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DRUG AND THERAPEUTICS NEWSLETTER

A publication of the CSU Pharmaceutical Sciences
Vancouver General Hospital, UBC Hospital, GF Strong

June 2008 *Volume 15, Number 2*

In This Issue...

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

This and other Drug and Therapeutics Newsletters are on the Web at **www.vhpharmsci.com**

Changes to Formulary

Additions

1. Lansoprazole 30 mg capsules and FasTabs (Prevacid®)
- Proton pump inhibitor (PPI) to replace both rabeprazole tablets and omeprazole MUPS for NG/PEG use
- See Therapeutic Interchange, page 2

2. Linezolid 600 mg PO/IV (Zyvoxam®)
- Restricted Antimicrobial Drug (RAD) for treatment of infections caused by susceptible strains of staphylococci and streptococci (including MRSA and VRE) in patients who cannot receive or have failed vancomycin, or if the pathogen is resistant to vancomycin
- See review page 4

3. Sativex® buccal Spray (delta-9-tetrahydrocannabinol and cannabidiol)
- Cannabinoid analgesic for use in patients with intractable neuropathic pain who are unresponsive or are intolerant to other medications used for this condition
- Sativex® is classified as a narcotic drug
- Restricted to Complex Pain, Palliative Care and those patients on this medication prior to admission

4. Galantamine tablets (Reminyl®) and Rivastigmine capsules (Exelon®)
- Cholinesterase inhibitors used for the treatment of mild to moderate Alzheimer's disease. These agents may improve functional and cognitive abilities, and delay time to institutionalization.
- Restricted to those patients on these drugs prior to admission. Pharmacare currently sponsors the Alzheimer's Drug Therapy Initiative and covers treatment costs for galantamine, rivastigmine, and donepezil (Aricept®) for outpatients only.
- Donepezil is already available on formulary for new starts with prescribing restricted to geriatricians, psychiatrists, neurologists, as well as those on this drug prior to admission.

Deletions

1. Rabeprazole (Pariet®) tablets
- Alternative: Lansoprazole (Prevacid®)

2. Omeprazole MUPS®
- Discontinued by manufacturer
- To be replaced with Lansoprazole FasTabs for NG/PEG use

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3. Diethylsilbestrol injection (Honvol®), Stilbestrol tablets

- Discontinued by manufacturer

4. Edrophonium injection (Enlon®)

- Discontinued by manufacturer

Updated Policies/Procedures

1. THERAPEUTIC INTERCHANGE: PROTON PUMP INHIBITORS (PPI)

Effective Jun 1, 2008, all PPIs ordered for oral or NG/PEG use will be automatically interchanged to lansoprazole 30 mg capsules or 30 mg FasTabs, respectively.

2. THERAPEUTIC INTERCHANGE UPDATE: CEFOTAXIME TO CEFTRIAXONE

A therapeutic interchange protocol was implemented in Sept 2007 to auto-substitute cefotaxime to genericized ceftriaxone. Recent revised labeling of ceftriaxone recommends avoiding the co-administration of this drug with IV solutions containing calcium following reports of 8 deaths in children up to 1 year of age who received this combination. This recommendation extends to both adults and children, even though there is no indication that a similar risk exists in adults. As a result, on June 16, 2008 the following revisions to the ceftriaxone interchange will be implemented:

- All patients on TPN will be excluded from this interchange; thus all patients on TPN will remain on cefotaxime as ordered
- For all ceftriaxone orders, pharmacy will screen patients for calcium containing TPN orders and contact the prescriber to switch to cefotaxime
- All ceftriaxone labels will have the notation “do not give concurrently with IV calcium”. This comment will also appear on the MAR for ceftriaxone.

3. PHARMACIST AUTHORITY

As part of the regional VCH pharmacist prescribing authority approved in March 2008, the following pharmacist authorities will be implemented on June 16, 2008 at Vancouver Acute (VA)

Unit-based clinical pharmacists can independently write orders for multivitamins (PO/enteral), Nicotine Replacement Therapy (NRT), Calcium/Vitamin D, dosage adjustment of anti-infective drugs based on renal function, and any laboratory test associated with monitoring of drug therapy without prior physician consultation. The following conditions must apply:

A. <u>Multivitamins</u>

Unit-based clinical pharmacists may order all formulary multiple vitamin preparations for ORAL and ENTERAL administration (as long as the patient is able to take medications via naso-gastric tube and is not NPO) at the usual recommended daily dose without a physician's order. Single entity vitamin and parenteral preparations must still be ordered by a physician.

i) Multivitamin supplements will be considered only if program patient care guidelines recommend a multivitamin supplement for patient’s condition, or if all the following criteria are met:
   - Patient is malnourished or at risk of nutritional deficiencies
   - Expected length of stay is greater than 7 days
   - Patient is unable to eat sufficient food/ supplements to meet daily recommended intake (DRI)
   - Patient is unable to modify dietary intake to meet DRI
   - If iron supplementation is problematic based on a patient’s co-existing condition (e.g. hemosiderosis, iron overload syndrome), then iron-containing multivitamin products (i.e. Centrum Forte®/Select®) should not be ordered without prior consultation with a physician.

ii) The pharmacist consults with the patient and the patient is agreeable to initiate therapy.

iii) The pharmacist communicates the order by writing a note in the history section of the chart to indicate the rationale for multivitamin therapy. A copy of this note is given to the resource pharmacist for the purpose of quality assurance.

B. <u>Nicotine Replacement Therapy (NRT)</u>

Unit-based clinical pharmacists may write an order for NRT using the pre-printed NRT order form (PPO #638) as long as:

i) NRT has been reviewed with the patient and there are no contraindications to use (refer to PPO). The risks/benefits to initiate NRT have been explained to the patient and the patient is willing to start therapy.

ii) NRT patient teaching sheet(s) are given to and discussed with patient.

iii) The pharmacist communicates the order by writing a note in the history section of the chart to indicate the rationale for NRT and follow-up plan. A copy of this note is given to the resource pharmacist for the purpose of quality assurance.

iv) The patient is monitored for desired therapeutic outcome.

C. Calcium and/or Vitamin D therapy

Unit-based clinical pharmacists may write orders for calcium and/or vitamin D therapy for the treatment or prevention of osteoporosis/bone disease as long as:

i) The patient was taking these preparations prior to admission; OR

ii) The dosage and/or formulation that was prescribed are different from what the patient was taking prior to admission and it is clear that this formulation and/or dosage is what the patient should be taking (e.g. calcium carbonate 500 mg (Tums) vs calcium carbonate 1250 mg (ApoCal = 500 mg elemental calcium).

iii) The pharmacist reviews the patient medications and disease states to rule out any contraindications (e.g. known hypercalcemia, end-stage renal disease).

iv) The pharmacist consults with the patient and the patient is agreeable to continue with therapy.

v) The pharmacist communicates the order by writing a note in the history section of the chart indicating the rationale for this therapy. A copy of this note is given to the resource pharmacist for the purpose of quality assurance.

vi) The patient is monitored for potential side effects.

D. Modify Dosage of Anti-Infective Drugs based on Renal Function

Unit-based clinical pharmacists may change the dose and/or frequency of oral or parenteral anti-infective drugs based on renal function to improve the safety and/or effectiveness of a regimen according to the following conditions:

i) The prescribed dose and/or frequency of the anti-infective agent is not appropriate for the patient's level of renal function.

ii) The pharmacist has access to appropriate clinical information to make the regimen change.

iii) The pharmacist ensures the modified dose is adequate for the indication.

iv) If the patient is being followed by the Infectious Diseases (ID) team, the pharmacist should liaise with the ID pharmacist prior to any dosage adjustments.

v) Recommendations are based on those listed in the VA PDTM or formulary.

vi) The pharmacist communicates this change by writing a note in the history section of the chart to indicate the rationale for the change and the follow-up plan. A copy of this note is given to the resource pharmacist for the purpose of quality assurance.

vii) The pharmacist continues to manage and monitor the drug regimen. It is the responsibility of the pharmacist taking care of the patient to ensure there is a transfer of care before leaving the service.

viii) The pharmacist ensures appropriate laboratory tests are ordered for on-going monitoring (i.e. serum creatinine, BUN, drug levels).

E. Order Serum Drug Levels and other Laboratory Tests Associated with Drug Therapy Monitoring

Unit-based clinical pharmacists may order serum concentrations of all measurable drug levels including (but not limited to) aminoglycosides (with serum creatinine), carbamazepine, cyclosporine, digoxin, lithium, phenobarbital, phenytoin (with serum albumin), tacrolimus, theophylline, valproic acid, and vancomycin (with serum creatinine).

Unit-based clinical pharmacists may order any laboratory test to guide in drug therapy decision making.

4. PDTM UPDATES

Updated policies include:

- **Fentanyl subcutaneous infusions:** both Palliative Care and Complex Pain Services may order SC fentanyl infusions for patients where IV access is an issue.
- **Sodium bicarbonate infusions** used for prevention of radiographic contrast dye-mediated nephropathy: it is no longer necessary to withdraw 150 mL from the 1 L D5W bag prior to the addition of 150 mL sodium bicarbonate (total volume = 1150 mL).
- Medications administered via **subcutaneous infusion** are ideally run at flow rates of 1-10 mL/hour in minimal volume; flow rates should not exceed 25 mL/hour.

5. PATIENT TEACHING SHEETS - NEW INTRANET LINK

The VGH patient teaching sheets are now located on the VCH Connect homepage. Click on the "Clinical" tab and then "VGH Patient Counselling Materials".

Linezolid (Zyvoxam®)

Tim T.Y. Lau, Pharm.D., Karen Shalansky, Pharm.D.

Pharmacology

Linezolid is a synthetic antibacterial agent of a new class, the oxazolidinones. It exhibits activity against Gram-positive pathogens, such as *Staphylococcus*, *Streptococcus*, and *Enterococcus* (including methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE)).

The mechanism of action of linezolid differs from other antibacterial agents. It binds to the 23S ribosomal bacterial RNA, and effectively inhibits protein synthesis. Due to this unique mechanism of action, cross-resistance to other classes of antibiotics is unlikely.

Linezolid is completely absorbed after oral dosing with an absolute bioavailability of 100%, which is not affected by the administration of food. Peak plasma levels are achieved within 1-2 hours. The oral route is preferred unless GI compromise is suspected. Linezolid is primarily metabolized by the liver (65%); dosage adjustments are not required in renal failure and mild-moderate hepatic dysfunction. Doses should be given post-hemodialysis, as approximately 30% of a dose is removed via dialysis.

Adverse Effects and Drug Interactions

Most common side effects include headache, diarrhea, and nausea/vomiting (Table 1). Myelosuppression (thrombocytopenia, neutropenia, anemia, and pancytopenia) may occur with use beyond 2 weeks. It is recommended to monitor CBC weekly if anticipated therapy is greater than 2 weeks, especially in patients with pre-existing bleeding, thrombocytopenia, myelosuppression or those who are on concomitant drugs that may suppress the bone marrow.

Linezolid is a weak MAO-A and MAO-B inhibitor. Patients should be monitored for excessive high blood pressure if receiving an interacting drug, such as adrenergic agents (e.g. epinephrine, pseudoephedrine), serotonergic agents (e.g. citalopram, fluoxetine, fluvoxamine, nefazodone, sertraline, venlafaxine), meperidine, dextromethorphan, and foods with high tyramine content (e.g. aged cheese, beer, red wine).

Comparison to Other Agents

Vancomycin is the treatment of choice for hospital-acquired MRSA. Daptomycin and tigecycline are 2 non-formulary agents available in Canada that have activity against both MRSA and VRE (Table 1). Daptomycin is the only agent that has bactericidal activity against VRE.

Indications for Use at VA and Dosage

Linezolid is a Restricted Antimicrobial Drug (RAD) at VA limited to the treatment of infections caused by susceptible strains of staphylcocci and streptococci (including MRSA and VRE) in patients who 1) cannot receive vancomycin due to hypersensitivity or intolerance; 2) have failed to respond to vancomycin; or 3) have a pathogen resistant to vancomycin.

The dosage is 600 mg PO/IV twice daily for 10-28 days depending on the infection. Special Authority is required as an out-patient for Pharmacare coverage unless prescribed by an Infectious Diseases Specialist.

Table 1. Comparison of Linezolid, Daptomycin, and Tigecycline

Drug	Linezolid (Zyvoxam®)	Daptomycin (Cubicin®)**	Tigecycline (Tygacil®)**
Class	Oxazolidinone	Lipopeptide	Glycylcycline (tetracycline-derivative)
Activity	MSSA, MRSA, Streptococcus/ *Enterococcus*/VRE	MSSA, MRSA, Streptococcus/*Enterococcus*/ VRE	MSSA, MRSA, Streptococcus/ *Enterococcus*/VRE, Enterobactericiae, *Bacteroides*
Dosage	600 mg PO/IV BID	4 to 6 mg/kg IV daily	100 mg IV x 1, then 50 mg IV Q12H
Renal Failure	No dose adjustments; give dose post-hemodialysis	< 30 mL/min = Q48H dosing	No dose adjustments
Adverse Effects	Headache, diarrhea, nausea, thrombocytopenia, neutropenia	Headache, insomnia, hypotension, nausea, renal failure, phlebitis, rash, anemia, abnormal LFTs, CPK	Nausea (20%), vomiting (13%), abdominal pain, photosensitivity, acute pancreatitis, anaphylaxis/ anaphylactoid reactions
Drug Interactions	Weak MOA-A and MAO-B inhibitor - see text	Caution with concomitant statins and aminoglycosides	May decrease clearance of warfarin; monitor INR
Cost*/day	$191 (IV); $141 (PO)	$138 (70 kg patient)	$165

*based on wholesaler costs; **non-formulary at VA