divided QID**	THERAPY MAY NEED TO BE EXTENDED BASED ON PATIENT RESPONSE SECONDARY PROPHYLAXIS IN IMMUNE COMPROMISED (MAINTENANCE THERAPY): FLUCONAZOLE 200 MG DAILY
COCCIDIOIDOMYCOSIS	PREFERRED AGENT **Dose:** **400 - 1000 mg daily**	LIMITED ROLE DUE TO LACK OF CLINICAL DATA – MAY BE CONSIDERED IN REFRACTORY CASES	NO ROLE	PREFERRED ONLY FOR DIFFUSE PNEUMONIA, FOLLOWED BY FLUCONAZOLE THERAPY **Dose:** **0.7 – 1 mg/kg/day**	ALTERNATIVE TO AMB FOR DIFFUSE PNEUMONIA AND INTOLERANT OF AMB, FOLLOWED BY FLUCONAZOLE THERAPY **Dose:** **5 mg/kg/day**	REFRACTORY MENINGITIS: CONSIDER INTRATHECAL AMB (CSMC GUIDELINE AVAILABLE) HTTP://WEB.CSMC.EDU/CLINICAL/DOCUMENTS/INTRATHECAL-AMB-FOR-COOCI-INFECTION-75030.PDF

1 Use intravenous formulation ONLY if NPO
2 Dose based on total body weight. For voriconazole, total body weight greater than 130kg not studied
3 Avoid intravenous Voriconazole if CrCl <50 ml/min unless benefit outweighs risk (such as documented invasive aspergillosis and NPO)
4 Liver failure (Child-Pugh >7) use Caspofungin 70 mg load dose, then 35 mg daily
5 No Clinical Correlation with reported MIC values
6 Dose Obese patients (TBW > 140% IBW) on adjusted body weight: ABW = IBW + 0.4(TBW-IBW)
7 Likely to tolerate AmB: Receiving chronic hemodialysis; CrCl > 50ml/min and not on other nephrotoxins and no multi-organ failure
8 Consider test dose of AmB 1mg over 20 minutes to assess for infusion reactions
9 Bolus Hydrate with 500 ml normal saline pre and post infusion. Diligent potassium replacement required (consult pharmacist)
10 Renal adjustment necessary when CrCl ≤ 40 ml/min, standard dose is 100 mg/kg/day PO divided QID
11 Susceptible dose dependent refers to a Fluconazole MIC of 16 to 32 mg/L
12. Consider drug level monitoring in patients with suspected treatment failure, ADEs or prolonged treatment course
13. Higher doses may be required in obese patients (TBW >140% IBW). Consider 6 mg/kg based on corrected body weight: CBW= iBW + 0.3(TBW-IBW). Round final dose to nearest 200 mg.14. Includes fully susceptible and S-DDF (susceptible dosage dependant) fluconazole isolates. S-DDF indicates that success of therapy depends on achieving maximum possible blood levels; therefore, increase fluconazole dose to 800 mg daily.

2011 CSMC TREATMENT RECOMMENDATIONS FOR FUNGAL INFECTIONS

Approved by: The Antibiotic Use Review Committee, The Pharmacy and Therapeutics Committee

These recommendations are not intended to supercede clinical judgement

HISTOPLASMOSIS	NO ROLE	NOT RECOMMENDED	NO ROLE	ALTERNATIVE TO ABLC IF LIKELY TO TOLERATE[7] **Dose:** **0.7-1 mg/kg/day**	PREFERRED AGENT **Dose:** **5 mg/kg/day** **DISSEMINATED DISEASE: CONTACT FACULTY OR AUR PHARMACIST**	ITRACONAZOLE MAY BE USED IN THE MEDICAL CENTER FOR HISTOPLASMOSIS, USUALLY AFTER AMPHO B INDUCTION THERAPY

1 Use intravenous formulation ONLY if NPO
2 Dose based on total body weight. For voriconazole, total body weight greater than 130kg not studied
3 Avoid intravenous Voriconazole if CrCl <50 ml/min unless benefit outweighs risk (such as documented invasive aspergillosis and NPO)
4 Liver failure (Child-Pugh >7) use Caspofungin 70 mg load dose, then 35 mg daily
5 No Clinical Correlation with reported MIC values
6 Dose Obese patients (TBW > 140% IBW) on adjusted body weight: ABW = IBW + 0.4(TBW-IBW)
7 Likely to tolerate AmB: Receiving chronic hemodialysis; CrCl > 50ml/min and not on other nephrotoxins and no multi-organ failure
8 Consider test dose of AmB 1mg over 20 minutes to assess for infusion reactions
9 Bolus Hydrate with 500 ml normal saline pre and post infusion. Diligent potassium replacement required (consult pharmacist)
10 Renal adjustment necessary when CrCl ≤ 40 ml/min, standard dose is 100 mg/kg/day PO divided QID
11 Susceptible dose dependent refers to a Fluconazole MIC of 16 to 32 mg/L
12. Consider drug level monitoring in patients with suspected treatment failure, ADEs or prolonged treatment course
13. Higher doses may be required in obese patients (TBW >140% IBW). Consider 6 mg/kg based on corrected body weight: CBW= iBW + 0.3(TBW-IBW). Round final dose to nearest 200 mg.14. Includes fully susceptible and S-DDF (susceptible dosage dependant) fluconazole isolates. S-DDF indicates that success of therapy depends on achieving maximum possible blood levels; therefore, increase fluconazole dose to 800 mg daily.

2011 CSMC TREATMENT RECOMMENDATIONS FOR FUNGAL INFECTIONS

Approved by: The Antibiotic Use Review Committee, The Pharmacy and Therapeutics Committee

These recommendations are not intended to supercede clinical judgement

INDICATION	FLUCONAZOLE[1] (FZ)	VORICONAZOLE [1,2,3] (VCZ)	CASPOFUNGIN[4,5]	AMPHOTERICIN B[6,7,8,9] (AMB)	ABLC[6,9]	OTHER CONSIDERATIONS
ZYGOMYCETES (RHIZOPUS, ABSIDIA, MUCOR, RHIZOMUCOR)	**NO ROLE**	NO ROLE	NOT RECOMMENDED	ALTERNATIVE TO ABLC IF LIKELY TO TOLERATE[7] **Dose:** **1-1.5 mg/kg/day**	PREFERRED AGENT **DOSE:** **5 mg/kg/day**	POSACONAZOLE MAY HAVE A ROLE FOR CERTAIN PATIENTS BUT DATA ARE LIMITED AND SUSCEPTIBILITY BREAKPOINTS ARE NOT ESTABLISHED: CONTACT AUR PHARMACIST OR ID FACULTY IF CEREBRAL INVOLVEMENT, CONTACT AUR PHARMACIST OR ID FACULTY

2010 Percent Susceptible for Candida spp. from All Sources (Number of isolates tested in parenthesis)

ORGANISM[1]	Fluconazole	Voriconazole	Amphotericin B
Candida albicans	100 (57)	100 (57)	100 (55)
Candida glabrata (torulopsis)	Percent Susceptible & S-DDF: 46 (35)[14]	54 (35)	100 (34)
Candida parapsilosis	88 (16)	94 (16)	100 (15)
Candida tropicalis	100 (12)	100 (12)	100 (10)

Revised 6/2011

References

- Spellberg BJ, Filler SG, Edwards JE. Current Treatment Strategies for Disseminated Candidiasis. CID 2006 ;42 :244-251.
- Pappas PG, Kauffman CA, Andes D, et al. Clinical Practice Guidelines for the Management of Candidiasis: 2009 Update by the Infectious Diseases Society of America. CID 2009 ; 48 :503-535
- Perfect JR, et al. Clinical Practice Guidelines for the Management of Cryptococcal Disease: 2010 Update by the Infectious Diseases Soceity of America. CID 2010 :50

1 Use intravenous formulation ONLY if NPO
2 Dose based on total body weight. For voriconazole, total body weight greater than 130kg not studied
3 Avoid intravenous Voriconazole if CrCl <50 ml/min unless benefit outweighs risk (such as documented invasive aspergillosis and NPO)
4 Liver failure (Child-Pugh >7) use Caspofungin 70 mg load dose, then 35 mg daily
5 No Clinical Correlation with reported MIC values
6 Dose Obese patients (TBW > 140% IBW) on adjusted body weight: ABW = IBW + 0.4(TBW-IBW)
7 Likely to tolerate AmB: Receiving chronic hemodialysis; CrCl > 50ml/min and not on other nephrotoxins and no multi-organ failure
8 Consider test dose of AmB 1mg over 20 minutes to assess for infusion reactions
9 Bolus Hydrate with 500 ml normal saline pre and post infusion. Diligent potassium replacement required (consult pharmacist)
10 Renal adjustment necessary when CrCl ≤ 40 ml/min, standard dose is 100 mg/kg/day PO divided QID
11 Susceptible dose dependent refers to a Fluconazole MIC of 16 to 32 mg/L
12. Consider drug level monitoring in patients with suspected treatment failure, ADEs or prolonged treatment course
13. Higher doses may be required in obese patients (TBW >140% IBW). Consider 6 mg/kg based on corrected body weight: CBW= iBW + 0.3(TBW-IBW). Round final dose to nearest 200 mg.14. Includes fully susceptible and S-DDF (susceptible dosage dependant) fluconazole isolates. S-DDF indicates that success of therapy depends on achieving maximum possible blood levels; therefore, increase fluconazole dose to 800 mg daily.

2011 CSMC TREATMENT RECOMMENDATIONS FOR FUNGAL INFECTIONS

Approved by: The Antibiotic Use Review Committee, The Pharmacy and Therapeutics Committee

These recommendations are not intended to supercede clinical judgement

- Leenders AC, Reiss P, Portegies P, et al. Liposomal amphotericin B (AmBisome) compared with amphotericin B both followed by oral fluconazole in the treatment of AIDS-associated cryptococcal meningitis. AIDS 1997 ;11 :1463-1471.
- Sharkey PK, Graybill JR, Johnson ES, et al. Amphotericin B Lipid Complex Compared with Amphotericin B in the Treatment of Cryptococcal Meningitis in Patients with AIDS. CID 1996 ;22 :315-321.
- Walsh TJ, Anaissie EJ, Denning DW, et al. Treatment of Aspergillosis : Clinical Practice Guidelines of the Infectious Diseases Society of America. CID 2008 ;46 :327-360.
- Wheat LJ, Freifeld AG, Kleiman MB, et al. Clinical Practice Guidelines for the Management of Patients with Histoplasmosis : 2007 Update by the Infectious Diseases Society of America. CID 2007 ;45 :807-825.
- Van Burik JA, Hare RS, Solomon HF, et al. Posaconazole is effective as salvage therapy in zygomycosis : a retrospective summary of 91 cases. CID 2006 ;42 :e61-65.
- Medical Letter Antifungal Treatment Guidelines 2008
- Groll Ah, et al. Distribution of Lipid Formulation of Amphotericin B into Bone Marrow and Fat Tissue in Rabbits. AAC 2000;44(2); 408-410.
- Antifungal Drugs. The Medical Letter. 2009.
- Limper AH, Knox SK, Sarosi GA et al. An official American Thoracic Society Statement: treatment of fungal infections in adult pulmonary and critical care patients. *Am J Respir Crit Care Med.* 2011; 183:96-128.

1 Use intravenous formulation ONLY if NPO
2 Dose based on total body weight. For voriconazole, total body weight greater than 130kg not studied
3 Avoid intravenous Voriconazole if CrCl <50 ml/min unless benefit outweighs risk (such as documented invasive aspergillosis and NPO)
4 Liver failure (Child-Pugh >7) use Caspofungin 70 mg load dose, then 35 mg daily
5 No Clinical Correlation with reported MIC values
6 Dose Obese patients (TBW > 140% IBW) on adjusted body weight: ABW = IBW + 0.4(TBW-IBW)
7 Likely to tolerate AmB: Receiving chronic hemodialysis; CrCl > 50ml/min and not on other nephrotoxins and no multi-organ failure
8 Consider test dose of AmB 1mg over 20 minutes to assess for infusion reactions
9 Bolus Hydrate with 500 ml normal saline pre and post infusion. Diligent potassium replacement required (consult pharmacist)
10 Renal adjustment necessary when CrCl ≤ 40 ml/min, standard dose is 100 mg/kg/day PO divided QID
11 Susceptible dose dependent refers to a Fluconazole MIC of 16 to 32 mg/L
12. Consider drug level monitoring in patients with suspected treatment failure, ADEs or prolonged treatment course
13. Higher doses may be required in obese patients (TBW >140% IBW). Consider 6 mg/kg based on corrected body weight: CBW= iBW + 0.3(TBW-IBW). Round final dose to nearest 200 mg.14. Includes fully susceptible and S-DDF (susceptible dosage dependant) fluconazole isolates. S-DDF indicates that success of therapy depends on achieving maximum possible blood levels; therefore, increase fluconazole dose to 800 mg daily.

U.S. Food and Drug Administration

Safety

Actos (pioglitazone): Ongoing Safety Review - Potential Increased Risk of Bladder Cancer

[UPDATED 08/04/2011] The U.S. Food and Drug Administration (FDA) is informing the public that the Agency has approved updated drug labels for the pioglitazone-containing medicines to include safety information that the use of pioglitazone for more than one year may be associated with an increased risk of bladder cancer.

[UPDATED 06/15/2011] Use of the diabetes medication Actos (pioglitazone) for more than one year may be associated with an increased risk of bladder cancer. Information about this risk will be added to the *Warnings and Precautions* section of the label for pioglitazone-containing medicines. The patient Medication Guide for these medicines will also be revised to include information on the risk of bladder cancer.

This safety information is based on FDA's review of data from a five-year interim analysis of an ongoing, ten-year epidemiological study. The five-year results showed that although there was no overall increased risk of bladder cancer with pioglitazone use, an increased risk of bladder cancer was noted among patients with the longes exposure to pioglitazone, and in those exposed to the highest cumulative dose of pioglitazone.

FDA is also aware of a recent epidemiological study conducted in France which suggests an increased risk of bladder cancer with pioglitazone. Based on the results of this study, France has suspended the use of pioglitazone and Germany has recommended not to start pioglitazone in new patients.

Additional Information for Patients, Information for Healthcare Professionals, and a Data Summary are provided in the Drug Safety Communication.

FDA recommends that healthcare professionals should:

- Not use pioglitazone in patients with active bladder cancer.
- Use pioglitazone with caution in patients with a prior history of bladder cancer. The benefits of blood sugar control with pioglitazone should be weighed against the unknown risks for cancer recurrence.

FDA will continue to evaluate data from the ongoing ten-year epidemiological study. The Agency will also conduct a comprehensive review of the results from the French study. FDA will update the public when more information becomes available.

[Posted 09/17/2010]

AUDIENCE: Endocrinology, Family Practice, Urology

ISSUE: FDA notified healthcare professionals and patients that the Agency is reviewing data from an ongoing, ten-year epidemiological study designed to evaluate whether Actos (pioglitazone) is associated with an increased risk of bladder cancer. Findings from studies in animals and humans suggest this is a potential safety risk that needs further study. At this time, FDA has not concluded that Actos increases the risk of bladder cancer. Its review is ongoing, and the Agency will update the public when it has additional information.

BACKGROUND: The drug manufacturer, Takeda, conducted a planned analysis of the study data at the five-year mark, and submitted their results to FDA. Overall, there was no statistically significant association between Actos exposure and bladder cancer risk. However, further analyses were also performed looking at how long patients were on Actos and the total amount of the drug they received during that time. An increased risk of bladder cancer was observed among patients with the longest exposure to Actos, as well as in those exposed to the highest cumulative dose of Actos.

RECOMMENDATIONS: Healthcare professionals should continue to follow the recommendations in the drug label when prescribing Actos. Patients should continue taking Actos unless told otherwise by their healthcare professional. Patients who are concerned about the possible risks associated with using Actos should talk to their healthcare professional.

Additional Information for Patients, Information for Healthcare Professionals, and a Data Summary are provided in the Drug Safety Communication.

Healthcare professionals and patients are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report Online: www.fda.gov/MedWatch/report.htm [1]
- Download form [2] or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to -800-FDA-0178

[08/04/2011 - Drug Safety Communication [3] - FDA]

[06/15/2011 - Drug Safety Communication [4] - FDA]

[09/22/2010 - Podcast [5] - FDA]

[09/17/2010 - Drug Safety Communication [6] - FDA]

[09/17/2010 - Note To Correspondents [7] - FDA]

Links on this page:

1. http://www.fda.gov/MedWatch/report.htm
2. /Safety/MedWatch/HowToReport/DownloadForms/default.htm
3. /Drugs/DrugSafety/ucm266555.htm
4. /Drugs/DrugSafety/ucm259150.htm
5. /Drugs/DrugSafety/DrugSafetyPodcasts/ucm226749.htm
6. /Drugs/DrugSafety/ucm226214.htm

CEDARS-SINAI MEDICAL CENTER

DEPARTMENT OF ENDOCRINOLOGY AND
DEPARTMENT OF PHARMACY SERVICES

ACTOS® (PIOGLITAZONE)
UPDATE ON IMPORTANT SAFETY INFORMATION

DATE: _____

DEAR _____**:**

Actos® (pioglitazone) and pioglitazone containing products such as Actoplus Met® (pioglitazone with metformin), Actoplus Met XR® (pioglitazone with metformin extended release), and Duetact® (pioglitazone with glimepiride), may be associated with an increased risk of bladder cancer when used for more than one year. Pioglitazone is a medication used to treat type 2 diabetes.

Recently, the Food and Drug Administration (FDA) has approved updated labeling for pioglitazone-containing medicines. The FDA has announced that patients should read the updated drug labeling and medication guide they receive along with their pioglitazone prescription as it explains the risks associated with its use. **It is recommended that patients contact their healthcare professional if they experience blood or a red color in the urine, an increased need to urinate, or pain with urination.** The FDA will continue to evaluate the data and update the public when more information becomes available.

Our records indicate that you have been prescribed pioglitazone, or a pioglitazone-containing product. If you are currently taking this medication, please CONTINUE taking this medication as prescribed and CONSULT with your doctor. Your doctor and you may choose to select an alternative medication.

Please see the link below for more safety information on pioiglitazone:
http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm226257.htm

A medication guide is also attached for more information

Please contact your doctor and/or the pharmacy where you have your pioiglitazone prescription filled with any further questions.

Thank you.

PROCEDURE

CEDARS-SINAI

Effective Date: Not Approved

Title: High-Alert Medications: Management of MM.01.01.03

Document Owner: Manukyan, Christine (Pharmacy Compliance Specialist)

Home Department: Department of Pharmacy Services

I. POLICY

A. Cedars-Sinai Medical Center (CSMC) safely manages high-alert medications.

B. Medications involved in a high percentage of external/internal medication errors and/or sentinel events and that carry a higher risk for abuse, errors, or other adverse outcomes are identified as high-alert medications. Additional medications may be added to the list based on reports of external/ internal errors and sentinel events.

C. CSMC identified high-alert medications include:

1. Chemotherapy agents for cancer indication (parenteral)
2. Direct thrombin inhibitors: argatroban and lepirudin infusions
3. Heparin
4. Insulin infusion
5. Intrathecal or epidural administration of medications
6. Magnesium sulfate infusion 25g/250ml
7. Neuromuscular blockers (ICUs and ED)
8. Opioid infusions including PCAs and PCEAs
9. Potassium chloride (KCL) vials (2mEq/1ml concentrated)
10. Propofol infusions (except OR setting)
11. Sodium chloride $\geq$ 3% bolus and infusion
12. Thrombolytic agents for therapeutic use: alteplase and reteplase

D. CSMC has defined processes for safe management of high-alert medications throughout the medication use process (i.e. procuring, storing, ordering, transcribing, preparing, dispensing, administering, and/or monitoring).

II. PURPOSE

To provide general guidelines for the management of high-alert medications.

III. PROCEDURE

A. Steps for procurement, storage, ordering and transcribing, preparation and dispensing, administration and documentation, and monitoring are outlined in table 1.

B. Definitions

Pharmacist (RPh) Independent double check - the pharmacist responsible for order transcription/verification, preparation or dispensing of high-alert medications will get a second pharmacist review of the medication. See table 1 for specific high alert medications requiring RPh independent double check.

- Upon transcription of chemotherapy orders for cancer indication, orders are evaluated for appropriateness of the drug, dose based on mg/m2, selection and volume of diluent, total number of doses to be administered (i.e. dose reconciliation), route and rate of administration, compatibility and interaction with other medications. See Policy and Procedure Chemotherapy Ordering and Checking MM.01.01.03a
- Upon preparation, pharmacist will review the medication label, expiration date, dose, diluents(s), rate of administration and compatibility
- Upon dispensing, pharmacist will review the medication label, expiration date, dose, diluents(s), rate of administration, and check patient's Medication Administration Record to assure the order is still active

Nurse (RN) independent double check – upon administration, the nurse responsible for the medication administration will obtain a second health care provider (RN, MD, RPh) verification of the medication before it is administered. The second verification will include two patient identifiers (inpatient: patient name and MRN#, outpatient: patient name and date of birth), a review of the medication, the IV line tubing setup, and the pump program set up (including medication name, dose, route, and timing).

IV. POLICY APPROVALS

- Phillip Zakowski, MD
  Chair, Pharmacy and Therapeutics Committee
- Steve Simons, MD, FACP, FCCP
  Medical Director, Medical Affairs

- Rita Shane, PharmD, FASHP
  Director, Pharmacy Services
- Linda Burnes Bolton, DrPH, RN, FAAN
  Vice President Nursing and Chief Nursing Officer

ORIGINAL EFFECTIVE DATE: **4/2010**

	Selection / Procurement		Storage			Order / Transcription ~		Preparation	Dispensing	Administration
	Use commercially available product only	*Limit & standard concentrations*	*RPh or TCT certified double check (Green sticker)*	*Red bins / tape in the Pharmacy*	*Perpetual inventory in the Nursing Units*	*Standard hospital protocol or order set*	*Restricted use to specific patient care area*	*RPh independent double check*	*RPh independent double check*	*RN independent double check*
Chemotherapy for cancer indication (parenteral)				X		X		RPh double check & dose reconciliation*	RPh double check & dose reconciliation*	X
Direct thrombin inhibitors: argatroban & lepirudin infusions		X				X			X	X
Heparin	standardized commercially available for anticoagulation	X	X	X		X			RPh double check for heparin infusions for anti-coagulation	bolus & infusion for anticoagulation
Insulin infusion		X				X				X
Intrathecal or epidural administration of medications									X	X
Magnesium sulfate infusion 25g/250ml	X	X		X			L&D, MFCU, ICU			X
Neuromuscular blockers bolus and infusions		X	X	X	X		ED, ICU		RPh double check for patient specific infusions	X
Opioid infusions, including PCA and PCEAs		X			X	X			RPh double check for patient specific customized PCA/PCEA	X
Potassium chloride (KCl) vials (2mEq/1ml concentrated)	X		X	X			6-OR			
Propofol infusions	X	X					ED, ICU			X
Sodium chloride ≥3% bolus and infusion	X						23.4% - ICU			X
Thrombolytic agents for therapeutic use (alteplase, reteplase)		X				alteplase		alteplase^	alteplase^	X

~Transcription of chemotherapy orders are independently double checked by two pharmacists, *Dose reconciliation accounts for doses prepared/dispensed, ^except in emergency situations

CEDARS-SINAI MEDICAL CENTER®

PATIENT / CAREGIVER EDUCATION RECORD

PATIENT I.D.

Taking Coumadin® (Warfarin)

THIS IS IMPORTANT INFORMATION FOR YOU

- When you get home, look at the list of discharge medications discussed and given to you by your nurse or physician. Take Coumadin® (warfarin) exactly as prescribed and remember to look at the information sheets for medication side effects or interactions.
- Look and become aware of the Danger Signals listed below.

1. **Self-Care:**
   - Tell your doctor if you have recently had a fall or other injury.
   - Brush and floss your teeth gently.
   - Be careful when using sharp objects, including razors and fingernail clippers.
   - Avoid picking your nose. If you need to blow your nose, blow it gently.
   - Avoid having any injections while taking this medication.
   - Carry an ID card or wear a medical alert bracelet to let any emergency caregivers know that you are using Coumadin®.
   - Make sure any doctor or dentist who treats you knows that you are taking Coumadin®.
   - You may need to stop using this medicine several days before surgery or medical tests.
   - Diet and medications can affect the PT / INR level.
   - Women: Using this medicine while you are pregnant can harm your unborn baby. Use an effective form of birth control to keep from getting pregnant. If you think you have become pregnant while using the medicine, tell your doctor right away.

2. **Activity / assistive devices:**
   - Coumadin® (Warfarin) increases the risk of bleeding so you may bleed more easily while you are using this medicine. Stay away from rough sports or other situations where you could be bruised, cut, or injured.
   - Call your doctor if you have recently had a fall or other injury.

3. **Nutrition:** ❑ Regular Diet ❑ Special Diet: _____
   - **For diet questions call Clinical Nutrition: (310) 423-3444**
   - You may take Coumadin® with or without food.
   - Eating foods that contain vitamin K can affect the way Coumadin® works.
   - Eat a consistent amount of foods with Vitamin K. Do not avoid food that contains Vitamin K.
   - Avoid major changes in dietary habits, or notify your health professional before changing habits.

Taking Coumadin® (Warfarin)

3. **Nutrition:** *(Cont'd)*
   - ***Do not*** vary the amount of food in your diet which is high in vitamin K.
     Examples of foods high in vitamin K are:

• Asparagus • Avocado • Broccoli • Brussel sprouts • Cabbage *(red and green)* • Cauliflower • Endive	• Garbanzo beans • Green onions *(scallions)* • Green tea • Leafy vegetables *(turnip or collard greens, kale, lettuce, spinach)* • Turnips	• Lentils • Liver • Seaweed • Soybeans • Oils (soybean, canola & olive) • Watercress

   - Other food products can affect the way Coumadin® works in your body:
     - **Food products** that may affect blood clotting include
       - cranberries / cranberry juice
       - garlic
       - ginger
       - licorice
       - turmeric
   - ***Do not take*** any supplements (vitamin pills) that contain vitamin E or vitamin K while you are taking this medicine.
   - Avoid supplements that contain Omega 3 fatty acids.
   - Avoid preparations that contain Fish Oils.
   - Avoid consuming large amounts of alcohol while you are taking this medicine

4. **Other Medications *(including over-the-counter, vitamin and herbal products):***
   - **Do not take** any medication including over-the-counter medication except on the advice of the physician or pharmacist.
     Also, do not stop taking any medication without the advice of a physician or pharmacist.
   - There are many other medicines, including nonprescription *(over-the-counter)* medicines and herbal products that you should not use while you are taking Coumadin®. Make sure your doctor or pharmacist knows about ALL other medicines you are using.
   - ***Avoid*** the following herbal supplements while taking warfarin:
     Alfalfa, cinchona bark, clove oil, ginkgo, garlic, ginger, ginseng, feverfew. Talk with your healthcare provider if you have concerns about these or other food products and their effects on Coumadin®.

5. **If a dose is missed:**
   - It is important that you take your medicine as prescribed by your doctor
   - If you miss a dose or forget to take your medicine, take it as soon as you can.

CEDARS-SINAI MEDICAL CENTER®

PATIENT / CAREGIVER EDUCATION RECORD

PATIENT I.D.

Taking Coumadin® (Warfarin)

5. **If a dose is missed:** *(Cont'd)*
   - If it is almost time for your next dose, wait until then to take the medicine and skip the missed dose.
   - Do not take extra medicine to make up for a missed dose.

6. **Do not miss** any scheduled doctor's / clinic appointments. Your blood will be checked regularly to assess your response to Coumadin®. **These blood tests will include PT / INR levels.**

7. **How to Store and Dispose of This Medicine:**
   - Store the medicine in a closed container at room temperature, away from heat, moisture, and direct light.
   - Ask your pharmacist, doctor, or health caregiver about the best way to dispose of any leftover medicine after you have finished your treatment.
   - Keep all medicine away from children and never share your medicine with anyone.

8. **Danger Signals you should immediately report to your physician:**
   - Trouble breathing
   - Swollen lips, tongue, throat, or face
   - Hives or painful rash
   - Black, bloody, or tarry stools
   - Blood in your urine
   - Vomiting or coughing up blood
   - Bleeding gums or sores in your mouth
   - Urinating less than usual
   - Yellowing of the skin or eyes (jaundice)
   - Dizziness
   - Unusual bleeding or bruising, including heavy menstrual periods
   - Severe headache
   - Purple discoloration of your toes or fingers
   - Sudden leg or foot pain
   - Chest pain
   - Confusion
   - Slurred speech
   - Weakness on one side of the body
   - Any other side effects you feel are due to this medication

9. **For questions and follow up appointment call (RN to provide on day of discharge):**
   - Date of next PT / INR blood draw: ❑ Within a week ❑ _____
   - **Contact Information for healthcare professional / clinic / office monitoring your anticoagulation therapy:**
     - Name _____
     - Phone _____

ID#	Signature / Title	Date	Time	Initials	Interpreter Signature	Date	Time
	Pharm.D.						
Initials	**Signature / Title**	**Date**	**Time**	**Initials**	**Signature / Title**	**Date**	**Time**
	RN				RN		

DEPARTMENT OF PHARMACY SERVICES
WARFARIN (COUMADIN®) PATIENT EDUCATION PROVIDED BY PHARMACIST

Date: _____ Time: _____

Information Provided to: ❑ Patient ❑ Caregiver / Family Member

Teaching Method: ❑ Reading ❑ Discussion ❑ Interpreter ❑ Video / TV

Response to Education: ❑ Verbalizes Understanding ❑ Needs Reinforcement

❑ Other: _____

Pharmacist Name: _____ / _____ / _____ / _____

print sign pager/cell # ID #

Form No. 10435 (Rev. 8/22/11)

Subject:	**Hypoglycemia Reactions: Adult / Pediatric/Newborn Treatment Protocol**

CCN00083 Supersedes: H-2	Effective: September 2011 Prev. Issued: July 2010, February 2010 , June 2008, March 2006, April 2004, March 2001, July 1998, March 1998

I. POLICY

Hypoglycemia Treatment Protocol

If a patient is found to have hypoglycemic blood glucose levels (see Definition), initiate the hypoglycemia protocol **UNLESS** otherwise ordered by the physician

Licensed personnel who have been certified to perform the capillary blood glucose monitoring may perform the procedure. A physician's order **is not necessary** prior to administration of glucose solution, Glucagon SQ or glucose tablets if hypoglycemia is suspected.

The nurse will write hypoglycemia protocol on the order sheet and the physician will co-sign within 24 hours.

Physician Notification

The physician is to be notified immediately for patients who require administration of glucose solution or glucagon.

The physician is to be notified prior to the next insulin or oral hypoglycemic agent dose for those patients who are treated with dextrose tablets.

II. DEFFINITION

Hypoglycemia:

Age Group	Blood Glucose
Adult	70 mg/dl or less
Child > 1 year	≤ 60 mg/dl
Infant 28 days to 1 year	≤ 55 mg/dl
Newborn 72 hours to 28 days	≤ 55 mg/dl
Newborn 48-72 hours	≤ 45 mg/dl
Newborn 2-48 hours	≤ 35 mg/dl
Newborn ≤ 2 hours	≤ 25 mg/dl

III. PURPOSE

To identify and provide standard, timely treatment for the patient with a hypoglycemic reaction.

IV. PROCEDURE / PROTOCOL

A. Assess patient for signs and symptoms of hypoglycemic reactions.

Subject:	**Hypoglycemia Reactions: Adult / Pediatric/Newborn Treatment Protocol**

CCN00083 Supersedes: H-2	Effective: September 2011 Prev. Issued: July 2010, February 2010 , June 2008, March 2006, April 2004, March 2001, July 1998, March 1998

B. Treatment Protocol

1. Adult patient with a blood glucose of 70 mg/dl or less, UNABLE TO SWALLOW, UNCONSCIOUS, OR NPO

STATE	SYMPTOMS	HAS IV ACCESS	NO IV ACCESS	INPATIENT	OTHER
Suspected hypoglycemia				• Stat capillary blood glucose test*	
Blood Glucose 51 - 70 mg/dl	No		Glucagon 1 mg Subcu	• Immediately call Attending MD or House Staff to obtain potential new orders PRIOR to giving the next insulin or oral hypo-glycemic agent dose.	• Immediately call RRT and notify MD
Blood Glucose 51 - 70 mg/dl	Yes	1 amp D50 (50 cc) IV push	Glucagon 1 mg Subcu	• Notify Attending MD or House Staff immediately. • Assess pt. and recheck bld. Glucose every 15 min until > 70 mg/dl	• Immediately call RRT and notify MD • Assess patient, recheck capillary glucose and repeat treatment q 15 minutes until glucose is greater than 70 mg/dL *(Outpatient - If no response or patient worsens after 2 attempts, transfer patient to the Emergency Dept)*
Blood Glucose 50 mg/dl or less	Yes or No	1 amp D50 (50 cc) IV push	Glucagon 1 mg Subcu	• Notify Attending MD or House Staff immediately. • Assess pt. and recheck bld. Glucose every 15 min until > 70 mg/dl	• Immediately call RRT and Notify MD. • Assess patient, recheck capillary glucose and repeat treatment q 15 minutes until glucose is greater than 70 mg/dL (*Outpatient - If no response or patient worsens after 2 attempts, transfer patient to the Emergency Dept)*

* see Blood Glucose, Capillary: Monitoring Bedside

Subject:	**Hypoglycemia Reactions: Adult / Pediatric/Newborn Treatment Protocol**

CCN00083 Supersedes: H-2	Effective: September 2011 Prev. Issued: July 2010, February 2010 , June 2008, March 2006, April 2004, March 2001, July 1998, March 1998

2. **Adult patient with blood glucose of 70 mg/dl or less, who is ABLE TO SWALLOW**

STATE	SYMPTOMS	Swallows	OTHER
Suspected hypoglycemia			• Stat capillary blood glucose test
Blood Glucose 51 - 70 mg/dl	Yes or No	4 ~~3~~(4 gm tablets) glucose tablets PO (total amount of glucose per treatment is 4 ~~3~~ tablets = 16 ~~12~~ gm) If the patient cannot chew or refuses glucose tablets, 120 ~~180~~ mls of orange juice* maybe used in place of 4 ~~3~~ glucose tablets. ~~1 tablet is equal to 60 ml juice. Give 1 additional glucose tablet if no response within 15-20 min~~	• Notify MD • Give 120cc of juice (orange or apple) • Assess patient, recheck capillary glucose and repeat treatment q 15 minutes until glucose is greater than 70 mg/dL (Once glucose is above 70 mg/dL the individual should consume a meal or snack to prevent recurrence of Hypoglycemia) *(Outpatient - If no response or patient worsens after 2 attempts, transfer patient to the Emergency Dept)*

* If a patient has chronic renal disease or is on a potassium-restricted diet **do not** use orange juice, use cranberry or apple. For patients being treated with Precose (Acarbose), Hypoglycemia **MUST** be treated with oral dextrose i.e., glucose tablets.

3. **Child > 1 year with a blood glucose of ≤ 60 mg/dl**

STATE	SYMPTOMS	CENTRAL LINE ACCESS	PERIPHERAL IV ACCESS	NO IV ACCESS	OTHER
Suspected hypoglycemia					• Stat capillary blood glucose test
Child > 1 yr Blood Glucose ≤60 mg/dl	Yes	D25W 2 cc/kg IV push (3-5 min)	D10W 5cc/kg IV push (3-5 min)	1 glucose tablet, or 60-120cc of juice (orange or apple)	• Notify MD immediately of patient's condition. • Assess patient, recheck capillary blood glucose and repeat treatment q15 minutes until hypoglycemia is resolved. • Notify MD if hypoglycemia persists. • When hypo-glycemia is resolved, recheck capillary blood glucose q1 hr x 2, then q2 hr until ordered otherwise by physician.

* If a patient has chronic renal disease or is on a potassium-restricted diet **do not** use orange juice, use cranberry or apple.

Subject:	**Hypoglycemia Reactions: Adult / Pediatric/Newborn Treatment Protocol**

CCN00083 Supersedes: H-2	Effective: September 2011 Prev. Issued: July 2010, February 2010 , June 2008, March 2006, April 2004, March 2001, July 1998, March 1998

4. Infant 28 days to 1 year with a blood glucose of ≤ 55 mg/dl

STATE	SYMPTOMS	CENTRAL LINE ACCESS	PERIPHERAL IV ACCESS	NO IV ACCESS	OTHER
Suspected hypoglycemia					• Stat capillary blood glucose test
Infant 28 days to 1 year old **Blood Glucose ≤ 55 mg/dl**	Yes	D25W 2 cc/kg IV push (3-5 min)	D10W 5 cc/kg IV push (3-5 min)	Juice 60-120cc (orange or apple)	• Notify MD immediately of patient's condition. • Assess patient, recheck capillary blood glucose and repeat treatment q15 minutes until hypoglycemia is resolved. • Notify MD if hypoglycemia persists. • When hypo-glycemia is resolved, recheck capillary blood glucose q1 hr x 2, then q2 hr until ordered otherwise by physician.

* If a patient has chronic renal disease or is on a potassium-restricted diet **do not** use orange juice, use cranberry or apple.

5. Newborn 72 hours old to 28 days with a blood glucose of ≤ 55 mg/dl

STATE	SYMPTOMS	CENTRAL LINE ACCESS	PERIPHERAL IV ACCESS	NO IV ACCESS	OTHER
Suspected hypoglycemia					Stat capillary blood glucose test
Newborn 72 hours to 28 days **Blood Glucose ≤ 55 mg/dl**	Yes		D10W 2 cc/kg IV push (3-5 min)		• Notify MD immediately of patient's condition. • **Increase IV rate by:** **D10W 1.2cc/kg/hr** **OR** **D12.5W 1ml/kg/hr** • Assess patient, recheck capillary blood glucose and repeat treatment q 30 minutes until hypoglycemia is resolved.

Subject:	**Hypoglycemia Reactions: Adult / Pediatric/Newborn Treatment Protocol**

CCN00083 Supersedes: H-2	Effective: September 2011 Prev. Issued: July 2010, February 2010 , June 2008, March 2006, April 2004, March 2001, July 1998, March 1998

6. Newborn 48 - 72 hours old with a blood glucose of ≤ 45 mg/dl

STATE	SYMPTOMS	CENTRAL LINE ACCESS	PERIPHERAL IV ACCESS	NO IV ACCESS	OTHER
Suspected hypoglycemia					• Stat capillary blood glucose test
Newborn 48-72 hours **Blood Glucose ≤ 45 mg/dl**	Yes		D10W 2 cc/kg IV push (3-5 min)		• Notify MD immediately of patient's condition. • **Increase IV rate by:** **D10W 1.2cc/kg/hr** **OR** **D12.5W 1ml/kg/hr** • Assess patient, recheck capillary blood glucose and repeat treatment q 30 minutes until hypoglycemia is resolved.

7. Newborn 2 - 48 hours old with a blood glucose of ≤ 35 mg/dl

STATE	SYMPTOMS	CENTRAL LINE ACCESS	PERIPHERAL IV ACCESS	NO IV ACCESS	OTHER
Suspected hypoglycemia					• Stat capillary blood glucose test
Newborn 2-48 hours old **Blood Glucose ≤ 35 mg/dl**	Yes		D10W 2 cc/kg IV push (3-5 min)		• Notify MD immediately of patient's condition. • **Increase IV rate by:** **D10W 1.2cc/kg/hr** **OR** **D12.5W 1ml/kg/hr** • Assess patient, recheck capillary blood glucose and repeat treatment q 30 minutes until hypoglycemia is resolved.

Subject:	**Hypoglycemia Reactions: Adult / Pediatric/Newborn Treatment Protocol**

CCN00083 Supersedes: H-2	Effective: September 2011 Prev. Issued: July 2010, February 2010 , June 2008, March 2006, April 2004, March 2001, July 1998, March 1998

8. Newborn ≤ 2 hours old with a blood glucose of ≤ 25 mg/dl

STATE	SYMPTOMS	CENTRAL LINE ACCESS	PERIPHERAL IV ACCESS	NO IV ACCESS	OTHER
Suspected hypoglycemia					• Stat capillary blood glucose test
Newborn ≤ 2 hours old **Blood Glucose ≤ 25 mg/dl**	Yes		D10W 2 cc/kg IV push (3-5 min)		• Notify MD immediately of patient's condition. • **Increase IV rate by:** **D10W 1.2cc/kg/hr** **OR** **D12.5W 1ml/kg/hr** • Assess patient, recheck capillary blood glucose and repeat treatment q 30 minutes until hypoglycemia is resolved.

C. Documentation

CS-Link

1. Order Entry Navigator: enter Hypoglycemia Protocol.
2. eMAR: administration glucose solution or Glucagon or glucose tablets; link Pyxis override medication with order.
3. Progress Note: hypoglycemia reactions
   - Signs and symptoms
   - Results of capillary blood glucose values
   - Time of onset and duration of symptoms
   - Treatment and response
   - Time and name of physician notified
4. Flowsheet: initial capillary blood glucose and repeat capillary blood glucose **every 15 minutes until blood glucose hypoglycemia is resolved.**

Centricity

1. Document the signs and symptoms, blood glucose results, medication administration, notification of MD, outcome and if transferred to the ED.
2. Progress Note: hypoglycemia reactions
   - Signs and symptoms
   - Results of capillary blood glucose values
   - Time of onset and duration of symptoms
   - Treatment and response
   - Time and name of physician notified and medications.
   - Instruction on carrying some for of fast acting sugar (hard candy, glucose tablets) and to always eat food every 4 – 5 hours when taking diabetes medications

Subject:	**Hypoglycemia Reactions: Adult / Pediatric/Newborn Treatment Protocol**

CCN00083 Supersedes: H-2	Effective: September 2011 Prev. Issued: July 2010, February 2010 , June 2008, March 2006, April 2004, March 2001, July 1998, March 1998

V. REFERENCE

- American Diabetes Association: Clinical Practice Recommendations
- Craig, J., (2008). Acute Hypoglycemia, Core Curriculum for Pediatric Critical Care Nursing. 416-417.
- National Association of Neonatal Nurses (1994). *Neonatal Hypoglycemia*
- *Guidelines for Practice*. Petaluma, California: Author

VI. KEY WORDS

- Insulin Reaction
- Low Blood Sugar

VII. COMPETENCY

- Blood Glucose Monitoring

VIII. POLICY ORIGINATOR(S) AND APPROVAL(S)

A. Originators

- Joyce Spalding, RN, MSN, CDE
- Eloisa de la Cruz, RN, CDE
- Mary Jane Vos, RN, CDE
- Sharon Cooper, RN, MSN, CNS

B. Approvals

- Rita Shane, Pharm.D.
  Director, Pharmacy Services
- Ruchi Mathur, MD, FRCP (C)
  Division of Endocrinology, Diabetes & Metabolism
- Linda Burnes Bolton, Dr.PH, R.N., FAAN
  Vice President, Nursing and Chief Nursing Officer

CEDARS-SINAI MEDICAL CENTER
PHARMACY SERVICES

RITUXIMAB (RITUXAN®) FOR NON-ONCOLOGICAL USES ORDER FORM

PROOF
This Form Has Not Been Approved to Print

PATIENT I.D.

TIME: _____ DATE: _____

1. Patient Name: _____ Date of Birth: _____ MRN: _____
2. Patient Height: _____ Weight: _____ BSA: _____
3. **Allergies / Intolerances:** ❑ **NKA**
   - ❑ **Allergies to:** _____
     - **Reaction:** ❑ anaphylaxis ❑ edema ❑ hives ❑ pruritus ❑ rash ❑ unknown ❑ other: _____
     - **Severity:** ❑ Severe ❑ Moderate ❑ Mild
   - ❑ **Intolerances to:** _____
4. Diagnosis:
   - ❑ Rheumatoid arthritis
   - ❑ Glomerulonephritis
   - ❑ Acute humoral rejection
   - ❑ ABO Incompatible Kidney Transplant
   - ❑ Systemic lupus erythematosus
   - ❑ Highly sensitized patients awaiting solid organ transplantation
   - ❑ Vasculitis
   - ❑ Other _____

- **Nurse Monitoring - please refer to IV Policy & Procedure for more information**
  - Nurse must be at bedside during the 1st 15 minutes of the infusion
  - Monitor and document vital signs and pulse oximetry at **baseline and then every 15 minutes for 1 hour** or until stable, and **hourly** thereafter until infusion is complete.

It is advisable to use methotrexate or other immunosuppressive medication as concomitant therapy in Rheumatoid Arthritis, Systemic Lupus Erythematosus, and Vasculitis to decrease the development of human anti-chimeric antibodies.

5. **Indication:**

Rheumatoid arthritis

❑ Patient has rheumatoid arthritis fulfilling ACR criteria which is active and has failed an adequate trial or is intolerant to a tumor necrosis factor blocking agent.

Systemic Lupus Erythematosus

❑ Patient has SLE fulfilling ACR criteria and has active moderate to severe thrombocytopenia or auto-immune hemolytic anemia and has failed to achieve remission with one or more courses of corticosteroid treatment.

❑ Patient has SLE fulfilling ACR criteria and has another active serious organ threatening manifestation of systemic lupus and has failed community standard of care treatment with corticosteroid, immunosuppressive, or cytotoxic treatment.

Vasculitis

❑ Patient fulfills classification criteria for Wegener's, Churg-Strauss, microscopic polyangiitis or cryoglobulinemic vasculitis and has active moderate to severe systemic vasculitis with internal organ involvement and has failed community standard of care treatment with corticosteroid, immunosuppressive, or cytotoxic treatment.

❑ TELEPHONE ORDER					R.N.	DATE	TIME
PHYSICIAN I.D. NUMBER	SIGNATURE OF PHYSICIAN				M.D.	DATE	TIME
SIGNATURE OF TRANSCRIBER	INIT.	TITLE	DATE	TIME	SIGNATURE OF NURSE (NOTED) R.N.	DATE	TIME

CEDARS-SINAI MEDICAL CENTER
PHARMACY SERVICES

RITUXIMAB (RITUXAN®) FOR NON-ONCOLOGICAL USES ORDER FORM

PROOF
This Form Has Not Been Approved to Print

PATIENT I.D.

5. **Indication:** *(Cont'd)*

Highly sensitized patients awaiting solid organ transplantation

❑ Patient has PRA > 30%, history of pregnancies/ blood transfusions/ previous transplants, or with positive crossmatch.

❑ **Acute humoral rejection in solid organ transplant recipients**

Glomerulonephritis

❑ Patient with biopsy proven FSGS, anti-GBM nephritis, immune complex nephritis, or IgA nephritis resistant to treatment with corticosteroid, immunosuppressive, or cytotoxic treatment.

6. **Other (Comments):** _____

_____

7. **Inclusion criteria**

Yes	No	
❑	❑	Patient has a negative tuberculin (TB) skin test or Quantiferon-TB Gold (QFT-Gold) test within the last 12 months *(prior to initial therapy only)* or if test is positive, treatment for latent tuberculosis has been initiated prior to therapy. Last TB skin test: Date: _____ Result: _____

8. **Exclusion criteria**

Yes	No	
❑	❑	History of progressive multifocal leukoencephalopathy (PML).
❑	❑	Symptoms of neurological deficits or dementia suggestive of PML are present.
❑	❑	History of use within 4 weeks or concomitant use of cyclophosphamide, anakinra or etanercept.
❑	❑	History of use within 8 weeks or concomitant use of infliximab, adalimumab or abatacept.
❑	❑	History of active infection including chronic hepatitis B.

9. **Dose** *(to be prepared and infused per IV P&P)*

❑ Rituximab 1000 mg IVPB x_____ doses on / for _____ *(Specify dates or frequency)*

❑ Rituximab: _____ mg / m2 IVPB ❑ weekly ❑ every other week ❑ monthly.

10. **Premedications**

❑ Methylprednisolone _____ mg IVP x1 *(mandatory for first treatment of rituximab).*

❑ Acetaminophen 650 mg PO x1.

❑ Diphenhydramine _____ mg PO x1.

11. Additional Orders: _____

_____

_____

_____

❑ TELEPHONE ORDER	R.N.					DATE	TIME
PHYSICIAN I.D. NUMBER	SIGNATURE OF PHYSICIAN M.D.					DATE	TIME
SIGNATURE OF TRANSCRIBER	INIT.	TITLE	DATE	TIME	SIGNATURE OF NURSE (NOTED) R.N.	DATE	TIME