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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

- 1. Gliclazide Modified Release 30 mg tablet (Diamicon MR®)**
 - Once daily formulation of gliclazide for management of type 2 diabetes
 - Added to formulary to a) provide continuity of care for patients on this formulation prior to admission; and b) provide a more convenient alternative for patients who fail or are intolerant to another sulphonylurea AND have demonstrated or are at risk of non-compliance
- 2. Blephamide® eye drops and ointment**
 - Antibacterial, anti-inflammatory eye preparation that contains sulfacetamide 10% plus prednisolone 0.2%
 - Replaces Vasocidin® eye drops which are no longer being manufactured
 - all orders for Vasocidin® will be interchanged to Blephamide®

2. Nicotine Inhaler (Nicorette® Inhaler)

- Nicotine replacement therapy (NRT) to aid in smoking cessation
- May be used in combination with Nicotine patch in patients who are not able to maintain abstinence with a single NRT therapy
- Patient teaching sheet available on-line (on the VCH homepage, click on Programs and Services, then Pharmaceutical Sciences-Vancouver Acute, then Patient Counseling Materials on the left hand side of page)
- Pre-printed Smoking Cessation orders that contain NRT choices (patch, gum, inhaler) and bupropion are available in printing (PPO # 638)
- See Page 3 for review and other NRT at VA

Deletions

- 1. Racemic epinephrine 2.25% solution (Vaponephrine®)**
 - Discontinued by manufacturer
 - Alternative: 5 mL (5 mg) l-epinephrine 1:1000 = 0.5 mL racemic epinephrine
- 2. Quinidine 200 mg tablets and Quinidine Bisulfate 250 mg (Biquin Durules®)**
 - Discontinued by manufacturer
- 3. Vasocidin® eye drops (Sulfacetamide 10% + Prednisolone 0.25%)**
 - Discontinued by manufacturer
 - Alternative: Blephamide® eye drops, ointment

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Updated Policies

1. MAGNESIUM SULPHATE IV INTERCHANGE

As a medication safety initiative, the Pharmacy Department will introduce a therapeutic interchange policy approved by the Drugs and Therapeutics Committee to standardize the prescribing of magnesium sulphate intermittent infusion orders (Table 1).

Table 1. Magnesium Sulphate IV Therapeutic Interchange	
Ordered As:	Interchanged to:
2.5 g or less	2 g in 50 mL D5W*
Greater than 2.5 g	5 g in 100 mL D5W*
*Default volume and solution if not specified	
NOTE: 1 g = 4 mEq = 8 mEq	

The interchange will be **effective March 26, 2007** and applies to all intermittent IV magnesium sulphate orders unless the physician writes "Do not Substitute". Nursing units exempt from this policy are BMT Day Care, MDCU, OR and CSICU.

Medication errors frequently occur with the preparation and administration of IV magnesium sulphate from the 10 mL vials of 50% solution (equivalent to 5g/10mL or 40 mEq/10mL). Doses may be compounded incorrectly on the nursing units due to confusion of the correct conversion for the dose ordered, i.e. grams vs mEq vs mMol vs mL.

To reduce the risk of medication errors associated with the administration of magnesium sulphate, the pharmacy will compound and dispense premixed bags of the above concentrations as a personal prescription to general nursing units instead of dispensing the 10 mL vials. For units that receive magnesium sulphate as wardstock (other than the above named exempt areas), the vials will be replaced with the same premixed bags.

All magnesium sulphate infusions must be administered by a pump. Labels on all premixed bags will include the administration rate, i.e. 2 g dose to be infused over at least 30 to 60 minutes by pump, and 5 g dose to be infused over at least 3 to 4 hours by pump.

2. AZITHROMYCIN PO INTERCHANGE

The Antibiotic Use Subcommittee had previously made the decision to have clarithromycin XL PO as our oral macrolide of choice for respiratory tract infections. Surveillance data suggest that the administration of azithromycin may be associated with a potential increase in *Streptococcus pneumoniae* resistance. Thus, **effective March 26, 2007**, a therapeutic interchange policy will take effect such that all doses of azithromycin PO will be interchanged to clarithromycin XL (Table 2). Exceptions to this policy include approved restricted uses for azithromycin PO (i.e. one time doses for chlamydial infections, and MAC prophylaxis in HIV patients), Infectious Diseases (ID) consult, or if "do not substitute" is written.

Table 2. Azithromycin PO Therapeutic Interchange	
Ordered As Azithromycin:	Interchanged to Clarithromycin XL:
250 mg PO daily	500 mg PO daily
500 mg PO daily	1000 mg PO daily
Exemptions: Azithromycin ordered for chlamydial infections (i.e. 1000 mg PO x 1 dose), MAC prophylaxis (i.e. 1200 mg PO weekly) or ID consult	

3. FORMULARIES 2007

The 2007 Vancouver Acute Formularies have been distributed to all nursing units. Note that only the pocket size version of this formulary is available now. The slightly larger blue binder formularies have been removed from all wards and replaced with this new 2007 (mauve cover) version. Please contact Karen Shalansky at (604) 875-4839 if any questions.

The formulary is also available on-line: on the VCH homepage, click on Programs and Services, then Pharmaceutical Sciences-Vancouver Acute, then Formulary (on right hand side of page).

4. RENAVITE® = REPLAVITE®

Note that Replavite®, the renal vitamin B and C plus folic acid formulation, is now being manufactured under the brand name Renavite®.

5. PDTM UPDATES

- **Digoxin Immune Fab (Digibind®) requires DPIC approval** prior to administration. While a small supply is kept in the Emergency Department, DPIC must still be called for approval to use this supply (604-682-5050).
- **The starting dose of argatroban has been reduced to 0.5-1 mcg/kg/minute.** PTTs should be checked 2 hours after initiating therapy to maintain PTTs 1.5-3 times baseline (not to exceed 100 seconds).

6. MODIFICATION TO HEPARIN PROTOCOLS

On Jan 16, 2007, the laboratory switched to new reagents for measuring PTTs. As a result, the new therapeutic PTT ranges for heparin are:

- **HEPARIN/WARFARIN STANDARDIZED PROTOCOL: 60-120 seconds**
- **LOWER TARGET HEPARIN PROTOCOL: 50-85 seconds**

New Drugs/Drug Products

Nicotine Inhaler (Nicorette®)

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Indication

The aim of nicotine replacement therapy (NRT) is to replace nicotine from cigarettes. Nicotine inhaler is indicated as a stop smoking aid to help reduce nicotine withdrawal symptoms. In addition, to providing adequate amounts of nicotine to help reduce the urge to smoke, the inhaler may also have additional benefit by providing a hand-to-mouth ritual similar to smoking.¹

Dosage

Nicotine inhaler consists of a mouthpiece and plastic cartridge which delivers 4 mg of nicotine (the major fraction of the total 10 mg nicotine in the inhaler is deposited in the oral cavity). The initial dosage is self-titrated to the level of nicotine the patient requires to reduce abstinence symptoms. Each cartridge has enough nicotine to last 20 minutes. The patient can continuously inhale 1 cartridge for 20 minutes (8 to 10 inhalations = ~1

cigarette; 1 cartridge can replace ~4 cigarettes).¹ Alternatively, the patient can try sessions of various duration e.g. 2 sessions of 10 minutes or 4 sessions of 5 minutes each to a total of 20 minutes. The number of cartridges used varies from 6 to 12 per day during the first 3 to 12 weeks of therapy. After 12 weeks, patients should gradually reduce the daily dose over the following 6 to 12 weeks. When daily use is reduced to 1 to 2 cartridges/day, the use of the inhaler should be stopped. The safety and efficacy of continued use of the inhaler beyond 6 months of therapy has not been studied.¹

Comparable Formulary Agents

Nicotine is available as a gum, patch and inhaler in Canada (Table 3).

Table 3. Nicotine Replacement Therapy

Dosage Form*	Peak Nicotine Levels	Initial Dose/day	Relative Cost
Nicotine Patch 7, 14, 21mg	5-6 hours after application	7-21mg daily	+
Nicotine Gum 2mg, 4mg	15-30 minutes after start of chewing gum	10-12 pieces per day (max 20/day)	+
Nicotine Inhaler	15 minutes after inhalation	6-12 cartridges per day	++

*combination NRT therapy (patch + gum, patch + inhaler) may be indicated in patients who are not able to induce or maintain abstinence while on a single NRT formulation

The Cochrane Review identified 123 RCT of which 103 compared NRT to placebo or no treatment, and 95 had greater than or equal to 12 months of follow-up.² All formulations of NRT were found to be effective in promoting smoking cessation with increased odds of quitting smoking of ~1.6-2 times compared to placebo/no treatment regardless of setting (Table 4). The nicotine inhaler had the highest odds ratio for abstinence amongst the three NRT formulations, although there were only 4 studies included in this group. The review concluded that choice of formulation should reflect patient needs, tolerability, and cost. The 4 mg gum was also more effective than the

2mg gum in highly dependent smokers. There is some evidence that combining products (e.g. patch plus either gum or inhaler) may be more effective than either product alone.^{2,3}

Table 4. NRT vs Placebo/No Treatment (Control) for Smoking Cessation at 6-12 months²

Comparison	Gum v control	Patch v control	Inhaler v control
Number of Trials (N)	52 (17,819)	37 (16,228)	4 (976)
Weighted Event Rates	18% v 12%	14% v 8.1%	17% v 9.1%
Odds Ratio for Abstinence (95%CI)	1.66 (1.52-1.81)	1.81 (1.63-2.02)	2.14 (1.44-3.18)
NNT (95%CI)	17 (15-20)	17 (15-20)	13 (9-25)

A randomized 12-week trial (N=504) comparing nicotine gum, transdermal patch, nasal spray and inhaler found no differences amongst the formulations in their effects on withdrawal discomfort, urge to smoke, or rates of abstinence.⁴ Compliance with NRT was highest for the patch and lowest for the inhaler. The inhaler was rated as the most embarrassing to use.

Adverse Effects/Caution

Mild localized irritation of the mouth or throat may occur, particularly during the early stages of use; symptoms are cough (27%), throat irritation (24%), pharyngitis (15%), stomatitis (15%) and rhinitis (8%). Systemic adverse effects include headache (26%), dyspepsia (14%), nausea (10%), and symptoms of withdrawal (3%). Symptoms of nicotine excess and withdrawal may overlap. More commonly, nicotine excess is associated with palpitations, nausea and sweating while withdrawal symptoms are associated with anxiety, nervousness and irritability.¹ Inhaled nicotine is an airway irritant and may cause bronchospasm; patches may be preferable for smokers with a history of severe airways reactivity.

While all forms of NRT can be used in patients with cardiovascular disease, they should be used with caution in patients who have had an acute coronary syndrome within the past 14 days, or serious arrhythmias.^{1,5}

Conclusions

All nicotine delivery systems (gum, patch, inhaler) appear similarly effective and no nicotine delivery system has been shown to be demonstrably superior to another. The nicotine inhaler represents the most expensive method of delivering nicotine, but may offer the advantage of having the patient performing a ritual similar to smoking. Patches may be preferable in patients with severe bronchospastic disease as the inhaler may cause direct airway irritation. Combination therapy (e.g. patch plus inhaler) could be considered for patients unable to quit smoking using a single NRT formulation. All nicotine products should be used in conjunction with a comprehensive behavioural smoking-cessation program.

References

1. Nicorette® inhaler product monograph, CPS 2006.
2. Silagy C et al. Nicotine replacement therapy for smoking cessation. Cochrane Database Syst Rev 2004;3:CD000146 (updated August 23, 2006)
3. Molyneux A. Nicotine replacement therapy. BMJ 2004;328:454-6.
4. Hajek P et al. Randomized comparative trial of nicotine polacrilex, a transdermal patch, nasal spray, and an inhaler. Arch Intern Med 1999;159:2033-8.
5. Anon. Guidance for health professionals on changes in the licensing arrangements for nicotine replacement therapy 2005. Available at: www.ash.org.uk/html/cessation/Smoking%20reduction/NRT051229.pdf

Pharmacy Awards

The Canadian Society of Hospital Pharmacists has awarded the following research awards to:

Nilu Partovi, in conjunction with Mary Ensom, Lillian Ting, Bob Levy, Wayne Riggs

- BC Branch Publication Award for their research paper "Limited sampling strategy for predicting area under the concentration-time curve of mycophenolic acid in adult lung transplant recipients".

Sean Gorman, Jane de Lemos, Harjinder Parwana, Richard Slavik, Lynne-Michelle Stewart

- Merck Frosst Rational Drug Use Award for their research paper "Feasibility of antibiotic short-course therapy for ventilator-associated pneumonia: FASTVAP".