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DRUG AND THERAPEUTICS NEWSLETTER

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Vancouver General Hospital, UBC Hospital, GF Strong

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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

Additions

1. Pregabalin capsules (Lyrica®)
- Anticonvulsant similar in structure and activity to gabapentin
- Approved for management of neuropathic pain and complex seizure disorders
- See page 3 for review

2. Risperidone long-acting depot injection (Risperdal Consta®)
- Antipsychotic depot drug used for management of schizophrenia and related psychotic disorders where relapse and/or non-compliance is present
- Added in response to new Pharmacare Special Authority coverage in order to support continuity of care and initiation in hospital setting
- Physician to complete a pre-printed order (PPO #642) & obtain Pharmacare Special Authority prior to initiation of therapy

Deletion

1. Penicillin GK 500,000 unit tablets
- Alternative: Penicillin VK 300mg

Updated Policies

1. PHARMACY-ADJUSTED VANCOMYCIN & AMINOGLYCOSIDE DOSING SERVICE

Effective June 11, 2007, **unit-based clinical pharmacists can independently write orders to change the dosage for intravenous (IV) aminoglycosides and vancomycin based on levels without prior physician consultation**. This is a revision to an existing policy (added section iii below).

Policy:

i. All patients with aminoglycoside and vancomycin serum drug concentration measurements will be reviewed by a clinical pharmacist from Monday to Friday.

ii. When necessary for monitoring or adjusting therapy in an individual patient, unit-based clinical pharmacists will order a serum drug level and/or serum creatinine for aminoglycoside or vancomycin therapy without prior consultation with a physician. The pharmacist will attempt, wherever possible, to incorporate measurements with other blood testing to avoid redundant venipunctures.

iii. Dose adjustments for aminoglycoside and vancomycin will be made independently by unit clinical pharmacists based on drug level interpretation and other patient

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 karen.shalansky@vch.ca

factors, including diagnosis, goals of therapy, clinical status, pharmacokinetic evaluation, and administration times.

iv. The pharmacist will document any dosage changes and drug level interpretations in the Physician's progress notes of the patient's chart.

2. ORAL MULTIVITAMIN ORDERING BY DIETICIANS

Effective immediately, **dieticians may independently order all formulary ORAL multiple vitamin preparations at VA without a physician order in the usual daily dose** (Table 1). Single entity vitamins and IV preparations must still be ordered by a physician.

Table 1. Multivitamins that may be ordered independently by a Dietician

Tablets	**Dose**
Multiple Vitamins (Multivites, Vitogen®)	1 tablet PO daily
Vitamins & Minerals (Centrum Forte®/Select®)	
Multiple Vitamins with Zinc (Z-Bec®)	
Vitamin B with C (Renavite®)	
Liquids*	
Infantol®	5-10mL PO daily

*Maltlevol®-12 must be ordered by a physician due to high alcohol content

Multivitamin supplements will be considered only if program patient care guidelines recommend a multivitamin supplement for a 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 multivitamins containing iron (i.e. Centrum Forte®/Select®) should not be ordered without prior consultation with a physician.

3. NEW NAUSEA & VOMITING ORDER SETS

Through input from the Departments of Anesthesia, Pharmacy and Nursing, the standard order set for the management of post-operative nausea and vomiting (PONV) at VA has been revised. Pharmacy is working with nursing and physicians to update pre-printed orders which contain PONV orders to change these to the new recommendations. Note that dolasetron is no longer recommended for management of PONV due to Health Canada concerns that dolasetron may cause life-threatening arrhythmias when used for this indication. At VA, ondansetron has replaced dolasetron for use in PONV as the 5-HT3 receptor antagonist in this class.

Both the order and dosage of antinauseant drugs have been updated as per below. 5-HT3 receptor antagonists are considered first-line as they have generally been found to be more effective than other agents. If a particular option fails to control PONV within 30 minutes, it is recommended to administer the next drug on the list.

Management of Post-Op Nausea and Vomiting

1. Ondansetron 1 to 4 mg IV Q8H PRN
   - 4 mg for nausea with emesis or retching; 1 mg for nausea with no emesis or retching
   - Inform physician if headache occurs

2. Metoclopramide 10 to 20 mg or 5 to 10 mg (if frail, elderly, weight < 50kg) IV Q6H PRN
   - Start at maximum dose in range; after 2 maximum doses, decrease to minimum dose in range
   - Avoid or D/C if GI bleed, bowel perforation, mechanical obstruction or extrapyramidal symptoms (e.g. dystonic reaction)

3. Dimenhydrinate 25 to 50 mg or 12.5 to 25 mg (if frail, elderly, weight < 50kg) IV Q6H PRN
   - Use maximum dose in selected range, unless significant sedation, delirium or confusion, then use minimum dose

4. Prochlorperazine 5 to 10 mg or 2.5 to 5 mg (if frail, elderly, weight < 50kg) IV Q6H PRN
   - Use maximum dose in selected range, unless significant sedation, delirium or confusion, then use minimum dose

New Drug/Drug Products

Pregabalin (Lyrica®)

Shari Pek B.Sc (Pharm), Bernie Leung B.Sc (Pharm), Eric Lun Pharm.D., Karen Shalansky Pharm.D.

Pregabalin has been added to formulary as an alternative to gabapentin for the management of neuropathic pain, complex seizure disorders, and for patients receiving this drug prior to hospital admission. Pregabalin is an anticonvulsant that is similar in structure and mechanism of action to gabapentin, but with differing pharmacokinetic and pharmacodynamic profiles.

Efficacy

Placebo-controlled trials have shown pregabalin to be effective in improving pain and quality of life in adult patients with diabetic peripheral neuropathy (DPN) and post-herpetic neuralgia (PHN). Response rates (≥ 50% reduction in pain) range from 40-48% (pregabalin) vs 15-18% (placebo) for PDN[1-3] and 26-52% vs 10-24% for PHN[4,5]. There are no head-to-head trials comparing pregabalin to gabapentin and most trials exclude enrolment of patients who have already failed on therapeutic doses of gabapentin.

Comparison to Gabapentin

The main differences between pregabalin and gabapentin are its more predictable absorption and faster onset of action, allowing for more rapid dose titration (Table 2). Because pregabalin does not require a carrier protein for transport, drug absorption after oral administration is more reliable and linear than that of gabapentin. A typical titration phase to target dose for pregablin is 2-3 weeks compared to 4-8 weeks or more with gabapentin. Side effect profiles of pregabalin and gabapentin are similar and include dizziness, drowsiness, peripheral edema, weight gain, blurred vision, and dry mouth. Pregabalin costs approximately twice that of gabapentin and is not a Pharmacare benefit.

Conclusions

There is lack of direct evidence to suggest that pregabalin offers any distinct advantages over gabapentin. However, clinical experience indicates that pregabalin is easier to use for pain management of DPN and PHN due to its more predictable dose response permitting easier and faster dose titration. The significant cost disadvantage of pregabalin and its lack of BC Pharmacare coverage needs to be considered when prescribing this medication.

Table 2. Comparison of Pregabalin and Gabapentin[6]

	Gabapentin	Pregabalin
Chemistry	Analogue of GABA	Substituted analogue of gabapentin
Absorption	Saturable	Non-Saturable
Bioavailability	60% - 300mg 35% - 1600mg	90%
Onset of Action	≥ 9 days	1-3 days
Efficacy: **Pain Control** **QOL**	 Similar Similar	 Similar Similar
Adverse Effects	Similar	Similar
Renal Elimination (Half-Life)	70-80% (5-7 hours)	90-99% (5-7 hours)
Dose* (Normal Renal Function)	300mg po TID; ↑ Qweek as tolerated to maximum 3600mg/day	75mg po BID; ↑ every 3-7 days as tolerated to maximum 600mg/day
Pharmacare Coverage	Yes (generic)	No

QOL = Quality of Life
*Doses of both pregabalin and gabapentin must be reduced for GFR < 60 mL/minute

References

1. Lesser H et al. Pregabalin relieves symptoms of painful diabetic neuropathy: a randomized controlled trial. Neurology 2005;63:2104-10.
2. Rosenstock J et al. Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo controlled trial. Pain 2004;110:628-38.
3. Richter RW et al. Relief of painful diabetic neuropathy with pregabalin: a randomized, placebo-controlled trial. J Pain 2005;6:253-60.
4. Sabatowski R et al. Pregabalin reduces pain and improves sleep and mood disturbances in patients with post-herpetic neuralgia: results of a randomized, placebo-controlled clinical trial. Pain 2004;109:26-35.
5. Frampton JE et al. Pregabalin: in the treatment of postherpetic neuralgia. Drugs 2005;65:111-8.
6. Clinical Pharmacology on-line resource: (www.clinicalpharmacology.com (accessed May 2007)

Adverse Drug Reaction Report 2006

There were 15 suspected adverse drug reactions (ADR) reported at VGH in 2006 (Table 3). Of these, 4 were considered to have been the cause of hospitalization. To notify Pharmacy of an ADR, call local 62481 (VGH site) or local 27249 (UBC site). Pharmacists will complete all ADR report forms and forward copies to the Canadian Adverse Drug Reaction Monitoring Program.

Table 3. Adverse Drug Reactions Reported in 2006

Drug	Suspected Reaction
Acetazolamide	Decreased level of consciousness (resulted in hospitalization)
Allopurinol	Maculopapular rash on ~90% of body surface area (resulted in hospitalization)
Cefuroxime	Pseudomembranous colitis
Gabapentin	Elevated liver function tests
Hydroxyzine	Leg Twitching
Iron Dextran test dose	SOB, throat swelling, skin erythema
Iron Gluconate (Ferrlecit®)	Hypotension, seizure
Iron Sucrose	Hand swelling, severe pain, burning (1); back and abdominal pain, N/V (1); nausea, indigestion, belching (1); swelling of ankles and left hand, burning calves (1)
Metformin	Lactic acidosis, hypoglycemia (resulted in hospitalization)
Pregabalin	Pulmonary embolism (resulted in hospitalization)
Quetiapine, Bupropion	Elevated liver function tests
Ranitidine	gynecomastia

Pharmacy Awards

1. *Addendum to last newsletter*: The study "Feasibility of antibiotic short-course therapy for ventilator-associated pneumonia: FASTVAP" won the national Merck Frosst Rational Drug Use Award for 2006. The complete list of authors was not included in the March 2007 newsletter. The authors for this study are:

- **Lynne-Michelle Stewart, Sean Gorman, Richard Slavik**, **Jane de Lemos**, Vinay Dhingra, Dean Chittock, Juan Ronco, **Harjinder Parwana**

2. The VGH ICU team won one of six 2007 BC Patient Safety Awards for their project "Improving Quality of Sedation in the ICU". The authors of this project are:

- **Jane de Lemos**, Dean Chittock, Denise Foster (with support from the ICU team)