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DRUG AND THERAPEUTICS NEWSLETTER

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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

Deletions

1. Framycetin gauze (Sofra-tulle®)
- Indefinite backorder
- Alternative: Chlorhexidine (Bactigras®) gauze dressing (available through Stores)

2. Tinzaparin injection (Innohep®)
- Alternatives: Dalteparin (Fragmin®) for prevention and treatment of deep vein thrombosis or pulmonary embolism; Enoxaparin (Lovenox®) for treatment of acute coronary syndromes
- See drug cost containment strategy, page 1

Updated Policies/Procedures

1. Further Drug Cost Containment Strategies

i) <u>Low Molecular Weight Heparins (LMWH)</u>

There are four LMWH for the prevention and treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) in Canada. In 2003, three of these drugs (enoxaparin, dalteparin, tinzaparin) were on formulary at the Vancouver Hospital sites. In the 2002/03 fiscal year, expenditures of these three LMWH were ~$245,000.

Due to the lower cost of dalteparin and data supporting an equivalent role of dalteparin and enoxaparin for DVT/PE management in a variety of settings, the following approach to the use of LMWH was implemented on January 20, 2004:

a) Dalteparin is now the low cost formulary LMWH for the prevention and treatment of DVT/PE and for management of non-acute coronary syndrome (non-ACS) indications (e.g. atrial fibrillation);
b) Enoxaparin is restricted to the management of ACS, i.e. unstable angina and non-ST-elevation myocardial infarction;
c) Tinzaparin has been deleted from formulary

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An annual drug acquisition cost avoidance of $60,000 is expected from this strategy.

ii) Amphotericin B Lipid-Based Formulations

Amphotericin B expenditures (conventional and lipid-based formulations) exceeded $800,000 at Vancouver Hospital in 2002/03 fiscal year making this agent the #1 anti-infective contributor to overall drug expenses.

In order to reduce the costs associated with the use of lipid-based amphotericin B formulations, pre-printed orders (PPO) have been created to ensure that conventional amphotericin B (Fungizone®, ~$50/day) is utilized first-line unless a "threshold creatinine clearance" is reached whereupon the lipid-based formulations (~$600-$1400/day) may be prescribed. These PPO were derived from a an in-house clinical trial in which a prescribing protocol guiding choice of amphotericin B formulation on a daily basis was found to reduce drug costs while preserving treatment outcomes.

There are two lipid-based formulations in Canada, Abelcet® and Ambisone®. These products are considered therapeutically equivalent. Abelcet® is considered to be the low cost alternative lipid formulation. Ambisone® is restricted by protocol for use in patients demonstrating severe infusion-related reactions to Abelcet®.

Effective January 20, 2004, new prescriptions for Abelcet® must be prescribed using a PPO. Four sets of PPOs for Abelcet® have been created according to specific patient groups: BMT/ Leukemia; Solid Organ Transplant (SOT); ICU (non-BMT, non-SOT patients); and balance of hospital (Table 1).

Table 1. Comparison of Abelcet® Pre-Printed Orders

Type of Patient	Creatinine Clearance Threshold
Leukemia/BMT	High Risk: 65 mL/minute Low Risk: 50 mL/minute
Solid Organ Transplant (SOT)	65 mL/minute
ICU*	30 mL/minute
Balance of Hospital**	30 mL/minute

*SOT and BMT patients in ICU will follow their respective protocols
**requires Infectious Diseases consult

An Infectious Diseases consult is required for Abelcet® for patients outside of the BMT/Leukemia, SOT and ICU settings. New prescriptions for conventional Amphotericin B do not require a PPO.

iii) Alteplase for Occluded Hemodialysis Catheters

Alteplase (tPA) is used to declot occluded central venous catheters. A modification to the existing hemodialysis catheter occlusion protocol was implemented January 20, 2004, whereupon the dose of alteplase was decreased from 2mg/catheter lumen to 1mg/lumen. This change was based on literature support and favourable experience at several hospitals across Canada. Alteplase is currently supplied to the renal unit in 1mL size syringes containing 1mg/mL. To instill the alteplase, 1mL (1mg) is added into each catheter lumen, followed by a volume of normal saline sufficient to fill the catheter volume plus 0.2mL. Alteplase is left *in situ* for either 1 hour or overnight until the next hemodialysis session, after which it is aspirated and then followed by a forceful 10mL saline flush. This change is expected to result in an annual drug cost avoidance of ~$35,000. Note that Pharmacy will still dispense alteplase in 1mg/mL - 2mL size syringes for non-hemodialysis-related central venous catheter occlusions.

iv) Modification to IV-PO Dosage Form Conversion: Ciprofloxacin

Our last newsletter (December 2003) outlines a pharmacist-managed intravenous (IV) to oral (PO) antibiotic conversion service that was implemented in November 2003. Through this service, clinical pharmacists were authorized to initiate step-down of various IV antimicrobials to PO therapy after 48 hours according to pre-established criteria. The IV-PO conversion for ciprofloxacin 400mg IV has been modified to include a PO dosage range of 500-750mg. This change is in recognition that a 400mg IV ciprofloxacin dose is equivalent to a 500mg oral dose of ciprofloxacin when area-under-the curve (AUC) is considered, and a 750mg oral dose when maximum serum concentration (Cpmax) is being compared. In clinical situations where a higher peak concentration of ciprofloxacin may be desired (e.g. management of infections involving difficult to penetrate tissues or fluids, or therapy against pathogens with intermediate susceptibility), the higher oral dose may be selected.

v) Antifibrinolytics in Cardiovascular Surgery

Antifibrinolytic drugs (aprotinin and tranexamic acid) are used to reduce excessive perioperative bleeding and minimize the need for blood transfusion with cardiac surgery. In the 2002/03 fiscal year, expenditures for these two drugs at Vancouver Hospital were ~$330,000. For a typical 4-hour procedure, tranexamic acid regimens cost $68-$113, while aprotinin regimens cost $504-$1008. Published clinical data support the use of tranexamic acid or low dose aprotinin regimens for many cardiac procedures. As such, modifications to the cardiac surgery pre-operative orders have been made to include a new risk-based antifibrinolytic protocol. For low or high risk patients, tranexamic acid is the preferred antifibrinolytic agent. Treatment options for very high risk patients or those undergoing thoraco-abdominal aortic aneurysm repair or aortic arch repair include either tranexamic acid, a low dose aprotinin regimen ("half Hammersmith", 1 million KIU, followed by 0.25 million KIU/hr) or a high dose aprotinin regimen ("full Hammersmith", 2 million KIU, followed by 0.5 million KIU/hr). An annual drug cost avoidance of ~$55,000 is expected from this strategy.

2. Automatic Stop Order Policy Revision

An automatic stop order takes effect if an order for a drug listed in Table 2 does not state the number of doses or days of therapy required. Physicians may override the automatic stop order policy by indicating a specific dose or time limit. The **maximum time limit** of 30 days has now been **extended to 6 weeks**. An exception to this policy is in the ECU and DPU where a maximum time limit of 90 days continues to exist.

Note that:

- All drug orders are automatically cancelled and must be re-written following surgery except for the following:
  a) diagnostic procedures which do not transgress the major body cavities;
  b) closed procedures done by means of catheter insertion;
  c) groin repair

For further detail, the full auto-stop policy is located in the Vancouver Hospital formulary, green section, page 17.

Table 2. Automatic Stop Orders For Drugs

Medication Category	Auto-Stop Time Limit
Restricted Antimicrobial Drugs (Ciprofloxacin IV, Cefotaxime, Ceftriaxone, Ceftazidime, Imipenem, Levofloxacin IV, Ticarcillin-Clavulanate)	3 days*
Narcotic and Controlled Drugs (except phenobarbital)	7 days
Anti-infectives (topical & systemic; TB drugs exempt)	7 days
Anticoagulants - oral	7 days
Inhalation solutions by nebulizer	7 days
Total Parenteral Nutrition (TPN)	7 days
Ophthalmic preparations except for glaucoma/lubrication	7 days
PRN orders other than those on the Routine Medication Order Form in the ECU & DPU	28 days

*7-day auto-stop for Bone Marrow Transplant & Medical Day Care Unit

Pharmacy Awards

The Canadian Society of Hospital Pharmacists (CSHP) has honoured various members of the Pharmaceutical Sciences CSU with the following awards:

- CSHP/Glaxo Smith Kline award for Pharmaceutical Care for the project: "Re-evaluation of the management of community-acquired pneumonia at a community hospital after implementation of a pre-printed order." **Vicki Wong**, Zahra Kanji, Rajesh Mainra, Michael Boldt.

- CSHP/Aventis award for Specialty Practice in Cardiology for the project: "A randomized trial of patient self-managed versus physician-managed oral anticoagulation." **Rubina Sunderji**, Ken Gin, **Karen Shalansky**, Cedric Carter, Keith Chambers, Cheryl Davies, Linda Schwartz, Anthony Fung.

Adverse Drug Reaction Report 2003

There were a total of 24 suspected adverse drug reactions (ADRs) reported at VH sites in 2003 (Table 1). Of note, 10 adverse reactions were considered to have been the cause of hospitalization and 3 resulted in prolonged 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 Pharmaceutical Sciences CSU, 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 1. Adverse Drug Reactions Reported in 2003

Drug	Suspected ADR	Drug	Suspected ADR
Allopurinol + IVIG	Toxic Epidermal Necrolysis (1)[a]	Erythropoietin	Seizures (1)
Atropine	Ventricular tachycardia (2)[a]	Fexofenadine/ Pseudoephedrine (Allegra D®)	PVCs and ventricular tachycardia (1)[a]
Azathioprine	Severe nausea/vomiting, abdominal pain, diarrhea (1)[a]	Iron Dextran (Infufer®)	Sternal pain, rash, severe itch (2)
Candesartan	Bronchospasm, dry cough (1)	Iron Sucrose (Venofer®)	Arthralgias, shortness of breath, sinus tachycardia (1)[a]
Cefazolin	Pruritis, shortness of breath and hypotension in previous penicillin skin test negative patient (1)	Methylprednisolone	Hiccoughs (2)
Colchicine	Proximal muscle weakness (1)[a]	Moxifloxacin + Quinine	Ventricular tachycardia (1)[a]
Cyclosporine (Neoral®)	Tonic-clonic seizure (1)[b]	Ranitidine	Thrombocytopenia (1)[a]
Darbepoetin	Leg weakness, myalgia (2)	Rosiglitazone	Bradycardia, biventricular failure (1)[a]
Drospirenone/ ethinyl estradiol (Yasmin®)	Deep Vein Thrombosis and Pulmonary Embolus (1)[a]	Simvastatin	Myositis (1)[b]
Eptifibatide	Pulmonary hemorrhage (1)[b]	Vancomycin + Gentamicin	Drug fever (1)

[a]hospitalized due to ADR ; [b]prolonged hospitalization due to ADR