Pharmacy and Therapeutics Committee Approvals, June 2011

P&T Date: April 5th, 2011 and May 3rd, 2011

AGENDA ITEM	P&T COMMITTEE DECISION	COMMENTS
• **ACETAMINOPHEN INTRAVENOUS INJECTION (OFIRMEV®)**	Do not add to formulary	***Indication:*** FDA approved Management of mild to moderate pain, management of moderate to severe pain with adjunctive opioid analgesics, and reduction of fever ***Mechanism of Action:*** Specific mechanism of action of acetaminophen has yet to be clearly elucidated. The analgesic affect appears to result from an increase in the pain threshold through inhibition of prostaglandin production, the nitric oxide pathway and modulation of various receptors and pathways (i.e. 5HT, cannabinoid, substance P, N-Methyl-D-aspartate and endogenous opioids). Its antipyretic effect likely comes from inhibition prostaglandin production and release. ***Adverse effects:*** Most common adverse side effects reported in the adult clinical trials include nausea, vomiting, headache and insomnia. In the pediatric population, common side effects include constipation, pruritus, agitation, atelectasis in addition to nausea and vomiting. Risk of hepatotoxicity is generally associated with doses that are higher than recommended. ***Precautions:*** Hepatic injuries have been reported in patients receiving higher than recommended doses of acetaminophen. Severe hepatotoxicity and even deaths have been reported in these scenarios. It is recommended that in patients with hepatic impairment, active liver disease, CrCl ≤ 30ml/min, severe hypovolemia, malnutrition (chronic) or alcoholism, acetaminophen should be used judiciously. Pregnancy Category C SEE OFIRMEV FACT SHEET FOR MORE INFORMATION  B2a1 Acetaminophen Fact S
• **PEGLOTICASE (KRYSTEXXA®) INTRAVENOUS INJECTION**	Do not add to formulary	***Indication:*** treatment of chronic gout in adult patients refractory to conventional therapy. ***Mechanism of Action:*** Pegloticase, a PEGylated, recombinant, mammalian uricase, reduces serum urate levels by catalyzing the oxidation of uric acid to allantoin. Allantoin is a more soluble derivative of uric acid that is renally excreted. ***Adverse effects:*** Anaphylaxis, infusion reactions, and gout flares were the most commonly reported serious adverse reactions. Most common adverse reactions include gastrointestinal effects (nausea, vomiting, constipation), chest pain, nasopharyngitis, and contusion or ecchymosis ***Boxed Warning:*** Anaphylaxis and infusion reactions have occurred during and after infusions of pegloticase. Pegloticase should be administered by a healthcare provider in a setting prepared for management of such reactions. Patients should receive antihistamines and corticosteroids as premedication. Serum uric acid levels should be checked prior to infusions, and discontinuation of therapy should be considered if there are two consecutive levels above 6 mg/dl. Due to these possible severe reactions, pegloticase is a risk evaluation mitigation strategy (REMS) medication. ***Precautions:*** Anaphylaxis has been reported to be up to 6.5%, despite premedication with intravenous corticosteroids, acetaminophen and/or oral antihistamine. Uric acid levels > 6 mg/dl have been associated with increased risk of anaphylaxis. Consider discontinuing pegloticase if 2 consecutive levels are > 6 mg/dL. Incidence of infusion reactions has been

		reported to be between 26%-41%, and has occurred in patients who received premedication. Gout flares may occur after beginning pegloticase due to the mobilization of urate from tissue deposits. These flares are more prevalent during the first 3 months of treatment with pegloticase. Non-steroidal anti-inflammatory drugs (NSAIDS) or colchicine should be administered 1 week prior to and at least 6 months after initiation of therapy to manage gout flares. Pregnancy Category C
• **NEBIVOLOL HYDROCHLORIDE (BYSTOLIC®) TABLETS**	Add to formulary; restrict to patients receiving nebivolol prior to admission	***Indication:*** Nebivolol (Bystolic™) is a third generation selective beta-1 receptor antagonist, FDA approved on 12/17/2007, for the treatment of mild to moderate blood pressure reduction as both monotherapy and adjuvant therapy ***Mechanism of Action:*** Nebivolol is a beta-1 (B1) adrenergic receptor antagonist with a mixture of both D- and L- enantiomers responsible for a dual mechanism of action. The D-enantiomer provides the high selectivity for B1 adrenergic receptors, whereas the L-enantiomer is responsible for nitric-oxide mediated vasodilatory activity. Based on its dual mechanism of action, nebivolol activity includes: decreased heart rate, decreased myocardial contractility, decreased tonic sympathetic outflow to the periphery from cerebral vasomotor centers, suppression of renin activity, vasodilation and decreased peripheral vascular resistance ***Adverse effects:*** Most common adverse drug reactions reported in clinical trials include (>2% in nebivolol group): dizziness (2.8-15.6%), bradycardia (11.1%); headache (5.6-7%), fatigue (2.8-3.6%), diarrhea (2.7-3.2%), and nasopharyngitis (2.4-2.9%). **Precautions***:* Contraindications include: bradycardia, >1st degree heart block, cardiogenic shock, decompensated heart failure, sick sinus syndrome (in the absence of an inserted pacemaker), severe hepatic impairment (Child Pugh >B), and known hypersensitivity to nebivolol or any of its components. Patients with bronchospastic disease should not receive beta blockers. Abrupt discontinuation of nebivolol may result in exacerbations of angina, myocardial infarction, and ventricular arrhythmias (taper over 1-2 weeks if possible). Pregnancy Category C
• **RETAPAMULIN (ALTABAX®) OINTMENT**	Do not add to formulary	***Indication:*** Retapamulin is a topical, pleuromutilin antibiotic that received FDA approval in 2007 for the treatment of impetigo due to *Staphylococcus aureus* (methicillin-susceptible isolates only) or *Streptococcus pyogenes*) in adults and pediatric patients aged 9 months and older. Retapamulin was considered a new molecular entity when approved and the first in the pleuromutilin drug class ***Mechanism of Action:*** Retapamulin 1% ointment is a bacteriostatic agent (bactericidal at very high concentrations) that selectively inhibits bacterial protein synthesis by binding to a distinct site on the 50s subunit of the bacterial ribosome, preventing normal formation of active 50S ribosomal submits. ***Adverse effects:*** Most common include headache, application site irritation, diarrhea, nausea, nasopharyngitis, increased creatinine phosphokinase ***Precautions:*** In the event of sensitization or severe local irritation, retapamulin use should be discontinued, the ointment wiped off the site of application, and alternate therapy instituted. Retapamulin 1% ointment is not been evaluated for intraoral, intranasal, ophthalmic, or intravaginal use. Epistaxis has been reported with the use of retapamulin on nasal mucosa. Pregnancy Category B.
REMOVALS FROM FORMULARY	• Human RhoD IV immunoglobulin (WinRho®)- remove from formulary due to risk of intravascular hemolysis in patients with immune thrombocytopenic purpura • Sodium thiosulfate 10%- continue to stock sodium thiosulfate 25% • Urised® (atropine sulfate 0.03mg, benzoic acid 4.5mg, hyoscyamine sulfate 0.03mg, methenamine 40.8mg, methylene blue 5.4mg, phenyl salicylate 18.1mg)- discontinued by	

<table>
<tr><td></td><td>manufacturer
• Fleets Phospho Soda®-discontinued by manufacturer
• Ganciclovir capsules</td></tr>
<tr><td>ADDITIONS TO FORMULARY</td><td>• Insulin NPH suspension 70% and Insulin Regular 30% (Novolin 70/30®)
• Insulin Lispro protamine suspension 75% and insulin lispro 25% (Humalog® 75/25)
• Leflunomide (Arava®)-allow for treatment of Polyomavirus</td></tr>
<tr><td>AUTOMATIC SUBSTITUTIONS</td><td>
<table>
<tr><th>Medication Ordered</th><th>Automatic Substitution</th></tr>
<tr><td>Percocet® 5/325 ½ tablet (oxycodone/acetaminophen)</td><td>Percocet® 2.5/325, same route a frequency</td></tr>
<tr><td>Fish oil 1000mg</td><td>Fish oil (Nature Made®) 3 caps (1080mg), same route and frequency</td></tr>
<tr><td>Tobramycin inhalation (TOBI®) 300mg via HHN BID (reverse previous tobramycin inhalation (TOBI®) 300mg via HHN BID to Gentamicin for injection 80mg via HHN TID autosubstitution)</td><td>Tobramycin for injection 80mg via HHN TID</td></tr>
</table>
Oral Calcium Automatic Substitutions (See below)
<table>
<tr><th>Calcium product Ordered</th><th>Automatic substitution</th></tr>
<tr><td>Calcium carbonate (Titralac®) 420 mg (168mg Ca^{+2})</td><td>Calcium carbonate 1250mg tablet (=500 mg Ca^{+2})</td></tr>
<tr><td>Calcium carbonate 325 mg (130mg Ca^{+2})</td><td>Calcium carbonate 1250mg tablet (=500 mg Ca^{+2})</td></tr>
<tr><td>Calcium carbonate 500 mg (200mg Ca^{+2})</td><td>Calcium carbonate 1250mg tablet (=500 mg Ca^{+2})</td></tr>
<tr><td>Calcium carbonate 650 mg (250mg Ca^{+2})</td><td>Calcium carbonate 1250mg tablet (=500 mg Ca^{+2})</td></tr>
<tr><td>Calcium citrate (Citracal®) Regular 1 tablet (250mg Ca^{+2}) (each tablet also contains 200 IU of Vitamin D)</td><td>Calcium carbonate 1250mg tablet (=500 mg Ca^{+2})</td></tr>
<tr><td>Calcium citrate effervescent tablet (Citracal Liquitab®) 1 tablet</td><td>REMOVE FROM AUTOSUBSTITUTION LIST (NO LONGER AVAILABLE)</td></tr>
<tr><td>Calcium carbonate (Caltrate®) 600mg (600mg Ca^{+2})</td><td>Calcium carbonate 1250mg tablet (=500 mg Ca^{+2})</td></tr>
<tr><td>Calcium gluconate 500mg - 1000 mg</td><td>Calcium carbonate 1250mg/5ml solution (500 mg</td></tr>
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</td></tr>
<tr><td>STATIN STANDARDIZATON</td><td>• Add rosuvastatin (Crestor®) 5mg, 10mg, 20mg to formulary
• Remove fluvastatin (Lescol®) from formulary
• Maintain atorvastatin (Lipitor®) as nonformulary. Pharmacy will continue to stock the 80mg strength for the ACS indication</td></tr>
<tr><td>PULMONARY RECOMMENDATIONS
LEVOALBUTEROL (XOPENEX®) AND BRONCHODILATOR ORDERS</td><td>• Xopenex® continues to be nonformulary at CSMC
• Starting 5/17/11, orders for all bronchodilators will be defaulted to: “every ___ hours while awake (unless the order specified “around the clock”)
 
Xopenex Considerations RT or</td></tr>
<tr><td>REGIONAL ANESTHESIA MINIMUM TIMING IN PATIENTS RECEIVING ANTITHROMBOTIC OR THROMBOLYTIC THERAPY</td><td>The regional anesthesia guideline has been updated to reflect minimium timing between placement/removal of regional anesthesia and various antithrombic or thrombolytic therapies
 
physician Guideline for Minimum Timing of</td></tr>
<tr><td>ANTICOAGULATION</td><td>• Dabigatran (Pradaxa®) Adverse Events Summary
 
B6A. Dabigatran Adverse Events Repc
• Dabigatran (Pradaxa®) Reversal Guidelines</td></tr>
</table>

	 B6B. Dabigatran Reversal Guidelines 0 • **Warfarin Reversal Revision**  B6D. Warfarin Reversal Guidelines R • **Anticoagulation Protocol-summary of changes**  B6C. Summary of Anticoagulation Proto
BOXED WARNINGS	• **2011 Boxed Warning Priority List** o *The following new drugs were added to the 2011 Boxed Warning Priority List: Clozapine, Foscarnet, Infliximab, Leflunomide, Methadone, Prasugrel, Sunitinib* o *The following drugs were removed from the 2011 Boxed Warning Priority List: Docetaxel, Enoxaparin/Dalteparin, Anti-thymocyte globulin (rabbit), IVIG, Paclitaxel, Propylthiouracil, Warfarin*  B7A 2011 BBW Priority list 03 11.pdf • **Terbutaline Boxed Warning** o *Due to the boxed warning, a request has been submitted to EIS to add a 72-hour expiration date to all terbutaline orders.* o *In the meantime, open-ended terbutaline orders will be processed with a 72-hour stop date*  B7B2. Terbutaline BBW details 02.11.pd
NORMAL SALINE AS THE STANDARD DILUENT IN SELECTED MEDICATIONS FOR NEURO PATIENTS	• The following medications should be mixed in normal saline as the default diluent in **NEURO ICU** patients: Fentanyl, heparin (in ½ NS), midazolam, nicardipine, norepinephrine, phenylephrine, vancomycin doses >1gm • If patient gets transferred from the ICU to Med/Surg areas, NS is to continue to be the standard diluent
ANTIBIOTIC USE REVIEW COMMITTEE	• **Gentamicin for Chorioamnionitis**  B14C. Chorioamnionitis AG C • **2011 Adult Antibiotic Empiric Treatment Recommendations**  Adult Antibiotic Empiric treatment_Ma • **2011 Pediatric Antibiotic Empiric Treatment Recommendations**  Pediatric Empiric Antibiotics_March 201 • **Proposed Obesity Dosing Recommendations for Commonly –Used Surgical Prophylaxis Antimicrobial Agents**  B14F. Surgical ppx obesity dosing recs 0

	• **Vancomycin Pharmacy Protocol-Revision**  B14H. Vanco for trauma patients 03.1 • **Five Day Autostop Date for Antimicrobials**  B14G. Auto-Stop for Antimicrobials 03.11.p • **Pediatric Gentamicin Protocol for Physicians**  B15B. Gentamicin ped protocol 03.11.p
OTHER TOPICS	• **Large Volume Paracentesis- Guideline for the use of Albumin 25%**  B17 Albumin - Post LV Paracentesis 03 11 • **Use of Intralipid® 20% in Patients With Local Anesthetic or Lipophilic Drug Induced Cardiac Arrest, Unresponsive to Standard Rescuscitative Therapy Guideline**  B16. Lipid Rescue Therapy 03.11.DOC • **Hypoglycemia Reactions: Adult/Pediatric/Newborn Treatment Protocol**  B18B. Hypoglycemia Reactions - Adult Ped

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

Darina Brezhnev, PharmD — *Pharmacy Program Coordinator*
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Rita Shane, PharmD, FASHP — *Director, Department of Pharmacy*

Acetaminophen [OFIRMEV™] FACT SHEET

- **New Route of Administration**
  OFIRMEV™ is a newly approved intravenous formulation of acetaminophen indicated for the management of fever and pain. It is an option in patients who cannot receive oral or rectal forms of acetaminophen.

- **Faster onset of action**
  Compared to oral and rectal formulations of acetaminophen, an earlier time to maximum concentration is seen with the intravenous formulation of acetaminophen. [Shortly after the 15 minute infusion vs. > 45 minutes]

- **Issues with drug administration**
  OFIRMEV™ is available as 10mg/ml 100ml vials and is administered undiluted as a slow intravenous infusion over 15 minutes. The manufacturer recommends that once the drug is removed from the vial, it should be used within 6 hours.

- **Risk of hepatotoxicity**
  Similar to other formulations of acetaminophen, there is risk for hepatotoxicity especially when recommended doses are exceeded.

- **Cost impact**
  Each dose of intravenous acetaminophen can be roughly 258 times the cost of a dose of oral acetaminophen. [$10.31 per 1g vial vs. $0.04 per 650mg oral tablet]

Xopenex Considerations

Efficacy and Safety Data
Levalbuterol (Xopenex®) Comparison to Albuterol

- Limited data to show that Xopenex® is clinically superior to racemic albuterol.
- No statistical differences in LOS and clinical improvement between albuterol and Xopenex® in most studies
- No statistical differences in adverse effects between albuterol and Xopenex® in several studies
  - 2007 *AAFP* article: "Levalbuterol tartrate appears to be no more effective and offers no improvement in the side-effect profile compared with albuterol. The higher cost may make it appropriate for only a limited group of patients." [1]
  - 2006 *Am J of Emerg Med* study: study was sponsored by Sepracor Inc."[2]
    - Headache (Lev 1.0%, Rac 3.2%)
    - Tremor (Lev 2.2%, Rac 2.2%)
    - Nervousness (Lev 3.2%, Rac 2.2%),
    - Tachycardia (Lev 1.9%, Rac 2.9%). [2]
  - 2005 *Annals Emerg Med*: Median change in pulse rate (levalbuterol vs albuterol)[3]
    - After first nebulization +9 vs +8; After third nebulization +22 vs +21; After fifth nebulization +18 vs +18

1. Michelle Hilaire, et al. Levalbuterol Tartrate (Xopenex HFA) for the Treatment of Bronchospasm. AAFP. 2007(75): *247-248*
2. Richard Nowak, et al. A comparison of levalbuterol with racemic albuterol in the treatment of acute severe asthma exacerbations in adults. *American Journal of Emergency Medicine.*2006(24): 259–267
3. F Qureshi, et al. Clinical efficacy of racemic albuterol versus levalbuterol for the treatment of acute pediatric asthma. *Ann Emerg Med*. 2005;46(1): 29-36

Current Expenditures and Prescribing Pattern

Expenditures

Xopenex® Expenditures

July 2009 – June 2010: $140,702

July 2010-Feb 2010 Annualized: $281,650

Cost Considerations

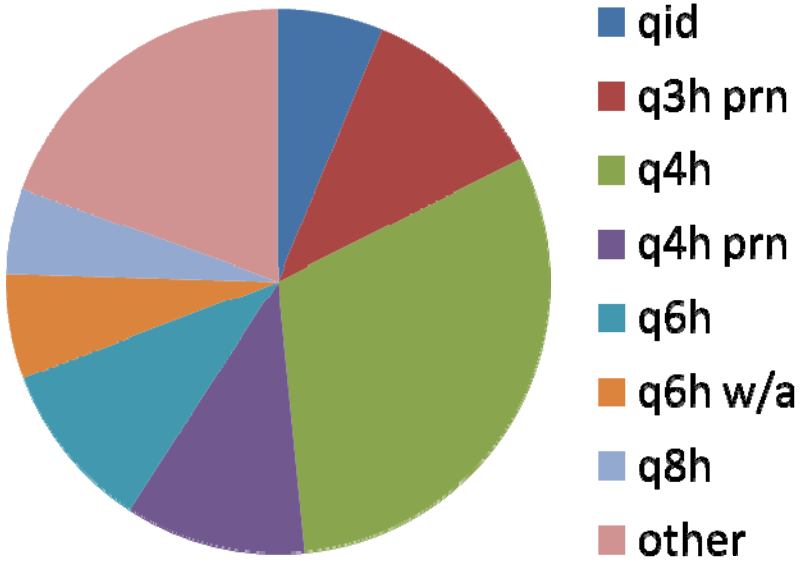
Albuterol: $0.34/dose; $2.04/day (q4h)

Xopenex®:$4.15/dose; $23.90/day (q4h)

12 doses/container; 7 day expiration upon opening

Prescribing Patterns

19 Different Frequencies Prescribed



Xopenex® – procedure for new orders starting on 5/17/11

- Xopenex® is nonformulary.
- Criteria for use:
  - Pediatric patient
  - Known sensitivity to S-isomer (rare)
  - Arrhythmia concern/ Hx of induction with albuterol
  - Severe tachycardia documented with albuterol and NOT with Xopenex®
  - Severe tremulousness documented with albuterol and NOT with Xopenex®
- If order meets any of the above criteria
  - Process order and document in an Ivent
- If the order meets any of the above criteria BUT the frequency is >Q6H
  - Contact prescriber to change the Xopenex frequency to Q6H or Q8H
- If the order doesn't meet criteria, please follow the steps below
  - Contact prescriber to change the order to albuterol
  - If prescriber insists in ordering xopenex, please contact gate keeper

Xopenex® – gatekeepers

- Dr. Dani Hacker – 423-2760 (pager 9800)
- Dr. Michael Lewis – 423-1832 (pager 4412)
- Dr. David Balfe – 423-1836 (1240)
- Dr. Ralph Potkin - 310-551-1178 (pager 310-596-0994)
- Dr. Steve Simons - 310-274-3444
- Dr. Harvey Brown - 213-742-0910

Nebulized bronchodilator administration

- Bronchodilators (beta agonists, anticholinergics) to be given **while awake and PRN**
  - **2200 to 0600** is the time frame to NOT wake patient for bronchodilator treatment (sleep time)
- **Procedure for new orders starting on 5/17/11:**
  - Unless the order specifies ATC, the default administration will be '…**every hours while awake**'
  - When entering the order, please choose the 'ordered frequency while awake'
    - Clarification policy will be revised to specify that no clarification of order is needed
    - No additional comments need to be entered under administration instruction
  - Prn orders will be processed as written.

PHYSICIAN GUIDELINE FOR MINIMUM TIMING OF ANTITHROMBOTIC OR THROMBOLYTIC AGENTS IN REGIONAL ANESTHESIA – Updated April 2011

Information below is based on administration of only 1 agent; risks of spinal hematoma are higher with multiple agents or in patients with coagulopathy.

Anticoagulant/ Anti-platelet/ Thrombolytic Agent	Timing of Last Dose → Insertion of Spinal Needle or Placement of Epidural Catheter	Restarting Medication after Placement (post-op)	Timing of Last Dose → Removal of the Epidural Catheter	Removal of the Epidural Catheter → First Dose
***THERAPEUTIC* DOSES of Anticoagulant Agents (NOT prophylaxis)**				
UFH	≥ 2-4 h post IV infusion[1]	≥ 1 hour after placement[1]	Ideally avoid while catheter is in place[2] > 2-4 h post IV infusion when anticoagulant effect is at minimum[1]	≥ 1 h[1]
Dalteparin (Fragmin®) 100 units/kg SQ q12h 200 units/kg SQ q24h	24 h*[1]	No specific recommendation available.[1]	Removal of catheter a minimum of 12 hours after the last dose	≥ 2 h[1]
Enoxaparin (Lovenox®) 1 mg/kg SQ Q12H or 1.5 mg/kg SQ Q24H	24 h*[1]	No specific recommendation available.[1]		≥ 2 hours[1]
Fondaparinux (Arixtra®)[4]	72 hours	Avoid while catheter in place.		2 hours
Lepirudin (Refludan®)[4,5]	8-10 hours and/or normal aPTT	Avoid while catheter in place.		2-4 hours
Argatroban[4, 5]	4 hours and/or normal aPTT	Avoid while catheter in place.		2 hours
Dabigatran (Pradaxa®)[5]	Avoid use in setting of neuraxial blockade.			
PO warfarin (Coumadin®)	OK if INR <1.5. If INR>1.5, hold warfarin until INR<1.5[1]	Avoid while catheter is in place[2]		OK if INR <1.5. If INR≥1.5, hold warfarin until INR<1.5.[1]
***PROPHYLACTIC* DOSES of Anticoagulant Agents**				
Dalteparin 5,000 units SQ q24h Enoxaparin 40mg SQ q24h Enoxaparin 30mg SQ BID	10-12 h*[1]	**Once daily dosing:** 1st dose: 6-8 hours after placement[1,3] 2nd dose: ≥ 24 hours after the 1st dose[1,3]**Twice daily dosing**:[1,3] 1st dose: ≥ 24 hours	Ideally avoid while catheter is in place[2] ≥ 12 hours after last dose[1]	≥ 2 h[1]
UFH SQ 5,000 units q12h/q8h	No Interaction, but may consider delaying heparin until after block if technical difficulty anticipated[2]			
Anti-platelet Agents				
NSAIDs/ASA*	There does not appear to be an interaction with these agents, unless in combination w/other agents that increase bleeding risk[1,2]			No specific recommendation available[1].
Clopidogrel (Plavix®)	7 days[1,3]	No specific recommendation available.[1] Ideally avoid while catheter is in place [2]		
Ticlopidine (Ticlid®)	10-14 days[1,3]			
Prasugrel (Effient®)[5]	7-10 days	No specific recommendation available.		6 hours
IIb/IIIa Inhibitors				
Abciximab (Reopro®)	24-48 hours[1,3]	No specific recommendation available[1]. Ideally avoid while catheter is in place[2]		No specific recommendation available.
Tirofiban (Aggrastat®)* Eptifibatide (Integrilin®)*	4-8 hours[1,3]			

Thrombolytic Agents (Full Dose)			
tPA (Alteplase/Activase®) Reteplase,(Retavase®),Streptokinase (Streptase®), Tenecteplase (TNKase®)	10 days[1]	Contraindicated, avoid while catheter is in place[1]	≥ 10 days[1]

- Presence of significant blood during needle and catheter placement, as identified by the anesthesiologist, will require delay of instituting injectable anti-coagulation for 24 hours. In this scenario, the first dose of LMWH should be a full dose, (e.g. dalteparin 5000 units) Post-operative time is defined as "the time the operative procedure ends".
- *Longer elimination times will be required in patients with impaired renal function. h = hours.

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References: (1) Horlocker TT, et al. Regional anesthesia in the anticoagulated patient: Defining the risks (The Second ASRA Consensus Conference on Neuraxial Anesthesia and Anticoagulation. Regional anesthesia and pain medicine.2003; 28(3): 172-197. (2) Nutescu E and Dager W. Managing Anticoagulation Patients in the Hospital: The Inpatient Anticoagulation Service Chapter 11. (3) Horlocker, TT, et al. Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy; American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (3rd Edition). Reg Anes Pain Med 2010;35:64-101.(4) University of Washington Anticoagulation Guidelines for Neuraxial Procedures. Updated January 2010. http://vte.son.washington.edu/docs/VTE_neuraxial_pathway.pdf. (5) Gogarten W. et al. Regional Anesthesia and Antithrombotic agents – Recommendations of the European Society of Anesthesiology. Eur J Anaesthesiol 2010;27:999–1015

SUMMARY OF DABIGATRAN (PRADAXA®) ADVERSE EVENTS

1) Cedars-Sinai Report from ED

- 70 year old male with atrial fibrillation transitioned from warfarin to dabigatran within the prior 2 weeks. Admitted via ED for GI bleed.

2) ISMP Report

- Full dose (150mg PO BID) ordered in a patient with Stage IV CKD: patient admitted to ICU with GI bleed requiring multiple units of FFP and PRBCs.

3) American College of Clinical Pharmacy Cardiology List Serv March 2011

- 82 year old male with ClCr <30ml/min on 150 PO BID. Admitted to ICU for UGIB and anemia; required transfusion and Vitamin K.
- 82 year old male with ClCr 17ml/min on 150 PO BID in addition to ASA 325mg PO for history of a.fib/PE/DVT. Admitted for syncopal episode with h/h 6.8/22.6; gross hematuria upon foley insertion. Required FFP, PRBCs and Vitamin K.

4) RE-LY Trial Reasons for Discontinuation from PI

- *Major GI bleeding occurred at a significantly higher rate with dabigatran 150mg PO BID versus warfarin: RR 1.5 (1.19-1.89) P<0.001

List-Serv/ISMP Reports	Cedars-Sinai Reports via ED/ RELY Trial Reasons for Discontinuation
ISMP 2/10/11 - In a recent report, Pradaxa® was prescribed by a cardiologist for a patient with Stage IV CKD. The dose of the medication was not adjusted for the patient's renal impairment. Instead of the recommended dose of 75 mg BID, the patient received 150 mg BID. Upon a follow-up visit with the cardiologist, the patient complained of weakness, black tarry stools, and was also found to have a low hemoglobin and hematocrit. The patient was admitted to the ICU with a massive GI bleed. The patient was given multiple units of FFPs and PRCBs, and eventually his H/H returned to safe levels. Among the precautions for Pradaxa® are several drug interactions and a recommended dose of 75 mg BID for patients with a CrCL of 15-30 mL/min.	**February 2011** **CHIEF COMPLAINT: Melena.** PMH: 70-year-old male with a history of A. fibrillation diagnosed in 2010. He was started on Coumadin at that time and has tolerated it well. About 2 weeks ago he was switched to Pradaxa®. He states he waited until his INR was 1.9 on Coumadin and then discontinued it and transitioned to Pradaxa®. He has had no known side effects until a week ago when he began to develop dark stool, maroon in color. He saw his cardiologist and mentioned this to her and was referred for GI evaluation. He was referred to the ED for admission for an urgent colonoscopy.
American College of Clinical Pharmacy Cardiology List Serv March 2011 1. 82 y/o male, 90.7 kg, CrCl < 30, taking dabigatran 150mg bid at home. Admitted to ICU with UGIB and severe anemia. Admission INR 4.3, aPTT 63.2, Hgb 7.8. Given Vit K 10mg subQ, 2 units PRBC in ED, following day received an additional 1 unit PRBC and Vit K 10mg IV. 2. 82 y/o male, 65.8 kg, CrCl 17, known history of CKD on erythropoietin, taking dabigatran 150mg bid and aspirin 81mg daily at home; h/o a fib, DVT and PE. Admitted s/p syncope with SOB found to have h/h 6.8/22.6, aPTT > 100, INR 2.6 (given Vit K and transfused with 2 units FFP plus 1 unit PRBC). Gross hematuria upon foley insertion.	**RELY Trial Reasons for Discontinuation from PI** *Major GI bleeding occurred at a significantly higher rate with dabigatran 150mg PO BID versus warfarin: RR 1.5 (1.19-1.89) P<0.001

CEDARS-SINAI MEDICAL CENTER

DABIGATRAN (PRADAXA®) REVERSAL GUIDELINES – DRAFT 3/7/11

Developed in Collaboration with the Departments of Laboratory Medicine, Transfusion Medicine
Emergency Medicine and Pharmacy Services

BACKGROUND:

1. Mechanism of Action: Direct thrombin inhibitor with an onset of action of approximately 2-3 hours.
   a. Thrombin converts fibrinogen into fibrin and allows for clotting to occur; also activates platelets.
   b. Dabigatran inhibits both free and clot bound thrombin as well as platelet aggregation[1]
   c. $T_{1/2}$ of approximately 12-17 hours in patients with normal renal function; prolonged $t_{1/2}$ in patient with CrCl ≤ 50 ml/min

2. Impact on laboratory parameters[1,2]
   a. Prolongs activated partial thromboplastin time (aPTT), ecarin clotting time (ECT) and thrombin clotting time (TT)
   b. Minimal effect on PT/INR
   c. **aPTT and TT are most reliable assays for determining presence or absence (rather than degree of anticoagulation) of dabigatran.**
      - Abnormal aPTT is most useful in determining the presence of dabigatran, not for measuring its anticoagulant effects. At therapeutic concentrations TT demonstrates linear dose-response; however, the sensitivity of the assay decreases with increasing plasma levels.
      - At a dose of 150mg twice daily, median peak aPTT was approximately 2x control (Cedars-Sinai median control = 30; range 22-37); 12 hours after the last dose, the median trough aPTT was 1.5x control.

3. Validated reversal guidelines do not yet exist. Review of current limited literature on this new drug and consensus from Cedars-Sinai faculty were used to create the following guideline to assist physicians in the care of patients with bleeding complications.

4. Initial recommended orders for all patients with suspected bleeding complications of dabigatran, regardless of the degree and severity of bleeding:

STAT Orders:

- Type and screen for hemodynamically stable patients with mild bleeding
- Type and Cross for blood for hemodynamically unstable patients with moderate to severe bleeding
- Thrombin time (** not available in ED lab)
- CBC
- Serum creatinine
- aPTT, PT/INR

Hematopathology Consultation:
Dr. Oxana Tcherniantchouk, Hematopathology, may be contacted for test interpretation as needed: 310-423-5471

References
1. Dabigatran (Pradaxa®) Prescribing Information. Boehringer-Ingelheim 2010.
2. Van Run, Joanne, et al. Dabigatran etexilate – a novel, reversible, oral direct thrombin inhibitor: Interpretation of coagulation assays and reversal of anticoagulant activity.
3. Cedars-Sinai Medical Center Guideline for Warfarin Reversal – P&T Approved December 2010
4. Shander, A. et al. Concensus Recommendations for the Off-Label Use of Recombinant Human Factor VIIa (Novoseven®) Therapy

S. Torbati, E. Klapper, O.Tcherniantchouk, S. Martin-Stone, R Aazami

March 2011

SUGGESTED GUIDELINE FOR MILD, MODERATE, SEVERE BLEEDING AND INTRACRANIAL HEMORRHAGE

Mild Bleeding	Moderate Bleeding	Severe Bleeding	Intracranial Hemorrhage
– Assess time of last dose – Hold next dose and monitor bleeding – Give PRBCs as needed	– Assess time of last dose – Hold next dose and monitor bleeding – Implement as needed **1. Volume resuscitation** a. Crystalloid b. PRBCs **2. Administer FFP 2-4 units** **3. Administer 1 unit of apheresis platelets** For Platelet < 50,000/mm^3 **4. Cryoprecipitate 10 units** **– Monitoring** 1. STAT aPTT, platelet count after above measures	– Assess time of last dose – Hold next dose and monitor bleeding – Implement options below as needed based on severity of bleeding and urgency of reversal/repletion. **1. Volume resuscitation** a. Crystalloid b. PRBCs **2. Administer FFP 2-4 units** **3. Administer 1 unit of apheresis platelets** For Platelet < 100,000/mm^3 **4. Cryoprecipitate 10 units** **5. Prothrombin Complex Concentrate (PCC): Factor IX Complex** (Profilnine®) – 25-50 units/kg IVP (2000-4000 units); repeat in 30 minutes if bleeding continues or aPTT/TT remains elevated.(Normal 22-37; median 30) – **Monitoring** a. Check aPTT, platelets in 30 minutes b. PCC/Factor IX Complex has initial/maximum effect within 10-30 minutes c. PCC/Factor IX Complex $T_{1/2}$ = 18-36 hours[3] *****For Continued bleeding, repeat Steps 1-5 above as needed*****	**Prothrombin Complex Concentrate (PCC): Factor IX Complex** (Profilnine®) – 25-50 units/kg IVP (2000-4000 units); repeat in 30 minutes if bleeding continues or aPTT remains elevated (Normal 22-37; median 30) – **Monitoring** a. Check aPTT in 30 minutes b. Initial/maximum effect within 10-30 minutes c. $T_{1/2}$ 18-36 hours[3] *****For Continued bleeding following 2 Doses of PCC/Factor IX Complex**:*** **Factor VII (Novoseven®)** – 70-90 mcg/kg IVP rounded to 1, 2 or 5mg vial; repeat in 15 minutes if bleeding continues or aPTT remains elevated (Normal 22-37; median 30) – **Monitoring** a. Check aPTT in 15 minutes b. Risk of arterial thrombosis is dose dependent c. $T_{1/2}$ 2-3 hours[4]

References

1. Dabigatran (Pradaxa®) Prescribing Information. Boehringer-Ingelheim 2010.
2. Van Run, Joanne, et al. Dabigatran etexilate – a novel, reversible, oral direct thrombin inhibitor: Interpretation of coagulation assays and reversal of anticoagulant activity.
3. Cedars-Sinai Medical Center Guideline for Warfarin Reversal – P&T Approved December 2010
4. Shander, A. et al. Concensus Recommendations for the Off-Label Use of Recombinant Human Factor VIIa (Novoseven®) Therapy

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March 2011

GUIDELINE FOR WARFARIN REVERSAL

Developed in Collaboration with the Departments of Laboratory Medicine, Transfusion Medicine and Pharmacy Services – April 2011

Product	Dosing			Onset/Duration	Special Considerations
Vitamin K *** Doses <2.5mg PO - use the IV formulation administered orally.**	**↓INR to Therapeutic Range within 1-2 days** *(no active bleeding)*	**↓INR to Normal within 24 hours** *(possible procedure within 24 hours)*	**↓ INR to Normal Rapidly[1,2]** *(ICH/Active Bleeding/Emergent Procedure)*	**4-24 hours** Patient dependent	•**SQ** not **not recommended for warfarin reversal** due to unpredictable distribution & reversal characteristics; appropriate for nutritional repletion (i.e. , with TPN therapy) •**Oral** Vitamin K not recommended in biliary disease •**Ineffective in severe liver disease** due to inability to synthesize coagulation factors • Anaphylaxis with slow IVPB ***(outweighed by life-threatening bleeding in a patient unable to take PO)***
	1-2.5mg PO/IVPB Repeat doses based on daily INR	**≤ 5mg PO/IVPB** Additional 1-2mg PO if INR remains ↑ (Grade 2C*)	**10mg IVPB** Repeat every 12 hours if needed based on clinical urgency/INR goal (Grade 1C*) Use with FFP, +/- PCC, to prevent rebound ↑ in INR	**IVPB** – initial effect at 4-6 hours; similar to PO at 24 hours **PO** – full effect at ~ 24 hours	
Prothrombin Complex Concentrate/ Factor IX Complex (PCC) – Profilnine®			**25-50 units/kg** (2000-3000 units) IVP Use with Vitamin K to prevent rebound ↑ in INR	**Initial/Full Effect[3]:** within 10-30 minutes	**Contains factors inhibited by warfarin[2]** • II, VII, IX and X in **>** concentrations than FFP; low FVII content •Possibly ↓ risk of thrombosis than rFVIIa
Fresh Frozen Plasma (FFP)			**15ml/kg** Use with Vitamin K to prevent rebound ↑ in INR	**Immediate, but only partial** replacement of factors due to volume/infusion time	• Variable amounts of factors •Lower amounts of factors than PCC •Large volume problematic in cardiac or fluid restricted patients.

1. Chest 2008;133;160S-198S
2. Hanley JP. J Clin Pathol 2004;57:1132-39
3. Leissinger CA, et al. Am J Hematol 2008. 83:137–143

***Grade 1C Recommendation:** strong recommendation, low or very low quality evidence
***Grade 2C Recommendation:** weak recommendation, low or very low quality evidence

SUMMARY OF MEDICAL CENTER ANTICOAGULATION PROTOCOL CHANGES

APRIL 5, 2011 PHARMACY & THERAPEUTICS COMMITTEE

ANTICOAGULATION PROTOCOL	REQUESTED CHANGES
Warfarin (Coumadin®)	Added/clarified the following statements: **1) MD/RX:** Added - Please see Physician Guideline for **MINIMUM** Timing of Antithrombotic/ Thrombolytic Agents in Regional Anesthesia (Last Page of Protocol) **2) MD/RX:** Removed existing reversal information and replaced with Warfarin Reversal Guidelines **3) MD/RX:** Removed nutrition consult order requirement **4) RX:** Added: NOTE: VAD Team manages the majority of their cases with a goal of 1.5-2. **5) RX:** Removed therapeutic INR table **6) RX:** Emphasized: **If MD discontinues LMWH/heparin prematurely, pharmacist must call and suggest either LMWH upon discharge or continuing UFH for a total of 5 days**.
Heparin	Added/clarified the following statements: **1) MD/RX:** Added - Please see Physician Guideline for **MINIMUM** Timing of Antithrombotic/ Thrombolytic Agents in Regional Anesthesia (Last Page of Protocol) **2) MD:** Continue LMWH/heparin until INR is **therapeutic and a total of 5 days of overlap therapy have been completed.** **3) MD:** Fluctuating/unanticipated aPTT trend, subtherapeutic/supratherapeutic aPTT despite increasing/decreasing doses, patients requiring >35,000 units/day: contact floor pharmacist for heparin level monitoring. **4) RX:** Warfarin should be initiated on Day 1 of heparin therapy unless clear contraindications have been documented. If warfarin is not initiated concurrently on Day 1, pharmacist to call prescriber to suggest initiation; if not initiated at that time, pharmacist to document reason for not initiating on the AMF, open an iVent and **recheck for warfarin initiation in 3 days** (based on regular business hours). **5) MD/RX:** Add VAD patients to highest bleeding risk category aPTT 60-75 **6) RX:** Emphasized: **If MD discontinues LMWH/heparin prematurely, pharmacist must call and suggest either LMWH upon discharge or continuing UFH for a total of 5 days**. **6) RX: Reversal of Heparin in Bleeding Patients (upon physician order):** Slow intravenous injection of protamine 1% solution at a dose of 1mg protamine for every 100 units of heparin that were administered within the last 2-4 hours. Maximum dose is 50mg slow IVP no more frequently than every 10 minutes.
Enoxaparin (Lovenox®) Dalteparin (Fragmin®)	Added/clarified the following statements: **Dalteparin:** **1)** Changed title to **DALTEPARIN (FRAGMIN®) PROTOCOL FOR TREATMENT OF DVT/PE AND MANAGEMENT OF ATRIAL FIBRILLATION** **2) MD/RX:** Added atrial fibrillation as indication. **3) MD/RX: DVT/PE:** Initiate warfarin concurrently on Day 1 in appropriate patients. A 5-day overlap of LMWH with warfarin and a therapeutic INR is essential to avoid thrombotic complications. Continue LMWH until INR is ≥2 **and** 5 days of overlap have been completed (even if INR is therapeutic prior to 5 days of overlap – i.e., INR 2.3 on Day 2 of warfarin therapy). **4) RX:** Emphasized: **If MD discontinues LMWH/heparin prematurely, pharmacist must call and suggest either LMWH upon discharge or continuing UFH for a total of 5 days**. **5) RX:** Warfarin should be initiated on Day 1 of heparin therapy unless clear contraindications have been documented. If warfarin is not initiated concurrently on Day 1, pharmacist to call prescriber to suggest initiation; if not initiated at that time, pharmacist to document reason for not initiating on the AMF, open an iVent and **recheck for warfarin initiation in 3 days** (based on regular business hours). **6) MD/RX:** Added - Please see Physician Guideline for **MINIMUM** Timing of Antithrombotic/ Thrombolytic Agents in Regional Anesthesia (Last Page of Protocol) **7) MD/RX:** Protamine - Maximum dose is 50mg slow IVP no more frequently than every 10 minutes.

2011 Priority Boxed Warnings

Drug Name	Summary of Boxed Warning	Recommended Pharmacist Actions	Recommended Nursing Monitoring (pending nursing review and approval)
Epoetin alfa (Epogen®, Procrit®)	Increased risk of death and serious cardiovascular events (thromboembolic events), stroke and increased risk of tumor progression or recurrence	Evaluate all Epoetin orders for indications For cancer patients, ensure the prescriber is enrolled in the APPRISE program and a completed APPRISE acknowlegement form is in the chart. Contact MD if patient is not receiving chemo therapy Monitor Hb daily for all patients receiving epoetin, and contact MD if Hb >12 x 3 days & patient did not receive blood transfusion within the last 3 days Contact MD if Hb remains >12 after 1 wk of dose reduction If no Hb is available after 3 days, order CBC	Contact MD if Hb >12g/dL Dispense medication guide
Fentanyl Transdermal (Duragesic®)	Contraindicated in patients who are not opioid-tolerant, in the management of acute or postoperative pain (including use in outpatient surgeries), and in the management of mild or intermittent pain. Using damaged or cut patches may lead to the rapid release of fentanyl and absorption of a potentially fatal dose of fentanyl. Use with strong and moderate CYP450 3A4 inhibitors may result in potentially fatal respiratory depression.	Evaluate all new orders for fentanyl patch and note MD ID/Name; was patient on a fentanyl patch prior to admission; Was it used for chronic pain: Indication - Is order consistent with guidelines (if not, describe clinical assessment to substantiate use); Amount of pain medication administered in the last 3 days; Whether dose was titrated per manufacturer's guidelines and rationale for dose escalation less than 72 hours if pertinent; Contact MD for changes if needed	Do not apply heat to patch area Do not use damaged or cut patches Monitor respiratory function

Drug Name	Summary of Boxed Warning	Recommended Pharmacist Actions	Recommended Nursing Monitoring (pending nursing review and approval)
Ketorolac Injectable (Toradol®)	Indicated for short term management of moderate to severe pain Maximum dose for based on age, weight. Increase dose will increase risk of adverse events. Increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which may be fatal. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. Increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach and intestines, which may be fatal.	Evaluate renal functions in patients receiving ketorolac and contact MD if patient has renal impairment Contact MD for renewed ketorolac orders (maximum allowed duration =5days per hospitalization) If no BMP is available at the initiation of therapy, order BMP If patient is ≥ 65yo, or < 50kg, or CrCl 10-50 mL/min. Autosub: Ketorolac 30mg IV x 1 **TO** 15mg IV x1 Ketorolac 30mg IV/IM Q4-6H TO 15mg IV/IM Q6H	Monitor UOP, Scr
Metformin containing products	Lactic acidosis is a rare, but serious, metabolic complication that may occur due to metformin accumulation during treatment. When it occurs, it is fatal in approximately 50% of cases.	Monitor BMP Q3days for patients receiving metformin If no BMP is available, order BMP at baseline and q3days. If patient receives IV contrast, hold metformin for 48 hours after IV contrast administration. Order BMP every other day x 3, beginning with am lab following IV contrast administration.	Monitor Scr Hold metformin for 48 hours after IV contrast administration

Drug Name	Summary of Boxed Warning	Recommended Pharmacist Actions	Recommended Nursing Monitoring (pending nursing review and approval)
Clozapine ****NEW****	**Agranulocytosis:** clozapine should be reserved for use in 1) treatment of severely ill pts with schizophrenia who fail standard antipsyhcotic treatment, or 2) for reducing the risk of recurrent suicidal behavior in pts with schizophrenia or schizoaffective disorder who are judged to be at risk of re-experiencing suicidal behavior. **Seizures:** increase risk at higher doses. **Increased Mortality in Elderly Pts with Dementia Related Psychosis** **Myocarditis** Increased risk of fatal myocarditis, esp during, but not limited to, the first month of therapy. **Other Cardiovascular And Respiratory Effects** Orthostatic hypotension, with or without syncope, can occur with clozapine treatment which is more likely to occur during initial titration in association with rapid dose escalation. Rarely, collapse can be profound and be accompanied by respiratory and/or cardiac arrest which has occurred in patients who were being administered benzodiazepines	Evaluate Clozapine orders for indications and to ensure patient's enrollment in the registry for this admission Contact MD if patient is admitted with or develops seizures, myocarditis, agranulocytosis, serious infections, or on BDZ ATC to notify the MD about the risks and to discuss whether the therapy (clozapine/BDZ) should be continued Order CBC with differential weekly (both new and continuation of outpatient regimen) if no CBC with differential is checked within the past week Monitor CBC, ANC weekly To avoid serious cardiorespiratory events, in pts who have a brief interval off clozapine (≥ 2 days since the last dose, both new and continuation of outpatient regimen),contact MD to reduce the dose to 12.5 mg once or twice daily; maximum dose increase of 50mg/day	Contact MD if patient misses more than 2 days, WBC < 3,500/mm3 Monitor signs and symptoms for orthostatic hypotention
Foscarnet (Foscavir®) ****NEW****	**Nephrotoxicity:** Renal impairment is the major toxicity of foscarnet sodium injection. Frequent monitoring of serum creatinine, with dose adjustment for changes in renal function, and adequate hydration with administration of foscarnet injection, is imperative. **Seizures**: related to alterations in plasma minerals and electrolytes have been associated with foscarnet injection treatment.	Only Infectious Disease Physician can initiate foscarnet therapy If hydration is not ordered, contact MD if for a hydration order. - 1st Infusion: 750 to 1000 mL of NS or D5W to establish diuresis. - Subsequent infusions, give 750 to 1000 mL of hydration fluid concurrently with 90 to 120 mg/kg dose; and 500 mL concurrently with 40 to 60 mg/kg dose Monitor BMP daily If BMP is not available, order BMP at baseline and daily.	Monitor renal function

Drug Name	Summary of Boxed Warning	Recommended Pharmacist Actions	Recommended Nursing Monitoring (pending nursing review and approval)
Infliximab ****NEW****	**Risk Of Serious Infection:** increased risk for developing serious infections that may lead to hospitalization or death. Higher risk in pts taking concomitant immunosuppressants such as methotrexate or corticosteroids. Pts should be tested for latent TB before infliximab use and during therapy. **Hepatosplenic T-Cell Lymphomas**: a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including infliximab. **Malignancy**: Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, including infliximab.	Only process orders if written on approved order set	Monitor for signs & symptoms of infection

Drug Name	Summary of Boxed Warning	Recommended Pharmacist Actions	Recommended Nursing Monitoring (pending nursing review and approval)
Leflunomide (Arava®) ****NEW****	Leflunomide is contraindicated in pregnant women, or women of childbearing potential who are not using reliable contraception. Severe liver injury, inclulding fatal liver failure, has been reported in some patients treated with leflunomide. Patients with pre-existing acute or chronic liver disease should not receive leflunomide. Patients with elevated serum alanine aminotransferase (ALT) > 2x ULN before initiating treatment should not receive leflunomide. Monitoring of ALT levels is recommended at least monthly for 6 months after starting leflunomide and thereafter every 6 to 8 weeeks. If the ALT rises to greater than 3 times the upper limit of normal while the patient is on leflunomide – leflunomide should be stopped while investigating the probable cause of the ALT elevation by close observation and additional tests.	Contact MD if leflunomide is ordered for pregnant patients (check H&P) Order LFT for patients (both new and continuation of outpatient regimen) if no LFT during current admission, at initiation of therapy. Contact MD if ALT > 2x ULN for new start or ALT > 3x ULN for continuation of therapy	NA

Drug Name	Summary of Boxed Warning	Recommended Pharmacist Actions	Recommended Nursing Monitoring (pending nursing review and approval)
Methadone ****NEW****	Deaths, cardiac and respiratory, have been reported during initiation and conversion of pain patients to methadone treatment from treatment with other opioids. Respiratory Depression QT interval prolongation and serious arrhythmia (torsades de pointes) have been observed during treatment with methadone, esp in pts receiving high doses of methadone Methadone treatment for analgesic therapy in patients with acute or chronic pain should only be initiated if the potential analgesic or palliative care benefit of treatment with methadone is considered and outweighs the risks.	Pharmacists to order baseline ECG if not ordered by MD in patients receiving >100mg/day Pharmacist will place the 'Dear Doctor' letter in the chart when the ECG is ordered to inform physicians The following instructions under medication instruction "This medication has been associated with QTc prolongation and arrhythmias. Monitor patient closely"	NA
Prasugrel (Effient®) ****NEW****	Prasugrel can cause significant, sometimes fatal, bleeding. - Do not use this drug in patients with active pathological bleeding or a history of TIA - In pts ≥ 75, prasugrel is generally not recommended - Do not start prasugrel in pts likely to undergo urgent CABG. Additional risk factors for bleeding include: <60 kg, propensity to bleed, concomitant medications that increase the risk of bleeding	Pharmacist reviews orders to ensure compliance with order set criteria Only cardiologists can initiate prasugrel therapy unless the patient was receiving Prasugrel prior to admission	Monitor for signs & symptoms of bleeding
Sunitinib (Sutent®) ****NEW****	Hepatotoxicity has been observed in clinical trials and post-marketing experience. It may be severe and deaths have been reported.	Order LFT for patients (both new and continuation of outpatient regimen) if no LFT during current admission, at initiation of therapy.	NA

Drug Safety and Availability
- Drug Alerts and Statements
- Importing Prescription Drugs
- Medication Guides
- Safe Use Initiative
- Drug Safety Communications
- Drug Shortages
- Postmarket Drug Safety Information for Patients and Providers
- Information by Drug Class
- Medication Errors
- FDA Drug Safety Newsletter
- Drug Safety Podcasts
- Drug Recalls

FDA Drug Safety Communication: New warnings against use of terbutaline to treat preterm labor

Safety Announcement
Additional Information for Patients
Additional Information for Healthcare Professionals
Data Summary
References

Safety Announcement

[02-17-2011] The U.S. Food and Drug Administration (FDA) is warning the public that injectable terbutaline should not be used in pregnant women for prevention or prolonged treatment (beyond 48-72 hours) of preterm labor in either the hospital or outpatient setting because of the potential for serious maternal heart problems and death. The agency is requiring the addition of a *Boxed Warning* and *Contraindication* to the terbutaline injection label to warn against this use. In addition, oral terbutaline should not be used for prevention or any treatment of preterm labor because it has not been shown to be effective and has similar safety concerns. The agency is requiring the addition of a *Boxed Warning* and *Contraindication* to the terbutaline tablet label to warn against this use.

Terbutaline is approved to prevent and treat bronchospasm (narrowing of airways) associated with asthma, bronchitis, and emphysema. The drug is sometimes used off-label (an unapproved use) for acute obstetric uses, including treating preterm labor and treating uterine hyperstimulation. Terbutaline has also been used off-label over longer periods of time in an attempt to prevent recurrent preterm labor.

Although it may be clinically deemed appropriate based on the healthcare professional's judgment to administer terbutaline by injection in urgent and individual obstetrical situations in a hospital setting, the prolonged use of this drug to prevent recurrent preterm labor can result in maternal heart problems and death. Terbutaline should not be used in the outpatient or home setting.

The decision to require the addition of a *Boxed Warning* and *Contraindication* is based on new safety information received and reviewed by the FDA. Specifically, FDA has reviewed postmarketing safety reports of terbutaline used for obstetrical indications (see Data Summary below), as well as data from the medical literature.[1-6] These label changes are consistent with statements from the American College of Obstetricians and Gynecologists (ACOG).[6]

Additional Information for Patients

- Be aware that serious side effects, including maternal heart problems and death, have been reported after prolonged use of terbutaline to manage preterm labor.
- There are serious situations where a healthcare professional may decide that the short-term use of injectable terbutaline in the hospital setting may benefit a pregnant woman.
- Oral terbutaline should not be used either to treat preterm labor or prevent recurrent preterm labor.
- If you are taking terbutaline for another medical condition (e.g., asthma), talk to your healthcare professional if you are pregnant or become pregnant to determine whether terbutaline is still right for you.
- FDA encourages patients to talk to their healthcare professional if they have concerns about any treatment they are receiving.
- Report any side effects from the use of oral or injectable terbutaline to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

Additional Information for Healthcare Professionals

- Be aware that death and serious adverse reactions, including increased heart rate, transient hyperglycemia, hypokalemia, cardiac arrhythmias, pulmonary edema, and myocardial ischemia have been reported after prolonged administration of oral or injectable terbutaline to pregnant women.
- Treatment with terbutaline administered by injection or by continuous infusion pump should not be used beyond 48 to 72 hours. In particular, injectable terbutaline should not be used in the outpatient or home setting.
- There are certain obstetrical conditions where the healthcare professional may decide that the benefit of terbutaline injection for an individual patient in a hospital setting clearly outweighs the risk.
- Oral terbutaline is contraindicated for the treatment or prevention of preterm labor.
- Report adverse events involving terbutaline to the FDA MedWatch program using the information in the "Contact Us" box at the bottom of this page.

Data Summary

In November 1997, FDA issued a Dear Colleague letter to notify healthcare professionals about concerns regarding the safety of long-term subcutaneous administration of terbutaline. The *Precautions* section of the labeling was revised to warn about serious adverse reactions, including cardiovascular adverse events that may occur after administration of terbutaline to women in labor.

Publications in the medical literature have reported a lack of safety and efficacy of terbutaline for the treatment of recurrent preterm labor.[2-5] Despite labeling changes, FDA's communication to the public, and professional association recommendations, prolonged use of terbutaline continues, with serious and sometimes fatal consequences.

FDA reviewed postmarketing reports of maternal death and serious cardiovascular adverse events submitted to the Adverse Event Reporting System (AERS) associated with obstetric use of terbutaline.

A search of AERS identified 16 maternal deaths that were reported since initial marketing of the drug in 1976 until 2009. Three of the 16 cases reported outpatient use of terbutaline administered by a subcutaneous pump, while nine cases reported use of oral terbutaline alone or in addition to subcutaneous or intravenous terbutaline. Of these nine cases, two reported use of oral terbutaline on an outpatient basis and seven cases involved inpatient use of oral terbutaline. The routes of administration in the remaining four cases were subcutaneous, intravenous, or unknown.

FDA identified 12 maternal cases of serious cardiovascular events associated with use of terbutaline that were reported to AERS between January 1, 1998 (after FDA issued the Dear Colleague letter) and July 2009. These events included cardiac arrhythmias, myocardial infarction, pulmonary edema, hypertension, and tachycardia. Three of the 12 cases reported use of the terbutaline administered by subcutaneous pump. Five cases involved use of oral terbutaline alone or in addition to subcutaneous terbutaline. Of these five cases, three cases involved use of oral terbutaline on an outpatient basis and two cases involved inpatient use of oral terbutaline.

In summary, based on this information, FDA has concluded that the risk of serious adverse events outweighs any potential benefit to pregnant women receiving prolonged treatment with terbutaline injection (beyond 48-72 hours), or acute or prolonged treatment with oral terbutaline. FDA is requiring the addition of a new *Boxed Warning* and *Contraindication* to the terbutaline drug labels to warn healthcare professionals about these risks.

References

1. National Asthma Education and Prevention Program (NAEPP). Working Group Report on Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment—Update 2004. NIH Publication No. 05-5236. Bethesda, MD: U.S. Department of Health and Human Services; National Institutes of Health; National Heart, Lung, and Blood Institute, 2004. Available from: http://www.nhlbi.nih.gov/health/prof/lung/asthma/astpreg/astpreg_full.pdf. Accessed November 19, 2010.

2. Wenstrom KD, Weiner CP, Merrill D, et al. A placebo-controlled randomized trial of the terbutaline pump for prevention of preterm delivery. *Am J Perinatol*. 1997;14:87-91.

3. Guinn DA, Goepfert AR, Owen J, et al. Terbutaline pump maintenance therapy for prevention of preterm delivery: a double-blind trial. *Am J Obstet Gynecol*. 1998;179:874-878.

4. Sanchez-Ramos L, Kaunitz AM, Gaudier FL, et al. Efficacy of maintenance therapy after acute tocolysis: a meta-analysis. *Am J Obstet Gynecol*. 1999;181:484-490.

5. Berkman ND, Thorp JM, Lohr KN, et al. Tocolytic treatment for the management of preterm labor: a review of the evidence. *Am J Obstet Gynecol*. 2003;188:1648-1659.

6. American College of Obstetricians and Gynecologists (ACOG). ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologist. No. 43. Management of preterm labor. *Obstet Gynecol*. 2003;101:1039-1047.

Related Information

- FDA Response to Citizen Petition on Terbutaline (PDF - 151KB) 2/17/2011
- FDA warns against certain uses of asthma drug terbutaline for preterm labor Press Release - 2/17/2011
- Terbutaline Information
- NDA Terbutaline Safety Labeling Change Letter (Injection) (PDF - 75KB)
- NDA Terbutaline Safety Labeling Change Letter (Oral) (PDF - 72KB)
- ANDA Terbutaline Safety Labeling Change Letter (Oral) (PDF - 50KB)
- ANDA Terbutaline Safety Labeling Change Letter (Injection) (PDF - 41KB)
- FDA Drug Safety Podcast for Healthcare Professionals: New warnings against use of terbutaline to treat preterm labor

Contact Us

Report a Serious Problem

1-800-332-1088

1-800-FDA-0178 Fax

MedWatch Online

Regular Mail: Use postage-paid FDA Form 3500

Mail to: MedWatch 5600 Fishers Lane

Rockville , MD 20857

Page Last Updated: 02/24/2011

Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

CEDARS-SINAI MEDICAL CENTER

March 2011

Gentamicin for the Treatment of Chorioamnionitis in Intrapartum Patients

Situation: Recently, there was a request from to clarify recommendations for the treatment of chorioamnionitis in intrapartum patients, particularly in regard to gentamicin.

Background: Chorioamnionitis is a cause of maternal and neonatal morbidity and death. Maternal complications include endometritis, bacteremia, hemorrhage, and cesarean delivery.

Treatment recommendations for intrapartum antibiotic therapy for chorioamnionitis include the following: Ampicillin + gentamicin 2 mg/kg loading dose (LD) then 1.5 mg/kg Q8H thereafter. If the patient has a penicillin allergy, vancomycin is used. Limited data exists for once-daily dosing in pregnant women as well as correct dosing weight to use, since most trials with aminoglycosides exclude pregnant women.

If caesarean birth is performed, it is recommended to add clindamycin or metronidazole. Therapy may be continued until the patient is afebrile and asymptomatic for at least 24 hours postpartum.

Assessment: Given the associated morbidity and mortality with chorioamnionitis and available evidence, traditional dosing of gentamicin should be used in addition to ampicillin to treat chorioamnionitis in intrapartum women. Limited data exists for the correct dosing weight to use for gentamicin. Available data suggests that an adjusted body weight should be used to calculate the dose in obese patients. Therefore, it is recommended to dose gentamicin based on total body weight, unless the patient is obese (>100 kg), where an adjusted body weight should be used to calculate the dose.

Recommendations: The following treatment recommendations can be used to treat intrapartum chorioamnionitis:
Ampicillin 2 gm Q6H (adjust for renal function). If PCN allergy: use Vancomycin
PLUS
Gentamicin 2 mg/kg loading dose (LD) then 1.5 mg/kg Q8H. Use TBW to calculate dose unless the patient's weight is >100 kg.

Suggested dosing range for maintenance doses include:

≤ 40 kg	(~ 90 lbs)	= 60 mg
41 - 50 kg	(~ 91 - 110 lbs)	= 80 mg
51 - 60 kg	(~ 111 - 130 lbs)	= 90 mg
61 - 70 kg	(~ 131 - 150 lbs)	= 110 mg
71 - 80 kg	(~ 151 - 176 lbs)	= 120 mg
81 - 90 kg	(~ 177 - 198 lbs)	= 140 mg
91 - 100 kg	(~ 199 - 220 lbs)	= 150 mg
> 100 kg	(> 220 lbs)	= use AdjBW to calculate dose. AdjBw = IBW + 0.4(Total Body Weight – IBW)

If caesarean birth: add clindamycin or metronidazole.

- The physician will discuss risks vs. benefits of treatment with each patient and document if the patient wishes to not receive treatment with gentamicin.

References:

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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, 43% Pseudomonas aeruginosa and 36% 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,] + 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
FEVER WITH NEUTROPENIA[6] (SEE PATHWAY FOR COMPLETE ALGORITHM)	Enterobacteriaceae Resistant GNB *Staphylococci* *Enterococci*	• Piperacillin/tazobactam[2,11] + tobramycin[3,4] **OR** • Cefepime[2,] + tobramycin[3,4] **MONOTHERAPY MAY BE CONSIDERED FOR UNCOMPLICATED PATIENTS:** cefepime[2] 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[17]
SEPSIS OF UNKNOWN SOURCE	Resistant GNB *S. aureus* /MRSA	• Piperacillin/tazobactam[2,11] + tobramycin[3,4] + vancomycin, **OR** • Cefepime[2,] + tobramycin[3,4] ± metronidazole + 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. Consider if patient has peak WBC≤15K AND peak SrCr ≤1.5x baseline. May give IV if unable to take PO.
14. ≥2 of the following characteristics of severe disease: Age >60 y/o, Temp >38.3C, Serum albumin <2.5mg/dL, immunosuppressed -OR- any 1 of the following: peak WBC≥15K, peak SrCr (1.5 x baseline), ICU admission, hypotension and/or shock, presence of ileus, pseudomembranes, or toxic megacolon
15. Hypotension, shock, ileus, or megacolon present
16. For initial or first recurrence of *C. difficile* infection. Discontinue inciting antimicrobials if possible.
17. May be stopped after 2 days if there is no evidence for a gram-positive infection

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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 + 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) NEC : piperacillin/tazobactam[3] + tobramycin	Not recommended
FEVER WITH NEUTROPENIA (see pathway for complete algorithm)	Enterobacteriaceae Resistant GNB *Staphylococci*	piperacillin/tazobactam[3,4] + tobramycin or cefepime + 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: TMP*/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	*S. aureus/S. epi*	cefepime + vancomycin	Externalization of shunt or hardware	Not recommended

(Neurosurgery or head trauma or VP shunt)	Enterobacteriaceae Resistant GNR *S. pneumoniae*	(trough 15-20)	usually necessary for sterilization. *Critically ill*[2]: meropenem + vancomycin (trough 15-20) ***Use maximum antibiotic dose***	

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

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2. Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice Guidelines for the Management of Bacterial Meningitis. CID 2004;39:1267-1284.
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5. Moellering et al. Current Treatment Options for Community-Acquired Methicillin- Resistant *Staphylococcus aureus* CID April 2008;46:1032-7
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CEDARS-SINAI MEDICAL CENTER

PROPOSED OBESITY DOSING RECOMMENDATIONS FOR COMMONLY-USED SURGICAL PROPHYLAXIS ANTIMICROBIAL AGENTS

Table 1. Surgical Prophylaxis Dosing Recommendations

DRUG	PATIENT WEIGHT	DOSE	
Aztreonam	< 80 kg (176 lbs.)	1 gm	
	≥80 kg (176 lbs.)	2 gm[8]	
Cefazolin	<80 kg (176 lbs.)	1 gm[1,8]	
	≥80 kg (176 lbs.)	2 gm[1,2,4,6,8]	
Cefotetan	<80 kg (176 lbs.)	1 gm	
	≥80 kg (176 lbs.)	2 gm[2,8]	
Cefuroxime	<80 kg (176 lbs.)	1.5 gm[1]	
	≥80 kg (176 lbs.)	3 gm[1]	
Clindamycin	<80 kg (176 lbs.)	600 mg	
	≥80 kg (176 lbs.)	900 mg[8]	Limited data
Metronidazole	<80 kg (176 lbs.)	500 mg	
	≥80 kg (176 lbs.)	500 mg	Limited data[8]

Table 2. Institution Survey

Institution	Obesity Dosing Recs?	Obesity Definition for Pre-Op Orders	Surgery Specific?
Palomar Pomerado Health	Yes	≥ 80 kg	No
University of Utah	Yes	>100 kg (cefazolin)	No
Johns Hopkins	Yes	<table><tr><th>Weight (kg)</th><th>Cefazolin *Q2-4h* (Cardiac Q2h)</th><th>Cefotetan *Q8h*</th><th>Vancomycin *Q12h*</th><th>Clindamycin *Q8h*</th><th>Metronidazole *Q8h*</th></tr><tr><td><70kg</td><td>2gm</td><td>2gm</td><td>1gm</td><td>600 mg</td><td>500 mg</td></tr><tr><td>71-99</td><td>2gm</td><td>2gm</td><td>1.25 gms</td><td>600 mg</td><td>500 mg</td></tr><tr><td>>100</td><td>2gm</td><td>2gm</td><td>1.5 gms</td><td>600 mg</td><td>500 mg</td></tr></table>	No
Holycross Hospital	Yes	≥80 kg (cefazolin)	No
SUNY Downstate Medical Center	Yes	> 80 kg – higher dosing recs used	No
The Hospital for Sick Children (Toronto)	Yes	Cefazolin: 30 mg/kg/dose; max 2 grams (Peds hospital)	No
Aurora Health Care – St. Luke's Medical Ctr.	Yes	80 kg for all surgeries and applied to cephalosporins, vancomycin, clindamycin, aztreonam In addition: Vanco ≥80 kg = 1.5 gm; >120 kg = 2 gram Cefazolin: ≥ 80 kg = 2 gm; >120 kg = consider 3 gm	No
New York Pres	Yes	> 80 kg = use high-dose cefazolin, aztreonam (2 gm)	No

References:

(1) IDSA Draft Recommendations for Colorectal Surgery; (2) Johns Hopkins; (3) Edmiston CE et al.; (4)Engelman; (5)Mandell; (6) Forse et al; (7) Waltrip et al.; (8) Bratzler; (9) Medscape; (10) Green B and Duffull SB.

11. TRAUMA PATIENTS:

Trauma patients are at a higher risk for drug – induced nephrotoxicity (i.e.: CT with IV contrast, hypovolemia, rhabdomyolysis, concomitant nephrotoxic drugs). The following monitoring parameters must be followed for trauma patients

- Draw two serum levels after loading dose to determine patient's specific vancomycin half-life and elimination rate constant.
- Maintenance dose and interval will be calculated based on the patient's specific PK parameters to achieve desired trough

  MD= (desired trough) X Vd X $(1-e^{-K\tau})/ e^{-Ke\tau}$ (Where τ is desired interval or Tau)
- Vancomycin trough level must be drawn daily until true trough or stead state is reached.
  - If level is <goal, continue current regimen and monitor trough daily until steady state is reached
  - If level is at goal <u>before</u> steady state, consider either adjusting dose or frequency.
  - If level is >goal, <u>hold</u> dose and readjust dose & frequency and repeat above process.
- Once vancomycin trough is reached, continue monitor parameters as outline in section 5 for high risk (ie. Hemodynamically unstable patients)

Auto-Stop for Antimicrobials

- Current Practice:
  - 5-day autostop
    - Piperacillin/tazobactam, cefepime, imipenem, meropenem, ciprofloxacin/levofloxacin, oseltamivir
  - 7-day autostop
    - All other antimicrobials except:
      - TMP/SMX (PO), pentamidine IV, antivirals, antiretrovirals, tuberculosis medications, anti-malaria medications, anthelminthics, interferon for hepatitis C, pyrimethamine

Approved 5-day Auto-Stop for All Antimicrobials Except:

- Anti-Helminthics
- Anti-Malaria Agents
- Anti-Retrovirals
- TB medications
- Wound Care Agents
  - Polysporin & bacitracin topical agents
  - Silver sulfadiazine
- Other
  - Amantadine (non-ID usage)
  - Interferon
  - Rifaximin 550 mg PO
- Prophylactic Use
  - Acyclovir/valganciclovir PO
  - Atovaquone
  - Azithromycin 1200 mg tabs
  - Ciprofloxacin 750 mg tablet
  - Clotrimazole PO
  - Dapsone
  - Norfloxacin PO
  - Nystatin PO
  - Pentamidine inhaled
  - Pyrimethamine
  - Ribavirin PO
  - TMP/SMX (PO)

Reasons for Change & Implementation Plan

- Reasons:
  - Improve consistency
  - Assist with de-escalation of prolonged antibiotic exposure and implementation of Senate Bill 1058
- Goal Implementation Date: Dec. 1st 2011

- Recommendations:
  - Educate physicians regarding 5-day autostop
    - Include in CPOE training
  - Send to P&T, CIC, COSAC, PICs and Division Meetings
    - Include in Pulse & Sutures
    - Send additional reminder in Nov. 2011

Pediatrics IV Gentamicin Protocol

Weight	Age in Days		
	0-7	7-28	> 28
0 – 0.999 kg	2.5 mg/kg Q24H	2.5 mg/kg Q24H	2.5 mg/kg Q12H
1 – 1.999 kg	3 mg/kg Q24H	4 mg/kg Q24H	2.5 mg/kg Q12H
2 – 2.999 kg	3 mg/kg Q24H	4 mg/kg Q24H	2.5 mg/kg Q8H
3 kg or above	3.5 mg/kg Q24H	4 mg/kg Q24H	2.5 mg/kg Q8H

- Gentamicin trough and peak with 3rd dose.
- Tr ½ hr before dose. Infuse over 30 mins. Pk ½ hr after end of infusion.

- Goal trough: ≤ 3.4 mg/kg/dose: < 2 mg/L
  ≥ 3.5 mg/kg/dose: ≤ 1 mg/L
- Usual Goal peak: 5 - 10 mg/L.

- For UOP < 1 ml/kg/hr in the past 12 hrs, notify MD. Check level and hold dose.

- Consult pharmacist for dosage adjustment.

Guideline:	**LARGE VOLUME PARACENTESIS; GUIDELINE FOR THE USE OF ALBUMIN 25%**
Effective:	
Prev. Issued:	None

OVERVIEW:

Large-volume paracentesis (LVP) is a common therapeutic procedure performed in outpatient and inpatient settings to manage refractory and symptomatic ascites in patients with advanced cirrhosis. Although some controversy exists in the medical literature, most authorities agree that it is reasonable to provide colloid replacement to patients receiving paracenteses greater than 5 liters to reduce the risk of post-paracentesis circulatory dysfunction--a syndrome characterized by hyponatremia, azotemia and increased plasma renin activity. Most consensus statements agree with the safety and efficacy of albumin for such volume expansion. (1-4)

DOSING AND ADMINISTRATION GUIDELINE:

1. For LVP with 5 - 7.5 Liters removed:
    a. Albumin 25%, 50 grams IVPB
2. For LVP with > 7.5 -10 Liters removed:
    a. Albumin 25%, 75 grams IVPB
3. Consider albumin replacement for patients receiving LVP less than 5 Liter in patients with underlying renal impairment, low serum albumin, significant edema, or active or suspected infections (including SBP) placing them at risk for intravascular volume depletion
    a. For fluid removal of 1.5-2 Liters, albumin 25%, 25 grams IVPB
    b. For fluid removal of >2-5 Liters, albumin 25%, 50 grams IVPB
4. Rate of administration:
    a. Administer each vial of Albumin 25% (25gm / 100mL) over 15 minutes.

REFERENCES AND CEDARS-SINAI SPECIALIST RECOMMENDATION:

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5. Communications with Cedars-Sinai Medical Center, Procedure Center.

Guideline:	**LARGE VOLUME PARACENTESIS; GUIDELINE FOR THE USE OF ALBUMIN 25%**
Effective:	
Prev. Issued:	None

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Guideline:	**GUIDELINE: USE OF INTRALIPID® 20% IN PATIENTS WITH LOCAL ANESTHETIC OR LIPOPHILIC DRUG INDUCED CARDIAC ARREST, UNRESPONSIVE TO STANDARD RESUSCITATIVE THERAPY**
Effective:	
Prev. Issued:	None

OVERVIEW:

Lipid rescue therapy (LRT) has been shown in numerous case studies to be an effective life saving treatment for patients suffering severe complications of local anesthetic and other lipophilic drug toxicities (1-12). The majority of case reports described lack of response to initial management with standard resuscitative measures, but all were successfully resuscitated after receiving lipid rescue therapy.

The lipid solution used for LRT is a 20% soybean oil based lipid product and is identical to that used in TPN therapy. No complications were reported in the case reports when used for resuscitative therapy (16, 17).

Based on these case reports, the immediate availability of LRT has been advocated by authorities for immediate use in emergency department and anesthesia settings (14,15).

The pharmacokinetics of lipid rescue therapy in the treatment of local anesthetic and lipophilic drug toxicity in not completely understood but likely involves the following mechanisms:

1. Sequestration of lipid soluble drugs within intravascular compartment 'Lipid Sink Theory' (13); reduction in 'free' drug
2. Potential energy source for cardiac muscle under stress
3. Fatty acids activate calcium channels, releasing intracellular calcium
    a. Increase in cardiac contractility
    b. Release of insulin, potentially increasing cardiac performance in 'shock'
    c. Enhanced blood pressure response in setting of alpha adrenergic vasopressors

DOSING GUIDELINE:

1. Initial Dose: Intralipid® 20%

- Adults: 100 ml (or 1.5 ml/kg) intravenous bolus injection over 2-3 minutes
- Children 1.5 ml/kg over 2-3 minutes
- May repeat 2 additional boluses if adequate circulation has not been restored.

2. Intralipid® 20% infusions (0.25 – 0.5 mL/kg/min for 30-60 minutes or longer) may be indicated after initial response to bolus dose.

- Consultation with the Poison Control Center (1-800-411-8080) on dosing and duration of the infusion is strongly recommended

CAUTIONS:

- Egg or soy allergy
- May exacerbate existing pancreatitis

These guidelines reflect current evidence based clinical practice. However, they are not to be considered absolute and universal recommendations. For individual patient application, these guidelines must be considered in light of the patient's clinical condition and latest evidence based care.

Guideline:	**GUIDELINE: USE OF INTRALIPID® 20% IN PATIENTS WITH LOCAL ANESTHETIC OR LIPOPHILIC DRUG INDUCED CARDIAC ARREST, UNRESPONSIVE TO STANDARD RESUSCITATIVE THERAPY**
Effective:	
Prev. Issued:	None

INTERACTIONS WITH LABORATORY TESTS:

Hemoglobin, hematocrit, white blood cell and platelet counts drawn immediately after LRT may be uninterpretable for several hours. Additionally, oxygen saturation may not be measurable and methemoglobin may be falsely elevated (18).

REFERENCES:

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2. Litz RJ, Popp M, Stehr SN et al. Successful resuscitation of a patient with ropivacaine-induced asystole after axillary plexus block using lipid infusion. *Anesthesia*. 2006; 61:800-1.
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7. Shah S, Gopalakrishnan S, Apuya J et al. Use of Inralipid in an infant with impending cardiovascular collapse due to local anesthetic toxicity. *J Anesth*. 2009; 23:439-41.
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Guideline:	**GUIDELINE: USE OF INTRALIPID® 20% IN PATIENTS WITH LOCAL ANESTHETIC OR LIPOPHILIC DRUG INDUCED CARDIAC ARREST, UNRESPONSIVE TO STANDARD RESUSCITATIVE THERAPY**
Effective:	
Prev. Issued:	None

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15. Lipid Infusion Protocol. Guy Weinberg, MD: http://www.lipidrescue.org. Accessed 2/7/2011.

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APPROVED BY:

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

CCN00083 Supersedes: H-2	Effective: July 2010 Prev. Issued: 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.

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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 pt. and recheck blood. Glucose every 15 min until > 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 pt. and recheck bld. Glucose every 15 min until > 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**

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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	3 (4 gm tablets) glucose tablets PO (total amount of glucose per treatment is 3 tablets = 12 gm) If the patient cannot chew or refuses glucose tablets, 180 mls of orange juice* maybe used in place of 3 glucose tablets. 1 tablet is equal to 60 ml juice. Give 1 additional glucose tablet if no response within 15-20 min	• Immediately call RRT and notify MD • Give 60 - 180cc of juice (orange or apple) • Assess pt. and recheck blood Glucose every 15 min until > 70 mg/dl. *(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.

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.

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.

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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

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- 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

V. REFERENCE

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VI. KEY WORDS

- Insulin Reaction
- Low Blood Sugar

VII. COMPETENCY

- Blood Glucose Monitoring

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

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