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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

- Atorvastatin 80 mg tablets (Lipitor®)**
 - Atorvastatin 80 mg tablets are now formulary. All other atorvastatin strengths will remain non-formulary; doses less than 80mg will continue to be interchanged to an equivalent simvastatin dose to a maximum of simvastatin 40mg daily.
 - Atorvastatin 80mg daily has greater lipid lowering effects compared to that of simvastatin 40mg daily. In addition, there is evidence supporting the use of high dose atorvastatin in improving cardiovascular outcomes in patients with acute coronary syndrome, stable CAD and stroke.

Deletions

- Peroglide (Permax®)**
 - Due to safety concerns of increased risk of cardiac valvulopathies, pergolide is only available through Health Canada's Special Access Program.

2. Neosporin® cream (polymixin B, neomycin, gramicidin)

- Discontinued by manufacturer
- All orders for Neosporin® cream will be interchanged to Neosporin® ointment (polymixin B, neomycin, zinc bacitracin)

Updated Policies

1. THERAPEUTIC INTERCHANGE: TRAVOPROST TO LATANOPROST

Travoprost and latanoprost are ophthalmic drops used for the treatment of glaucoma and are considered therapeutically equivalent. A Therapeutic Interchange has been implemented whereby all travoprost orders are automatically interchanged to latanoprost, at the same dose and frequency, unless "do not substitute" is specified.

2. Y-SITE COMPATIBILITY CHART UPDATE

The general nursing unit Y-site compatibility charts have been updated with the Nov 2007 version. The colour of this chart has changed from white to blue. Please contact Dr Karen Shalansky if you require a chart (875-4839).

3. HEPARIN 5000 units Subcutaneous (SC)

As of Jan 16, 2008, all heparin orders for 5000 units SC will be dispensed with heparin 10,000 units/mL - 1 mL vials (ie. 5000 units/0.5 mL). These are multidose vials and contain two 5000 units doses per vial. This switch is to improve medication safety by limiting the availability of higher concentrations of heparin.

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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,

4. NICOTINE REPLACEMENT THERAPY (NRT)

Jane de Lemos Pharm.D.

On May 31 2008, all hospitals will be going smoke-free, inside and out. Tobacco is the leading cause of preventable death in Canada. Statistically, 15-20% of patients admitted to hospital smoke; 50% of smokers die prematurely as a result of a smoking related disease, and 70% of smokers want to quit. Based on modeled data, Table 1 shows the relative decrease in mortality associated with smoking cessation compared to other interventions, as well as the number of patients needed to treat (NNT) to save one life.

Table 1. Risk reduction with Smoking Cessation

Intervention	Relative mortality reduction ¹	NNT ²	Cost per life year saved ³
Smoking cessation	36%	9	\$2000 to \$6000
Statin therapy	29%	34	\$50,000 plus
Beta blockers	23%	120	-
Blood pressure control	-	31	\$9000 to \$26,000
ACE inhibitor	23%	-	-
ASA	15%	143	-

Any patient who smokes and is receiving medical treatment for ischemic heart disease, hypertension, CHF, diabetes, atrial fibrillation or COPD is considered only partially treated if they have not been advised to quit by a health care professional. Canadian and international consensus guidelines for these conditions reflect the importance of smoking cessation as part of the bundle of care. Smoking cessation may also decrease the risk of fractures in patients with osteoporosis and the risk of recurrent ulcers. For patients with COPD, smoking cessation is associated with a slower decline in lung function.

A health care professional's advice and provision of NRT doubles the success rate of quitting. Patient teaching sheets are available on the VHnet for the various NRT products. As well, a NRT pre-printed orders form is available through printing ([PPO #638](#) - see insert). Health professionals can offer NRT to patients to support during abstinence in hospital. The patient's hospital stay provides an excellent

opportunity to inform patients of the health benefits if they stopped smoking for good. (Table 2).

Table 2. Patient Promotion of Smoking Cessation

Ask	Have you ever smoked?
Advise	The most important advice I can give you is to stop smoking. This may be a time to think about quitting (relate benefits in the patient's personal context given medical conditions, decrease risk of MI, stroke, etc.).
Assess	How willing are you to quit smoking? Assess level of nicotine dependence (see NRT orders).
Assist	Would you like some help to quit? Initiate the NRT prescriber order form. Provide patient information sheets.
Arrange	Point out resources for follow-up – QuitNow www.quitnow.ca or 1-877-455-2233.

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4. Srivastava P et al. BMJ 2006;332:1324-1326.

5. VINCRISTINE VIA MINIBAG ONLY

Effective February 1, 2008, all adult doses of vincristine will be dispensed in a 50 mL minibag. This is due to several fatalities that have occurred with inadvertent intrathecal administration of vincristine when dispensed in a syringe. A standard warning will appear on each minibag stating: "Warning: Fatal if given intrathecally. Do not use infusion pump for peripheral administration."

Pharmacy Awards

The Canadian Society of Hospital Pharmacists, BC Branch has awarded two VGH residency projects as the best in BC for 2006/07. The winning projects are:

- **Karen G Lee, Peter Loewen, Eric Lun**
"Implementation of a Quality Indicator for Inpatient Drug Therapy within a Large Urban Health Region"
- **Jennifer Samilski, Eric Lun, Tim TY Lau, Dean Elbe, Amneet Aulakh**
"A Personal Digital Assistant-Based Drug Use Evaluation of a Respiratory Quinolone: Moxifloxacin"

Updates in Drug Therapy

Treatment of Community-acquired Methicillin-Resistant *Staphylococcus aureus* (CA-MRSA)

Crystal Amos, BSc(Pharm), Reviewed by Tim TY Lau, Pharm.D.

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a pathogen that is emerging world-wide.¹ In the United States, MRSA has become an epidemic, with some cities reporting MRSA rates of over 70% of total *S. aureus* isolates.² In the past, MRSA was considered a hospital-acquired infection that occurred in patients with risk factors such as recent hospital contact, surgery, residence in a long-term care facility, dialysis, or presence of invasive medical devices.³ Currently, community-acquired MRSA (CA-MRSA) has made its way into Canada, and its incidence is increasing.

Some risk factors that have been associated with CA-MRSA include homelessness, parenteral drug use, and patients with *S. aureus* infection who are not responding to initial treatment with a beta-lactam antibiotic.⁴ Infections commonly caused by CA-MRSA are generally associated with skin and soft tissue infections, which may present as boils (furuncles), abscesses pyomyositis, folliculitis, impetigo, wound infections, bursitis, and cellulitis.⁴ CA-MRSA may also present as pneumonia. Patients who present with risk factors or with severe infection should be suspect for CA-MRSA.

The genes that code for CA-MRSA resistance are different from the hospital-acquired strain.⁵ For this reason, CA-MRSA is susceptible to more classes of antibiotics than hospital-acquired MRSA and more therapeutic options are available. In general, CA-MRSA tends to be susceptible to co-trimoxazole (TMP-SMX) and tetracyclines (e.g. doxycycline, minocycline). Clindamycin may also be used depending on local susceptibility patterns.⁴ For recurrent CA-MRSA infections, rifampin or fusidic acid may be considered in addition to co-trimoxazole or doxycycline.

In contrast to hospital-acquired MRSA, vancomycin is not required as a first-line agent for CA-MRSA and should be reserved for proven multi-drug resistant isolates. Linezolid is also effective against CA-MRSA, but should be avoided as initial therapy due to its high cost (~\$150/day) and the fact that other less expensive antibiotics are as effective.⁴ Fluoroquinolones (e.g. ciprofloxacin, moxifloxacin) should also be avoided because resistance to these

agents tends to occur rapidly when treating CA-MRSA infections.⁴

Clinicians should keep in mind that co-trimoxazole is often not effective for infections due to group A *Streptococci*, which is also a common cause of skin infections and abscesses.⁵ Therefore, if group A *Streptococcus* is suspected, the addition of a beta-lactam antibiotic (e.g. cephalexin) is necessary for empiric coverage. In contrast, clindamycin may cover both group A *Streptococcus* and CA-MRSA depending on susceptibilities.

The optimal dose of co-trimoxazole for treating CA-MRSA is still unknown, although more aggressive dosing is recommended.⁶ The suggested dose is co-trimoxazole DS two tablets orally twice daily for skin and soft tissue infections. For more severe infections, co-trimoxazole 15-20 mg TMP/kg/day (divided two to three times daily) is suggested, which is similar to doses used to treat more serious infections such as *Pneumocystis carinii* (PCP) or *Stenotrophomonas maltophilia*.⁶

Personal hygiene is essential in preventing the spread of CA-MRSA infections. Patients should be told of the importance of frequent and thorough hand washing, and to not share personal-care items such as towels, soaps, or razors. If a patient has a draining wound, the wound should be covered, and patients should avoid the use of whirlpools or saunas.

Despite the growing evidence of an increasing incidence of CA-MRSA in Canada, low-risk patients who present with an infection that is not suspect of CA-MRSA should be empirically treated with an appropriate first-line beta-lactam antibiotic. This is to prevent the development of resistance to alternate antibiotics. If CA-MRSA is suspected, a new pre-printed order (PPO) for Vancouver Acute is now available for patients admitted to the Emergency Department (ED) to assist clinicians in selecting an appropriate antibiotic for outpatients. This PPO is entitled "VGH ED Outpatient Treatment of Suspected/proven CA-MRSA Skin and Soft Tissue Infections" (PPO # 63).

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New Prescribing Restrictions for Rosiglitazone (Avandia, Avadamet, Avandaryl).

Crystal Amos, BSc(Pharm), Reviewed by Anar Dossa, B.Sc (Pharm)

Health Canada has recently imposed new prescribing restrictions for rosiglitazone in Type 2 diabetic patients.¹ Rosiglitazone will no longer be approved as monotherapy, or in combination with a sulfonylurea, except in instances when metformin is contraindicated or not tolerated. Rosiglitazone is now also contraindicated in patients with **any** stage of heart failure (NYHA Class I, II, III, or IV).

These new restrictions are in light of Health Canada's recent assessment of the cardiac safety of rosiglitazone, such as risk of myocardial infarction (MI) in addition to heart failure (HF). Their assessment included a review of the recently published and much debated meta-analysis conducted by Nissen and Wolski in the *NEJM*.²

Nissen and Wolski's results suggested a significant increase in the risk of MI with rosiglitazone compared to placebo or other antidiabetic regimens (odds ratio (OR) 1.43; 95% CI, 1.03-1.98; p=0.03), and a trend towards an increased risk of death from cardiovascular (CVS) causes which did not reach statistical significance (OR 1.64; 95% CI, 0.98-2.74; p=0.06). However, there are several shortcomings of the meta-analysis including the absence of primary or time-to-event data, and the inclusion of trials that were not originally intended to investigate CVS outcomes.^{2,3} Although this meta-analysis does not prove that rosiglitazone causes heart attacks, it is important in that it raises questions about the safety of rosiglitazone, and of the thiazolidinedione (glitazone) class as a whole.⁴

Pioglitazone (Actos[®]) has also been under surveillance to determine whether the concerns with rosiglitazone also apply to pioglitazone. Many experts cite the PROactive trial (Prospective Pioglitazone Clinical trial in Macrovascular Events) as proof that pioglitazone is safer than rosiglitazone. This trial was designed to determine whether pioglitazone reduces macrovascular morbidity and mortality in high risk people with Type 2 diabetes.⁵

While the primary combined endpoint was not statistically different, the secondary composite endpoint of death, MI, or stroke was significantly lower in the pioglitazone group compared to placebo (Harm Reduction (HR) 0.84; 95% CI, 0.72-0.98, p=0.027). However, the possible reduction in the risk of heart attack and stroke was at the expense of an increased risk of symptoms of heart failure and hospitalization for heart failure.

Subsequent to the rosiglitazone meta-analysis, Nissen and Wolski and co-investigators also conducted a meta-analysis evaluating the risk of CVS events with pioglitazone. Their results suggested that pioglitazone is associated with a lower risk of death, MI or stroke compared to controls (HR 0.82; 95% CI 0.72-0.94 p=0.005).⁶ Although these results favour pioglitazone, this meta-analysis has similar shortcomings as the rosiglitazone analysis in that it includes trials not originally intended to assess CVS outcomes.

Based on the uncertainty surrounding the safety of rosiglitazone, it would be prudent to use it judiciously. For newly diagnosed diabetics, who are not controlled by diet or exercise, initial therapy with metformin should be considered. If treatment goals are not reached, insulin or a sulfonylurea should be added before a glitazone. If a glitazone is required, they can be used, but are best avoided in any patient with heart failure. Keep in mind that glitazones are not approved for use with insulin, or as triple therapy (e.g. with a sulfonylurea and metformin), because the risk of heart failure is higher with these combinations.^{1,7}

References

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