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Changes to Formulary

In order to align with the BCHA Formulary, the following medications have been added to formulary and are stocked at Vancouver Acute. A list of BCHA P&T approved deletions follows. For further information, see Formulary Update (page 4).

Additions

1. **Perindopril 2 mg, 4 mg, 8 mg tablets (Coversyl®)**
 - Angiotensin-converting enzyme inhibitor (ACEI)
 - Note that all ACEIs other than ramipril, perindopril and captopril are therapeutically interchanged to trandolapril.
2. **Montelukast 10 mg tablets (Singulair®)**
 - Leukotriene modifier for use in asthma
3. **Oxybutynin 5 mg long-acting tablets (Ditropan XL®)**
 - Genitourinary smooth muscle relaxant

4. **Tolterodine 2 mg tablets (Detrol®)**
 - Genitourinary smooth muscle relaxant
5. **Sodium Chloride 1 g capsules**
6. **Insulin Lispro 100 units/mL injection (Humalog®)**
 - Rapid-acting insulin
 - See Therapeutic Interchange of all rapid-acting insulins to Insulin Lispro (page 3).
7. **Bumetanide 1 mg, 5 mg tabs (Burinex®)**
 - Loop diuretic indicated for treatment of edema
 - Bumetanide 1 mg produces a diuretic response similar to furosemide 40 mg; although bumetanide and furosemide are both sulfonamide derivatives, bumetanide does not appear to exhibit cross-sensitivity to patients allergic to furosemide.
8. **Indapamide 1.25 mg, 2.5 mg tabs (Lozol®)**
 - Thiazide-type diuretic
9. **Oxycodone 10 mg, 20 mg, 40 mg, 80 mg long-acting tablets (OxyNeo®)**
 - OxyNeo® has replaced Oxycontin® in Canada. To prevent abuse potential, the OxyNeo® formulation is harder to cut, chew, break, or crush, and if dissolved in liquid, forms a viscous gel which cannot be injected or snorted. More details on page 4.
 - OxyNeo® 5 mg long-acting tablets are also not available. See Therapeutic Interchange Policy (page 4).

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10. Dabigatran 75 mg, 110 mg, 150 mg capsules (Pradax[®])

- Oral anticoagulant restricted to patients on this medication prior to admission
- As opposed to warfarin, dabigatran does not require any coagulation monitoring (e.g. INR); however, it is contraindicated in patients with eGFR less than 30 mL/minute.
- See page 6 for oral anticoagulants comparison chart.

11. Levocarnitine 330 mg tablet, 1 g injection (Carnitor[®])

- Restricted to metabolic disorders

12. Citrulline enteral powder

- Used in management of metabolic disorders

13. L-arginine 250 mg/mL injection and powder

- Used in management of metabolic disorders

14. Loratadine 10 mg tablets (Claritin[®])

- Second-generation long-acting histamine-1 receptor antagonist used for seasonal allergic rhinitis or chronic urticaria
- To replace fexofenadine (Allegra[®])
- See Therapeutic Interchange of all second generation antihistamines to loratadine (page 3).

15. Cyproheptadine 4 mg tablets (Periactin[®])

- First-generation histamine-1 receptor antagonist

16. Escitalopram 10 mg, 20 mg tabs (Ciprallex[®])

- Antidepressant; selective serotonin reuptake inhibitor
- S-enantiomer of citalopram
- Restricted to patients on this medication prior to admission.

17. Collagenase 250 units/g ointment (Santyl[®])

- Topical debridement agent restricted to debridement of dermal ulcers

18. Indigotindisulfonate sodium 40 mg/5 mL injection (Indigo Carmine[®])

- Diagnostic agent for kidney function

19. Patent blue 50 mg/2 mL injection

- Diagnostic dye indicator

20. Pinaverium 50 mg tablets (Dicetel[®])

- GI tract calcium channel blocker used for relief of symptoms of irritable bowel syndrome

21. Nicotine 2 mg, 4 mg lozenges (Nicorette[®])

- Nicotine lozenge to aid in smoking cessation

22. Salmeterol 50 mcg diskhaler (Serevent[®])

- Long-acting beta-2 agonist inhaler for use in asthma

23. Budesonide 3 mg capsules (Entocort[®])

- Corticosteroid, anti-inflammatory agent for use in Crohn's disease

23. Posaconazole 40 mg/mL suspension (Posanol[®])

- Antifungal antibiotic
- Restricted to the prophylaxis or treatment of invasive fungal infections in patients 13 years or older who can tolerate a full fat meal **and** as indicated below:

1. Prophylaxis:

- a. Neutropenic patients, where neutropenia is present for 10 days or longer plus one of the following:
 - colonized with *Aspergillus* species, and/or receiving corticosteroids greater than 1 mg/kg/day
 - AML or MDS receiving induction chemotherapy
 - Acute Lymphocytic Leukemia
 - Burkitt's Lymphoma

- b. Allogeneic stem cell transplant patients with steroid-refractory GVHD treated with intensive immunosuppressive therapy

2. Treatment of invasive fungal infections, including zygomycetes, in L/BMT patients for the following situations:

- a. intolerant **or** resistant to other appropriate antifungals (e.g. amphotericin B, voriconazole, itraconazole, micafungin) **OR**
- b. where oral step down therapy is appropriate and cost effective

24. Desmopressin 0.1 mg tablets (DDAVP)

- Vasopressin oral analogue used for treatment of central diabetes insipidus

25. Acarbose 50 mg tablets (Prandase[®])

- Oral antidiabetic agent; inhibits breakdown of di- and poly-saccharides in the intestine

26. Benzylpenicilloyl polylysine 6 x 10⁻⁵ Molar injection (Pre-Pen[®])

- Major determinant mixture to be used as part of the penicillin skin test procedure

Deletions

1. **Cafergot[®] tablets (ergotamine/caffeine)**
2. **Varenicline tablets (Champix[®])**
3. **Danazol capsules (Cyclomen[®])**
4. **Chloroprocaine 2% injection (Nesacaine[®])**
 - Discontinued by manufacturer
 - There are no ester-type local anesthetics for injection available in Canada. See page 4 for recommendations for suspected allergy to local anesthetics.
5. **Tetracaine injection (Pontocaine[®])**
 - Discontinued by manufacturer
6. **Prilocaine 4% dental cartridge (Citanest[®])**
7. **Fexofenadine tablets (Allegra[®])**
 - Alternative: Loratadine 10 mg tablet (Claritin[®])
 - See Therapeutic Interchange of fexofenadine to loratadine (page 3).
8. **Trimeprazine tablets (Pancetyl[®])**
 - Alternatives: diphenhydramine (Benadryl[®]), hydroxyzine (Atarax[®])
9. **Actifed[®] tablets (triprolidine 2.5 mg/ pseudoephedrine 60 mg)**
 - Alternatives: diphenhydramine or hydroxyzine plus pseudoephedrine as individual agents
10. **Ipratropium nasal spray (Atrovent[®])**
11. **Salbutamol tablets (Ventolin[®])**
 - Alternative: salbutamol inhaler
12. **Terbutaline inhaler (Bricanyl[®])**
 - Alternatives: salbutamol inhaler (Ventolin[®]), formoterol turbuhaler (Oxeze[®])
13. **Methylprednisolone tablets (Medrol[®])**
 - Alternatives: prednisone, dexamethasone
14. **Chlorpropamide tablets (Diabinese[®])**
 - Alternatives: glyburide, gliclazide
15. **Testosterone Cyprionate injection (Depo-Testosterone[®])**
16. **Estradiol transdermal patches (Estraderm[®], Estradot[®])**

17. Insulin Aspart injection (Novorapid[®])

- Alternative: Insulin Lispro
- see Therapeutic Interchange Policy of short-acting insulins to Insulin Lispro (page 3)

Updated Policies

1. AUTOMATIC STOP DATE POLICY UPDATE

- Oral anticoagulants (e.g. warfarin, rivaroxaban, dabigatran) no longer have a 7-day stop date.
- For Residential Care Units, topical steroid creams, ointments and lotions have a stop-date of 28 days.

2. INSULIN LISPRO THERAPEUTIC INTERCHANGE POLICY

Insulin Lispro is the rapid-acting insulin product added to formulary that has replaced Insulin Aspart. Starting July 30, 2012, all orders for rapid-acting insulins will be converted 1:1 to Insulin Lispro as per Table 1.

Table 1. Therapeutic Interchange of Rapid-acting Insulins to Insulin Lispro

Drug Ordered	Drug Dispensed
Insulin Glulisine	Insulin Lispro - same number of units and frequency
Insulin Aspart	

3. LORATADINE THERAPEUTIC INTERCHANGE POLICY

Loratadine is the long-acting second-generation histamine-1 antagonist added to formulary that has replaced fexofenadine. All orders for second-generation antihistamines are now interchanged to loratadine 10 mg daily as per Table 2.

Table 2. Therapeutic Interchange of Second-generation Antihistamines to Loratadine

Drug Ordered	Drug Dispensed
Cetirizine any dose	Loratadine 10 mg PO daily
Desloratadine any dose	
Fexofenadine any dose	

4. OXYNEO® ADMINISTRATION AND 5 MG TABLET THERAPEUTIC INTERCHANGE

OxyNeo® is the only long-acting oxycodone preparation available in Canada. OxyNeo® is bioequivalent to Oxycontin®, but unlike Oxycontin®, the tablets are formulated such that they are harder to cut, chew, break or crush to prevent abuse potential. If dissolved in water, the tablets form a viscous gel. OxyNeo® **should be swallowed whole and taken with enough water** to ensure complete swallowing, immediately after placing in the mouth. Patients should not pre-soak, lick, or otherwise wet the tablet prior to ingestion. OxyNeo® must not be administered via any feeding tube as it may cause obstruction.

Also, unlike Oxycontin®, OxyNeo® is not available in a 5 mg strength. All orders for oxycodone 5 mg long-acting tablets will be therapeutically interchanged to oxycodone immediate release tablets according to Table 3.

Table 3. Therapeutic Interchange of Oxycodone 5 mg Long-acting Tablets

Drug Ordered	Drug Dispensed
Oxycodone long-acting 5 mg PO daily	Oxycodone immediate release 2.5 mg PO BID
Oxycodone long-acting 5 mg PO BID	Oxycodone immediate release 2.5 mg PO QID
Oxycodone long-acting 5 mg PO TID	Contact Prescriber

5. ALLERGY TO LOCAL ANESTHETICS

There are two chemically distinct groups of local anesthetics (LA): ester-type and amide-type. With the recent discontinuation of chlorprocaine and tetracaine, there are no longer any injectable ester-type LA products available in Canada. Historically, the option for those reporting an allergy to an amide-type of LA would be to give an agent from the ester group, and vice versa.

Most LA allergies are not true allergies but adverse effects or anxiety-related. Epinephrine, present in some LA products, may be inadvertently introduced into the blood resulting in tachycardia and/or palpitations. The presence of preservatives and/or latex may also cause adverse reactions. True hypersensitivity to LA products are rare. Skin testing is almost always negative.

If a patient reports an allergy to an amide-type LA, then a different amide-type local anesthetic may be trialed. The risk of cross-sensitivity is considered very low. Using an epinephrine-free and preservative-free product, if available and appropriate for the indication, is preferable.

Adapted from VIHA Medication Posting June 19, 2012 and Sunnybrook Health Centre Allergy to Local Anesthetics Update 2006.

6. FORMULARY UPDATE AND BCHA FORMULARY ALIGNMENT

The British Columbia Health Authorities (BCHA) Pharmacy and Therapeutics (P&T) Committee was created in 2009 with the mandate to create a single provincial Health Authority (HA) Formulary applicable to all hospitals across BC. The objective is for all patients in BC to have the same access to medications regardless of which HA delivers their care.

Under the BCHA Formulary Alignment Initiative, a provincial formulary list was finalized and approved by the BCHA P&T Committee in the fall of 2011.

Between April 2012 and June 2013, the BCHA Formulary will be implemented at hospitals throughout the province. This means that the existing VA formulary will be transitioned to the new BCHA Formulary.

The 2012 edition of our printed formulary is now available on all nursing units and reflects BCHA changes made to the VA formulary up to April 2012. Note that the printed version lists only formulary medications that will be stocked (inventoried) at VA (VGH, UBC, GF Strong). Other BCHA formulary medications with negligible or no use at VA (e.g. pediatric, obstetric, oncology medications) are not included. For a more comprehensive list of all BCHA formulary drugs added to date, please refer to the on-line formulary. The on-line formulary will have the notation "not stocked" for formulary agents that are not inventoried at VA. However, any formulary medication (even if not stocked) will be supplied by pharmacy if prescribed.

Two new charts have been added to the Therapeutic Tools section of the formulary: "Antibiotic Cross-Sensitivity Chart" and "New Oral Anticoagulants Comparison Chart".

7. FLUTICASONE INHALER THERAPEUTIC INTERCHANGE POLICY

Fluticasone MDI inhaler and budesonide turbuhaler remain the corticosteroid inhalers on formulary. Other corticosteroid MDI inhalers: beclomethasone (QVAR[®]) and ciclesonide (Alvesco[®]) will be therapeutically interchanged to fluticasone (Flovent[®]) MDI inhaler at an equivalent dose as per Table 5.

Table 5. Therapeutic Interchange of Steroid MDI Inhalers to Fluticasone

Drug Ordered	Drug Dispensed
Beclomethasone 100 mcg (QVAR [®])	Fluticasone 125 mcg (same number of puffs & frequency)
Ciclesonide 200 mcg once daily	Fluticasone 125 mcg BID
Ciclesonide 400 mcg once daily	Fluticasone 250 mcg BID
Ciclesonide 400 mcg BID	Fluticasone 500 mcg BID

8. COUNTERSIGNATURE ON THERAPEUTIC INTERCHANGES NO LONGER REQUIRED

The Prescriber's countersignature on all Therapeutic Interchanges (TIPs) and Prescription Interpretations (PIPs) are no longer required. All TIPs and PIPs will eventually be modified to show a requirement for a Pharmacist's signature, printed name, and college ID only.

9. PDTM UPDATES

- **Abciximab infusions** may be administered by nurses in NICU for management of an acute thromboembolic event complicating cerebral aneurysm coil embolization.
- **ECG monitoring is no longer required for administration of droperidol IV** when used for management of PONV in the lower recommended dose of 0.625-1.25 mg IV. A 12-lead ECG may be considered for patients at increased risk of prolonged QTc interval (e.g. electrolyte abnormalities including hypokalemia and hypomagnesemia; receipt of concurrent medication that prolong the QT interval; liver function impairment).
- The dosage section for fluconazole has been revised to reflect the most current guidelines for management of candidal infections and cryptococcal meningitis.

10. ONDANSETRON HIGH DOSE WARNING

The manufacturer of ondansetron (Zofran[®] - GlaxoSmithKline) has conducted an in-depth study on the effects of ondansetron on the QT interval. Preliminary results suggest that a single dose of ondansetron 32 mg IV may prolong the QT interval, which could predispose patients to development of *torasade de pointes*. Patients most at risk include those with congenital long QT syndrome, heart failure, bradyarrhythmias, electrolyte abnormalities (ie. hypokalemia, hypomagnesemia), and concomitant use of other QT-prolonging medications. The manufacturer will revise the ondansetron monograph to remove the 32 mg single IV dose, and specify that no single IV dose should exceed 16 mg.

Reference

Lexicomp on-line: Special Alerts, QT Prolongation with Ondansetron June 2012.

Pharmacy Awards

The *Clostridium difficile* Infection (CDI) Quality Assurance Initiative Project was awarded an Excellence in BC Health Care Collaborative Solutions Award of Merit by the Health Employers Association of BC.

The CDI project is a collaborative effort between Pharmacy, Infection Control, and Infectious Diseases at VGH, which aims to optimize the management of patients diagnosed with CDI. This Quality Assurance Initiative entails all patients to be followed by ward-based clinical pharmacists who intervene, as necessary, to enhance CDI treatments. The initiative resulted in improved treatment of CDI – effective treatment of patients increased from 9% to 69% - and shortened the length of hospital stays from 50 to 32 days. Overall, this ongoing initiative helped to improve patient health outcomes, while reducing complications and mortality.

This award represents an outstanding achievement for our clinical pharmacists and infection control practitioners, and demonstrates the high level of care that we offer our patients. This also shows the successes of a multi-disciplinary health care team partnership between Pharmacy, Infection Control, and Infectious Diseases.

Table 6. Warfarin and New Oral Anticoagulants Comparison Chart

Drug	Warfarin (Coumadin®)	Dabigatran ¹ (Pradax®)	Rivaroxaban ² (Xarelto®)	Apixaban ³ (Eliquis®)
Indications/Dose⁴ <u>Orthopedic Prophylaxis</u>	Dosing based on target INR 1.5-2.3	220 mg daily or 150 mg daily ⁵ TKR x 10 days THR x 28-35 days	10 mg daily TKR x 14 days THR x 35 days	2.5 mg BID TKR x 10-14 days THR x 32-38 days
<u>Stroke Prevention in Atrial Fibrillation</u>	Dosing based on target INR 2-3	150 mg BID or 110 mg BID ⁶	20 mg daily with food or 15 mg daily with food ⁷	-
<u>VTE Treatment</u>	Dosing based on target INR 2-3	-	15 mg BID x 3 wks, then 20 mg daily with food	-
Target Inhibition	Vitamin K epoxide reductase complex	Factor IIa (Thrombin)	Factor Xa	Factor Xa
Monitoring	INR	Not needed	Not needed	Not needed
Oral Bioavailability	99%	6-7%	66-100%	50%
Peak Onset	36-72 hours ⁸	2 hours	2-4 hours	3-4 hours
Half-life	20-60 hours	14-17 hours	9-13 hours	8-15 hours
Elimination	Hepatic (Cytochrome P450)	80% renal, 20% biliary	66% renal (36% unchanged), 33% biliary	27% renal, 73% biliary
Adjust Dose for Renal Failure	No	YES (contraindicated if eGFR < 30 mL/min)	YES (contraindicated if eGFR < 30 mL/min)	YES (contraindicated if eGFR < 15 mL/min)
CYP Metabolism	YES - CYP 2C9, 1A2, 3A4, 2C19	NO	YES - 30% CYP3A4	YES - 15% CYP3A4
P-glycoprotein Substrate	No	Yes	Yes	Yes
When to Hold Dose Prior to Surgery	5 days	<u>eGFR 50 mL/min or greater</u> Minor surgery: 1 day Major surgery: 3 days <u>eGFR 30-49 mL/min</u> Minor surgery: 2-3 days Major surgery: 4 days	Minor surgery: 1 day Major surgery: 2 days	

¹ Dabigatran is formulary restricted to patients on this medication prior to admission

² Rivaroxaban is formulary restricted to orthopedic prophylaxis only

³ Apixaban is a non-formulary drug

⁴ Approved indications in Canada

⁵ eGFR 30-50 mL/min, dabigatran dose for orthopedic prophylaxis = 150 mg daily

⁶ eGFR 30-50 mL/min and patient 75 years or greater + risk factors for bleeding, consider dabigatran 110 mg BID for stroke prevention in atrial fibrillation

⁷ eGFR 30-50 mL/min, rivaroxaban dose for stroke prevention = 15 mg daily

⁸ Full antithrombotic effect delayed for 72-96 hours after initiation

TKR = Total Knee Replacement; THR = Total Hip Replacement; VTE = Venous Thromboembolism; CYP = Cytochrome P450