

In This Issue...

Changes to Formulary	1
Cefamandole Interchange to Cefazolin	2
Alternative to Racemic Epinephrine	2
Antiemetic Prophylaxis for PONV	3
Amoxicillin-Clavulanate (Clavulin®)	4
Awards - CSU Pharmaceutical Sciences	5
Infusion Program Updates	5
Adverse Drug Reaction Report 1998	6

All formulary changes and policy/procedure updates have been approved by the Drugs and Therapeutics Committee (D&T) and Medical & Academic Advisory Council (MAAC).

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Changes to Formulary

Additions

- Amoxicillin/clavulanate 500/125 mg, 875/125 mg (Clavulin®)**
 - Oral antibiotic possessing broad spectrum antibacterial activity
 - See page 4 for drug review
- Garasone® eye/ear drops (gentamicin 3mg/mL and betamethasone 1.0mg/mL)**
 - antibacterial and anti-inflammatory drops
 - Cost: \$12.82/7.5mL
- Dakin's Solution 1:8,1:16 (dilute sodium hypochlorite)**
 - the **1:16** dilution will be the default strength supplied if a strength is not speci-

fied

Deletions

- Cefamandole 1g, 2g vials (Mandol®)**
 - on March 15, 1999, all orders for cefamandole will be interchanged to cefazolin (gram for gram)
 - see page 2 for interchange policy
- Cortisporin® ear drops (polymixin B/ neomycin/hydrocortisone)**
 - alternative: Garasone® eye/ear drops
- Tolcapone tablets (Tasmar®)**
 - new antiparkinsonian agent recently suspended by manufacturer due to safety concerns
 - may still be obtained through the Special Access Program (SAP)

Updated Policies/Procedures

1. Revised Drug Administration Policies

- Alteplase (t-PA) may now be administered direct IV by nurses in ICU, CCU-1, Emergency-Acute and Cardiac Cath Lab.

EDITORIAL STAFF:

Karen Shalansky, Pharm.D.
Peter Loewen, Pharm.D.
Rubina Sunderji, Pharm.D.
Peter Jewesson, Ph.D.

Any comments, questions or concerns with the content of the newsletter should be directed to the editors. Write to CSU Pharmaceutical Sciences Vancouver General Hospital, 855 W12th Ave, Vancouver BC V5Z 1M9, send a FAX to 604-875-5267 or email kshalans@vanhosp.bc.ca Find us on the Web at www.vhpharmsci.com

2. Cefamandole Interchange to Cefazolin

Carlo Marra, Pharm.D., Luciana Frighetto, B.Sc. (Pharm), Peter Jewesson, Ph.D.

Effective March 15, 1999, all orders for cefamandole will be subject to a therapeutic interchange with an equivalent regimen of cefazolin (Table 1). The previous cefamandole to cefuroxime interchange will no longer apply. Cefuroxime will still remain on formulary. Cefamandole is being deleted as it offers no advantage over other formulary antibiotics, is more expensive than cefazolin, and its use has declined significantly. At VHHSC, cefamandole no longer demonstrates *in vitro* superiority over cefazolin with respect to *Staphylococcus epidermidis*. The Division of Medical Microbiology has previously discontinued reporting susceptibility patterns for cefamandole.

Table 1. Cefamandole to Cefazolin Conversion

Cefamandole Dose	Cefazolin Dose Conversion
1 g IV q6h or q8h	1g IV q8h
2g IV q6h or q8h	2g IV q8h

In this institution, cefamandole has been used primarily for surgical prophylaxis in cardiac, orthopedic, and vascular procedures. As part of the Standardized Orders for Antimicrobial Prophylaxis (SOAP) initiative, a review of the antimicrobial surgery prophylaxis literature was recently conducted by members of the CSU Pharmaceutical Sciences. Guidelines were subsequently developed in collaboration with representatives from various surgical divisions for different procedures. The Divisions of Cardiac, Orthopedic, and Vascular Surgery have adopted cefazolin as their antibiotic of choice for surgery prophylaxis in non-beta-lactam allergic patients. Preprinted orders are now being created for many surgical procedures reflecting standard protocols for both pre-operative and post-operative antimicrobial prophylaxis.

Under the therapeutic interchange policy, if

cefamandole is prescribed, it will be interchanged to the same dose of cefazolin at an equivalent interval (Table 1). This policy has been approved by the Antibiotic Utilization Subcommittee, D&T (November 1998) and MAAC (January 1999).

3. Alternative to Racemic Epinephrine

Racemic epinephrine, used in the treatment of reversible bronchospasm and laryngeal edema, has been back-ordered indefinitely by the manufacturer. Racemic epinephrine contains equal amounts of the d- and l-isomers of epinephrine, with the l-isomer being more pharmacologically active.

The alternative to nebulized racemic epinephrine is nebulized l-epinephrine. L-epinephrine has been shown to be as effective as racemic epinephrine with no additional adverse effects.¹⁻³ The dose for l-epinephrine 1:1000 (1mg/mL) is 10-fold the volume required for racemic epinephrine. The adult dose is :

5 mL (5mg) l-epinephrine 1:1000 = 0.5mL racemic epinephrine 2.25%

Due to the volume required, l-epinephrine does not need to be further diluted for nebulization. The solution should be administered over 10-15 minutes. CSU Pharmaceutical Sciences will clarify all orders for racemic epinephrine with the physician and these will be corrected to l-epinephrine. L-epinephrine 1:1000 30mL injectable will be supplied.

L-epinephrine and racemic epinephrine both contain metabisulphite and should not be used in patients with sulphite hypersensitivity.

References

1. Kanji Z. Shortage of racemic epinephrine - is epinephrine an alternative? BCCH Pharmacy Informer. Spring/Summer 1998.
2. Waisman Y et al. Prospective randomized double-blind study comparing l-epinephrine and racemic epinephrine aerosols in the treatment of laryngotracheitis (croup). *Pediatr* 1992;89:302-6.
3. Nutman J et al. Racemic versus l-epinephrine aerosol in the treatment of post-extubation laryngeal edema: results from a prospective, randomized, double-blind study. *Crit Care Med* 1994;22:1591-4.

4. Antiemetic Prophylaxis for Post-Operative Nausea and Vomiting

Luciana Frighetto, B.Sc. (Pharm), Carlo Marra, Pharm.D., Peter Loewen, Pharm.D.

Post-operative nausea and vomiting (PONV) are commonly reported adverse events after surgery and can contribute to the development of aspiration, wound dehiscence, and increased bleeding.^{1,2} Prophylaxis with antiemetics has been shown to reduce the incidence of PONV as well as improve patient satisfaction, decrease recovery and discharge times, and reduce hospital readmissions.³⁻¹⁰ There are many studies supporting the use of prophylactic antiemetics to reduce the incidence of PONV in patients at high risk for PONV.^{3,7-9,11-18} Several different antiemetics have been studied for the prevention of PONV including metoclopramide, perphenazine, droperidol, ondansetron and dolasetron.^{3-5,7,11,19-21} These agents have all been associated with varying degrees of success.

Currently, there are no standard guidelines for the prophylactic use of antiemetics in the management of PONV in our institution. CSU Pharmaceutical Sciences, in collaboration with the Department of Anesthesia, have developed standard protocols for the prevention and immediate post-operative treatment of patients with nausea and vomiting for both the ambulatory and inpatient settings. For the prevention of PONV, preprinted orders for anesthesia and Surgical Daycare Centre (SDCC) have been created for patients considered at high risk for PONV and include various antiemetic agents such as droperidol, dolasetron, and metoclopramide. Dolasetron, a Limited Access Drug at VHHSC, has now been approved by the Drugs and Therapeutics Committee and Medical Academic and Advisory Committee for use in the prophylaxis of PONV. This agent can be prescribed using a preprinted anesthesia or SDCC pre-op order form. Preprinted orders have also been created for the treatment of PONV in the post anaesthesia recovery and surgical daycare settings. These orders reflect a standard approach for the treatment of PONV in these settings.

postoperative nausea and vomiting. *Can J Anaesth* 1997;44:173-81.

Amoxicillin/Clavulanate (Clavulin®)

Carlo Marra, Pharm.D., Luciana Frighetto, B.Sc. (Pharm)

Amoxicillin/clavulanate is a combination product containing amoxicillin, a semi-synthetic penicillin, and the β -lactamase inhibitor, clavulanate potassium. Clavulanate enhances the antibacterial spectrum of amoxicillin by acting as an irreversible "suicide" inhibitor of intracellular and extracellular β -lactamases and, thus protecting deactivation of amoxicillin.^{1,2} With the continued increase in resistance mediated by the bacterial production of β -lactamases, the addition of amoxicillin/clavulanate to the VHHSC drug formulary appears warranted. Addition of amoxicillin/clavulanate was proposed by the Antibiotic Utilization Subcommittee in October 1998, and approved by the D&T and MAAC in November 1998 and January 1999, respectively.

Spectrum of Activity

Amoxicillin/clavulanate provides additional coverage over amoxicillin of *Staphylococcal aureus*, *Hemophilus influenzae*, *Escherichia coli*, *Moraxella catarrhalis*, *Klebsiella pneumoniae*, *Bacteroides fragilis* and *Proteus* species.^{1,2} Consequently, this agent can be used as an alternative to 2nd and 3rd generation oral cephalosporins and/or cotrimoxazole for skin and soft tissue infections including bite wounds, lower respiratory tract infections, and urinary tract infections. In a recent meta-analysis that pooled three decades of trial results from more than four hundred publications and 38,500 patients, amoxicillin/clavulanate was equal or superior to other antibiotics for the treatment of upper and lower respiratory infections, skin structure infections, dental infections, head and neck infections, and selected urinary tract infections. In addition, when the results of these trials were grouped by annual and triennial publication dates, the efficacy of amoxicillin/clavulanate did not appear to have changed over time indicating its continued usefulness.

Dosage

The established adult oral dosing regimen for amoxicillin/clavulanate is 500/125 mg given every eight

New Drug/Drug Products

Amoxicillin/Clavulanate (Clavulin®)

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Dosage

The established adult oral dosing regimen for amoxicillin/clavulanate is 500/125 mg given every eight hours; however, some recent adult

trials have indicated that the administration of a new 875/125 mg oral preparation twice daily is as effective as the three times daily regimen for lower respiratory tract infections⁴ and acute bacterial maxillary sinusitis.⁵ Table 2 compares the dosage and cost of amoxicillin/clavulanate to amoxicillin alone and other formulary alterna-

Table 2. Cost comparison of Clavulin® to other oral formulary alternatives

Drug	Dose	Daily Cost ^a
Amoxicillin/ Clavulanate	500/125mg tid 875/125mg bid	\$4.00 \$4.63
Amoxicillin	500mg tid	\$0.27
Cefuroxime axetil	500 mg tid	\$11.88
Cefixime	400 mg daily	\$4.47
Cotrimoxazole	1 DS tablet bid	\$0.22

^a based on VHHSC acquisition costs

tives.

Adverse Effects

The incidence and spectrum of adverse effects with amoxicillin/clavulanate is similar to amoxicillin alone. Adverse effects are typically gastrointestinal in nature and include diarrhea, nausea, vomiting and indigestion. The 875/125 mg bid dosing schedule has resulted in a lower rate of gastrointestinal complications than the 500/125mg tid dosing regimen.^{4,5} There have been rare reports of hepatic dysfunction associated with the use of this agent, mainly in elderly patients receiving prolonged or repeated treatment courses.²

References

- Todd PA et al. Amoxicillin/clavulanic acid. An update of its antibacterial activity, pharmacokinetic properties and therapeutic use. *Drugs* 1990;39:264-307.
- Ball P et al. Amoxicillin clavulanate: an assessment after 15 years of clinical application. *J Chemother* 1997;9:167-98.
- Neu HC, Wilson APR, Gruneberg RN. Amoxicillin/clavulanic acid: A review of its efficacy in over 38,500 patients from 1979 to 1992. *J Chemother* 1993;5:67-93.
- Calver AD et al. Dosing of amoxicillin/clavulanate given every 12 hours is as effective as dosing every 8 hours for treatment of lower respiratory tract infections. *Clin Infect Dis* 1997;24:570-4.
- Seggev JS et al. A combination of amoxicillin and clavulanate every 12 hours vs. every 8 hours for treatment of acute bacterial maxillary sinusitis. *Arch Otolaryngol Head Neck Surg* 1998c; 124(8):921-5.

Pharmacy Awards

CSU Pharmaceutical Sciences is pleased to announce it has received the following national Canadian Society of Hospital Pharmacists (CSHP) Awards:

- **Organon Award** (Residency Project Award) Sunderji R, Campbell L, Shalansky KF, Fung A, Carter C, Gin K for "*Outpatient self-management of warfarin therapy: a pilot study.*"
- **Hoffman LaRoche Award** (Specialty Practice Award) de Lemos J, Carr R, Shalansky KF, Bevan D, Ronco J for "*Paralysis in the critically ill: intermittent bolus pancuronium compared with continuous infusion.*"
- **Novartis Award** (Pharmacoeconomics Award) Frighetto L, Marra C, Loewen P, Doleman J for "*Cost effectiveness of prophylactic dolasetron or droperidol for prevention of postoperative nausea and vomiting in outpatient gynecologic surgery.*"

Infusion Program Updates

Did you know that...

- The Home IV Antibiotic Program has been operating successfully for over 36 months, has enrolled over 265 patients who received over 6,200 outpatient antibiotic treatment days.
- A 1997 13-month cost benefit analysis of the Home IV Antibiotic Program revealed an estimated net cost avoidance of over \$440,000. In other words, for every 12 cents VHHSC contributes to the program, a cost avoidance of \$1.00 is achieved.
- All patients who are enrolled into the Home IV Antibiotic Program are asked to complete a satisfaction survey at the end of treatment. A 1998 18-month analysis of surveys revealed that on a 10-point scale, the median rank of patient satisfaction with the program is 10. In fact, 95% of patients enrolled in the program state they would participate again if the need arose.

Infusion Device Facts and Tips:

- Mechanical phlebitis is the most common side effect of a newly inserted PICC. It will appear within 72 hours and usually resolves well with moist, continuous heat for 24 hours.
- The primary cause of a "positional" PICC is a twisted or kinked line between the suture wing and the PICC hub.
- A PICC dressing will always have a gauze dressing under the occlusive dressing for the first 24 hours only (for occasional bleeding); subsequent dressings will only have the occlusive dressing.
- A gauze dressing should not be placed **under** an occlusive dressing for longer than 24 hours as it traps heat and moisture and will increase the risk of infection.
- If you see fluid under an occlusive dressing, check to see that the extension tubing is firmly attached to the PICC hub.
- When doing IV/CVC site preparation, use firm pressure, moving from the centre outwards.
- Following the removal of a CVC, the best dressing to apply is a gauze and occlusive dressing. These should be removed again in 24 hours.
- Four benefits of a Groshong close-ended catheter are that no heparin flush is required, no clamp is necessary, bleeding from the catheter is unlikely and air emboli is extremely uncommon.
- Huber point needles are now available in a 20 gauge, 3/4" length for leaner patients. This size is adequate for blood withdrawal and administration of medications.
- A patient teaching booklet entitled "**Total Parenteral Nutrition - A guide for Patients and Their Families**" is available for distribution and can be ordered from Lori Mason at

Adverse Drug Reaction Report 1998

There were a total of 40 suspected adverse drug reactions (ADRs) reported at VHHSC in 1998 (Table 3). Of note, 12 reactions were considered to have been the cause of hospitalization. The continued reporting of all suspected ADRs by nurses, physicians and pharmacists aids in an improved assessment of the magnitude and nature of adverse events. To notify Pharmacy of an ADR, either fill out a yellow ADR alert card, available on all nursing units, and send to CSU Pharmaceutical Sciences, or call local 62481 (VGH site) or local 27249 (UBC site). Pharmacists complete all ADR report forms and forward copies to the B.C. Regional ADR Centre. This Centre does preliminary analysis of the data and then forwards all reports to the Canadian ADR program in Ottawa who then forward them to the World Health Organization.

Table 3. Adverse Drug Reactions Reported in 1998

Drug	Suspected ADR	Drug	Suspected ADR
Abciximab (in conjunction with heparin & ticlopidine)	thrombocytopenia (4)	Levothyroxine ^a	chest pain/tightness (in relation to dose increase (1)
Allopurinol ^a	rash, lip swelling, conjunctival discharge, fever, eosinophilia (1)	Lithium ^a (interaction with hydrochlorothiazide)	tremors, ataxia, decreased level of consciousness, required hemodialysis (1)
Amitriptyline	ventricular tachycardia (1)	Methotrimeprazine	granulocytopenia (1)
Anileridine	pruritic rash on back and abdomen (1)	Niacin	flushing (1)
Bupropion	erythematous rash (1)	Nitrofurantoin ^a	pulmonary fibrosis (1)
Carbamazepine	neutropenia, falling platelet count (1)	Phenytoin	rash, fever with rigors (1)
Cefazolin	angioedema, swollen lips, flushing (1)	Phenytoin/Carbamazepine ^a	hypersensitivity reaction (1) (rash, fever, periorbital swelling, lymphadenopathy)
Ciprofloxacin	myoclonic jerks (1)	Propylthiouracil	neutropenia (1)
Cisapride	increased saliva and drooling (1)	Ranitidine ^a	pruritic rash, periorbital and lip swelling (1); delirium (1)
Cotrimoxazole	elevated LFTs (1)	Rifampin ^a	acute interstitial nephritis (1)
Donepezil	excessive drooling, rhinorrhea (1)	Tamoxifen ^a	deep vein thrombosis (1)
Droperidol	intense dysphoria, altered mental state, nightmares x 6 weeks after dose (1)	Ticlopidine ^a	thrombotic thrombocytopenic purpura (1)
Enalapril/ Hydrochlorothiazide ^a	agranulocytosis (1)	Tolcapone ^a	anxiety, agitation (1)
Fludrocortisone + Valerian	hypokalemia (1)	Vancomycin	nephrotoxicity (1)
Glucosamine	gastritis (1)	Warfarin ^a	rash (1); GI bleed (1, in conjunction with ASA and ticlopidine), GI bleed (1, in conjunction with ASA)
Iron Dextran	rash, chest pain, chills (1); back pain (1)	Zopiclone	black-out, fall (1)
Ketorolac	anaphylaxis (known allergy to NSAIDS) (1)		

^ahospitalized due to ADR