

# Pharmacy Informer

Children's and Women's Health Centre of BC, Department of Pharmacy

Winter 2015

## Updates from C&W Pharmacy, Therapeutics and Nutrition (PT&N) Committee

Jennifer Kendrick, BScPharm, PharmD

**The C&W PT&N Committee has been busy in 2014. The Committee serves as the Pediatric Subcommittee to the Provincial Pharmacy and Therapeutics Committee. We continue to have representation from other Health Authorities, in addition to our membership from C&W.**

### 1. Policies & Procedures:

The following policies & procedures have been approved and are being posted on the C&W intranet:

**High Alert Medications** list updated to include parenteral nutrition

**Hazardous Drugs Handling Policy**

**Intranasal Fentanyl** approved for use in Medical Day Unit

**Inhaled Nitrous Oxide** approved for use in Orthopedic Clinic

**BCCH Empiric Antibiotic Guidelines** updated for 2014

**Women's Hospital Patient Controlled Analgesia and Epidural Analgesia**

### 2. Additions to Formulary:

The following medications have been added to formulary at C&W:

**Isopropyl myristate/cyclomethicone (Resultz®):** an alternate pediculicide to permethrin (Nix®), for the treatment of resistant head lice. The manufacturer's application instructions should be followed, as they differ between products.

**Cetirizine:** an alternative second generation antihistamine to loratadine. While there is no compelling evidence that any antihistamine provides a significant clinical advantage over another, there may be interpatient variability in response. Cetirizine is more sedating than loratadine but may have a faster onset.

**Florababy® probiotic** (bifidobacterium and lactobacillus strains) has been added to formulary for the prevention of necrotizing enterocolitis in select preterm newborns. The Neonatal ICU has developed guidelines and a protocol for its use.

### 3. Medication Backorders:

We continue to face shortages of a substantial number of medications, anticipated to continue for the coming weeks and months due to problems with active pharmaceutical ingredients and manufacturing challenges. The Pharmacy Department continues to monitor supplies and usage. We are reviewing all affected medications in a systematic fashion in order to minimize the impact on direct patient care.

We appreciate all the assistance in reviewing options to mitigate the shortages (using oral/rectal routes, changing to alternative medications, changing to other brands and strengths, etc).

Be aware that some of the changes can arise from acute, unanticipated shortage and staff should be mindful of the potential for medication errors as any changes are considered or implemented.

### 4. Pre-printed Orders:

The C&W PT&N Committee has been busy approving pre-printed orders as part of the Clinical Systems Transformation in addition to our C&W-specific pre-printed orders. The following C&W pre-printed orders have been approved in the past year:

**Acute Kidney Rejection**

**Appendicitis Preoperative (Pediatric) and Appendicitis Postoperative (Pediatric)**

**Burn Bath Sedation and Analgesia**

**C Difficile (Adult) and C Difficile (Pediatric)**

**Fever and Neutropenia: Stable Patient**

**Eating Disorder Admission**

**Group B Streptococcus Prophylaxis: Intrapartum**

**HIV Postpartum and HIV Intrapartum and HIV Infant of HIV Infected Mother**

**Intravenous Immune Globulin (IVIG) Infusion**

**Inpatient Asthma**

**Lumbar Puncture Oral Sedation**

**Transfer to Clinical Decision Unit**

**Women's Hospital Post Anesthesia Care Unit**

**Women's Hospital Critical Hyperbilirubinemia Admission**

**Women's Hospital Fever in Labour**

**Women's Hospital Induction of Labor – Prostaglandin**

**Women's Hospital Oxytocin for Labor Augmentation**

**Women's Hospital Postpartum Prophylaxis: Newborns at Risk of Sepsis**

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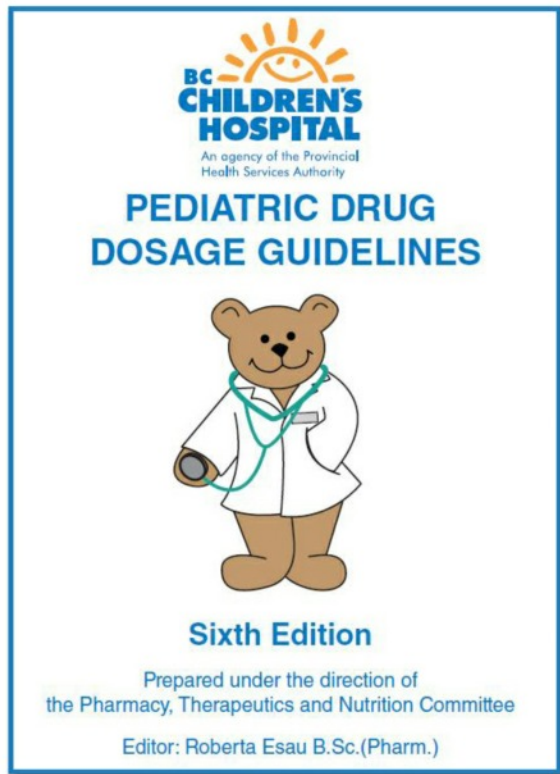
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The following monographs in the C&W Pediatric Drug Dosing Guidelines have been updated:

- **ampicillin** pneumonia added to list of serious infections
- **cephalexin** dosing updated and Q12H option removed
- **chloral hydrate** procedural sedation dose updated
- **fomepizole** is a new monograph that has been added
- **oseltamivir** dosing updated
- **piperacillin/tazobactam** dosing frequency changed to Q6H
- **vancomycin** update to C difficile dosing
- **voriconazole** dosing updated for children under 12 years and added information about therapeutic drug monitoring

Please update your paper copies. The updated versions of the monographs can be found on the C&W Intranet or on the internet at [www.pedmed.org](http://www.pedmed.org) (this site is still being piloted - your feedback to our [survey](#) on this resource would be appreciated).



Dr Nelson's Improved Inhaler, New Orleans Pharmacy Museum, New Orleans, LA. Photo: Dean Elbe

## Useful Online Medication Resources

Dean Elbe, BScPharm, PharmD, BCPP



Know a young person taking one or more medications regularly and who is experimenting with substance use? Help them **Get the Facts** about the risks of mixing medicine, booze and street drugs with the new, first-of-its-kind, dedicated website [DrugCocktails.ca](http://DrugCocktails.ca) which was developed by the professionals right here at BC Children's.

Launched in September 2013, this free site is an update of the beloved print resource "Cocktails" first published in 2002. The site is easily searchable by brand or generic medication name for over 235 different prescription and over-the-counter medications commonly used by youth. It will even help with the spelling of the medication names. Personal information is *never* collected from youth who use the site.

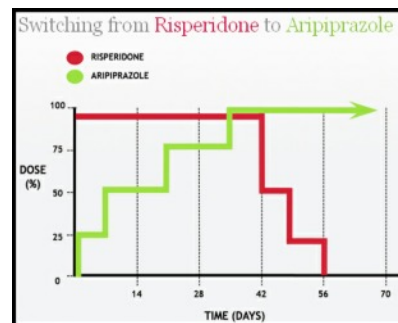
Inside, potential risks of mixing each of 10 different classes of substances (e.g. alcohol, cannabis, opioids, cocaine and more) with the chosen medication are listed in youth-friendly language, all presented in a clean, easy-to-use interface. Many of the ever-changing list of substance nicknames are included, along with information about the health risks of using various substances (provided courtesy of the Centre for Addictions Research of BC). Best of all, a professional version is available, [DrugCocktails.ca/pro](http://DrugCocktails.ca/pro) (requires FREE one-time registration) which includes robust clinical details of the interactions, with full references to medical literature.



For many years, the task of switching between antipsychotic drugs when lack of response or intolerable adverse effects occur has been a challenge for clinicians, with a multitude of proposed switch strategies documented in the literature. With more available antipsychotic drugs than ever, each with slightly different receptor affinities, pharmacokinetics and pharmacological effects, some guidance is welcome.

Enter [SwitchRx.ca](http://SwitchRx.ca). This free online tool was developed with the goal of providing accessible and up-to-date guidance to prescribers in the optimal transition of patients between antipsychotic drugs. Content is based on published evidence (where available) and the collective expertise of a panel of Canadian psychiatry and psychopharmacology experts. Pharmaceutical industry sponsor involvement was limited to reviewing the accuracy of the information. Funding for site development was provided via unrestricted educational grants.

Suggested time frames, dose (percentage) increments or decrements and potential clinical effects that may result from differences in receptor affinities between drugs is presented in an easy to understand graphical format.



## Medications and Peanut Allergy

Sonia Jeffries, BScPharm, ACPR  
edited by Karen Ng BScPharm, PharmD, BCPS

The [January 2013 issue of the Canadian Adverse Reaction Newsletter](#) presented a case where a 7-year-old child experienced an anaphylactic reaction minutes after receiving Cerumol® (active ingredients: arachis oil and chlorobutanol) ear drops to loosen ear wax, and was subsequently treated in the emergency room.[1] She had a known peanut allergy but her caregivers were unaware of the warning on the box that the product contained peanut oil.

This case serves as a good reminder of the importance of checking not only the medicinal, but also the non-medicinal ingredients and allergy warnings contained in prescription, non-prescription, and natural health products including topical preparations when a patient has an allergy. Reading labels carefully is especially important as medications with the same or similar brand names may contain different ingredients as they may be produced by different manufacturers, different varieties and sizes of the same brand may contain different ingredients, and manufacturers occasionally change the ingredients in products.[2]

### Peanut and Soy Allergy

Peanut and soy are both legumes that are phylogenetically and antigenically similar to each other.[3] While peanut-allergic individuals have been found to have extensive IgE binding to other legumes, including soy, clinical observations of co-reactivity to peanut and soy may be as low as 0.8% to 6.5%.[3] Many peanut-allergic individuals are able to safely eat soy products and vice-versa. Soy allergies are far less commonly responsible for anaphylaxis and life-threatening reactions compared to peanut allergies. Soy products used in medications, such as soy lecithin or soybean oil, are rarely a problem for peanut-allergic patients as both products contain a very small amount of soy protein (if any).[4]

Drug products that contain peanut oil (may be stated as "arachis oil" on labels) include:[4-6]

- Contraindicated in patients with peanut allergy:
  - Cerumol® ear drops (chlorobutanol otic) as described in the case above
  - Prometrium® capsules (progesterone)
  - Oily Calamine lotion (oily formulation only)
  - Sustanon 250 (testosterone) solution for injection
- Use with caution in patients with peanut allergy
  - Derma-Smothe/FS®, DermOtic® (fluocinolone topical oils)
  - BAL in oil (dimercaprol injection)

Drug products containing soy include:[4,7]

- Propofol (oil in water emulsion containing soybean oil)
- Isotretinoin (various brands)
- Vimpat® (lacosamide) film-coated tablets
- Atrovent® (ipratropium) inhalers previously contained soy lecithin; however the current formulation does not contain soy lecithin and is NOT contraindicated in patients with peanut or soy allergy.
- Combivent® (ipratropium/salbutamol) metered-dose inhalers used to contain soy lecithin, but are no longer available in Canada.
- Ipratropium nasal spray and solution for nebulization do not contain soy lecithin.
- Many other medications contain soy in the form of soybean oil or soy lecithin; an extensive list will not be provided here. The allergic potential for these ingredients, as mentioned above, is extremely low, but may affect specific patients.

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## Health Canada Advisories

Jennifer Kendrick, BScPharm, PharmD

Two new Health Canada advisories were released in January 2015:

1. [Risk of extrapyramidal adverse effects of metoclopramide in children.](#)

The manufacturers have recommended that metoclopramide be contraindicated in children less than one year of age and that the maximum daily dose for children older than one year of age be revised downward to 0.5 mg/kg/day.

2. [Risk of ventricular arrhythmias with domperidone.](#)

This was an update to a previous advisory warning that patients over 60 years, using daily doses greater than 30 mg, or having predisposing factors for QT prolongation were at a small increased risk of ventricular arrhythmias with domperidone. In the past 30 years, Health Canada has received 19 reports of cardiac events associated with domperidone. The manufacturers have recommended that domperidone be contraindicated in patients with predisposing factors: prolongation of cardiac conduction intervals (particularly QT), significant electrolyte disturbances, cardiac disease, moderate or severe liver impairment, receiving QT-prolonging drugs and potent CYP3A4 inhibitors.

Neither advisory was based on new information. With careful risk-benefit assessment and monitoring, some clinicians and patients may elect to continue metoclopramide or domperidone when a safe and effective alternative is not available. The BCCH Pediatric Drug Dosage Guidelines will be updated with the above information.



Keep up to date with Health Canada Advisories, Warnings and Recalls of health products by adding the [MedEffect™ Canada website](#) to your bookmarks, sign up for [mobile alerts](#) or follow the [@HealthCanada](#) Twitter feed.

## Research and Publications

Karen Ng, BScPharm, PharmD, BCPS

### Research

Kiang TKL, Wilby KJ, **Ensom MHH**. Clinical pharmacokinetic drug interactions associated with artemisinin derivatives and HIV-antivirals. *Clin Pharmacokinet* 2014;53:141-53. [Abstract](#)

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Ma C, **Decarie D**, **Ensom MHH**. Stability of clonidine suspension in oral plastic syringes. *Am J Health-Syst Pharm* 2014;71:657-61. [Abstract](#)

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**Kendrick J**, **Ensom MHH**, Steer A, White C, **Kwan E**, **Carr RR**. Standard-dose versus high-dose acyclovir in children treated empirically for encephalitis: A retrospective cohort study of its use and safety. *Pediatric Drugs* 2014;16:229-34. [Abstract](#)

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**Ensom MHH**, **Decarie D**. Stability of extemporaneously-compounded clonidine in glass and plastic bottles and plastic syringes. *Can J Hosp Pharm* 2014;67:308-10. [Full Text](#)

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**Ensom MHH**, **Decarie D**. Stability of extemporaneously-compounded pyridoxine in glass and plastic bottles and plastic syringes. *Can J Hosp Pharm* 2014;67:394-6. [Full Text](#)

**Ensom MHH**. Forty-five years of the CJHP: never closed, always renovating. *Can J Hosp Pharm* 2014;67:405-6. [Full Text](#)

**Paquette VC**, Culley C, Greanya E, **Ensom MHH**. Lacosamide as adjunctive therapy in refractory epilepsy in adults: A systematic review. *Seizure* 2015;25:1-17. [Abstract](#)

Turgeon RD, Wilby KJ, **Ensom MHH**. Antiviral treatment of Bell's palsy based on baseline severity: A systematic review and meta-analysis. *Am J Med* 2015; doi: 10.1016/j.amjmed.2014.11.033. [Abstract](#)

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Lo E, Wilby KJ, **Ensom MHH**. Use of proton pump inhibitor in management of gastro-esophageal varices - A systematic review. *Ann Pharmacother* 2015;49:207-19. [Abstract](#)

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**Elbe D**, Bezchlibnyk-Butler KZ, Virani AS, Procyshyn RM (eds). Clinical Handbook of Psychotropic Drugs for Children & Adolescents, 3rd Edition. Hogrefe Publishing, Boston, MA. [Link to Resource](#)

**Li, D** was author and consultant for the "Anxiolytic Medications" section in Best Practice Guidelines for Mental Health Disorders in the Perinatal Period. BC Reproductive Mental Health Program and Perinatal Services BC. March 2014. [Full Text](#)



Large Mortar, New Orleans Pharmacy Museum, New Orleans, LA. Photo: Dean Elbe

## **Ivacaftor (Kalydeco®): A New Channel of Drugs for Cystic Fibrosis**

Karin Ng, BScPharm, ACPR  
edited by Eva Cho, BScPharm, ACPR  
reviewed by Dr. Mark Chilvers, Respiratory Medicine

### **Background [1,2]**

Cystic fibrosis (CF) is an autosomal recessive disorder caused by mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene, which functions to transport chloride and bicarbonate ions. In the lungs, the absence of CFTR function results in dehydration of the airway luminal surface and thickened mucus, which leads to infection and inflammation, ultimately causing structural damage to the lungs, bronchiectasis, and respiratory failure.

The mainstay of therapy involving mucolytic agents, antibiotics, inhaled beta-agonists, and other anti-inflammatory agents have always just been aimed at controlling symptoms. A new treatment targeting the CFTR defect is now available. Ivacaftor, approved by Health Canada in November 2012, is indicated for the treatment of CF in patients 6 years and older who have a G551D mutation in the CFTR gene. G551D is the third most common CF-causing mutation, but only affects ~4% of CF patients. G551D is a class III mutation, characterized by normal numbers of CFTR on the cell plasma membrane but defective gating of the CFTR (protein cannot open to transport chloride ions). In June 2014, the indication for ivacaftor use was expanded to include 9 additional gating mutations: G1233E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R and G970R. Currently, in BC, ivacaftor is a part of the orphan drug program, and each patient is applied for individually and evaluated on a case by case basis to determine eligibility for drug coverage. Some private insurance companies also cover the cost of ivacaftor. Annual cost of ivacaftor therapy is approximately \$300,000 per patient.

### **Proposed Mechanism of Action [1,2]**

Ivacaftor acts as a 'potentiator' of CFTR gating mutations, by inducing CFTR channel opening either dependent or independent of ATP binding and hydrolysis.[3]

### **Clinical Evidence**

Ramsey et al.[4] conducted a randomized, double-blind, controlled trial comparing ivacaftor 150 mg BID to placebo in 167 patients with CF and G551D mutation on at least one allele, who were 12 years of age and older with a forced expiratory volume in 1 second (FEV1) of 40-90% predicted.

At 24 weeks and 48 weeks there were significant improvements in FEV1, pulmonary exacerbation frequency, Cystic Fibrosis Questionnaire (CFQ-R) quality of life, and sweat chloride concentrations in the treatment group compared to placebo.[4] At 24 weeks, there was a 10.4% absolute increase in FEV1 from baseline in the ivacaftor group, as compared to a 0.2% decrease in the placebo group. At 48 weeks, 67% of patients in the ivacaftor group were free from pulmonary exacerbations, as compared to 41% of patients in the placebo group. Ivacaftor was generally well tolerated, having a frequency of adverse events similar to placebo. Please see summary of results in Table 1 (at right).

With the positive results observed in the Ramsey trial, more trials were done to expand the use of ivacaftor for CF patients. Another similar phase III study evaluating the efficacy and safety of ivacaftor monotherapy in 52 patients with CF patients and G551D mutation on at least one allele, who were aged 6-11 (N=52), found that ivacaftor 150 mg BID significantly increased FEV1% predicted from baseline 12.6% compared to 0.1% in the placebo group over 24 weeks.[5] Other significant improvements in the ivacaftor-treated groups included a mean weight gain of 2.8 kg.

**Table 1. Ivacaftor Trial Results (Ramsay et al.)[4]**

Outcome	Outcomes Compared to Baseline			
	Week 24		Week 48	
	Ivacaftor (N=83)	Placebo (N=78)	Ivacaftor (N=83)	Placebo (N=78)
FEV1% predicted absolute change	+10.4 (p<0.001)	-0.2	10.1	-0.4
Sweat chloride (mmol/L)	-48.7	-0.8	-48.7	-0.6
Pulmonary exacerbations, number of subjects	18	35	28	44
Weight change (kg)	3	0.2	3.1	0.4

The incidence of adverse events was also similar between treatment and placebo.[5]

Ivacaftor was then studied in CF patients with other gating mutations. KONNECTION is a 2 part, double-blind crossover study for 8 weeks, followed by a 16 week open-label extension, evaluating the efficacy and safety of ivacaftor in CF patients greater than 6 years of age, with a non-G551D gating mutation on at least one allele.[7] Part 1 of the study found that ivacaftor 150 mg BID significantly increased FEV1% predicted from baseline 7.5 % compared to -3.2% in the placebo group over 8 weeks. Other significant improvements in the ivacaftor-treated group included BMI, sweat chloride and CFQ-R. All improvements were sustained and noted through to week 24. The incidence of adverse events was also similar between treatment and placebo.

Recently, an open label study looked at safety, pharmacokinetic, pharmacodynamic, and effectiveness of ivacaftor in CF patients aged 2-5 years with a gating mutation. The study has not yet been published, but the company has already submitted a New Drug Application for the use of ivacaftor in children ages 2-5.

### **Adverse Reactions [6]**

- CNS: Headache (17%), dizziness (5%)
- Resp: Upper respiratory tract infection (16%), nasal congestion (16%), rhinitis (6%)
- Nausea (10%), abdominal pain (<1%)
- Rash (10%)
- Arthralgia (5%)
- Elevation of transaminases (ALT or AST) (<1%)
- Hypoglycemia (<1%)

### **Dosing and Administration [6]**

Adults and pediatric patients ≥ 6 years old: 150 mg tablet every 12 hours taken orally with fat-containing food. Reduce dose with moderate or severe hepatic impairment and when used with moderate or strong CYP3A inhibitors.

### **Drug Interactions [6]**

Ivacaftor is a major CYP3A substrate and weak inhibitor of CYP3A4; may inhibit CYP2C9. Possible interactions include:

- CYP3A inducers (e.g. rifampin, phenobarbital, rifabutin, carbamazepine, phenytoin) → decreased ivacaftor levels
- CYP3A inhibitors (e.g. ketoconazole, voriconazole, clarithromycin, erythromycin) → increased levels of ivacaftor
- CYP and P-glycoprotein substrates → potential altered levels of concomitant drugs
- Grapefruit juice → may increase plasma concentrations of ivacaftor
- Herbal products (e.g. St. John's Wort) → may decrease efficacy of ivacaftor

For specific drug interactions and recommended dosage adjustments, please refer to the product monograph.

Currently ivacaftor is the only marketed treatment available to patients that correct the underlying defect at the level of the CFTR protein. Although there is still no known cure for CF, this development has advanced the understanding of CFTR therapies and has paved the way for other novel drugs which are currently being studied to target other mutations or to correct the CFTR defect.

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### **Use of Oseltamivir for Treatment of Influenza in Children**

*Karen Ng, BScPharm, PharmD, BCPS  
Reviewed by Dr. Ashley Roberts, Infectious Diseases and Antimicrobial Stewardship*

Immunization is the main preventive measure for influenza viruses, however for patients who develop influenza infection, oseltamivir can be an important treatment option to reduce the severity and duration of symptoms, risk of complications, use of antibiotics, and potentially mortality. [1-3] Oseltamivir is rapidly metabolized into its active metabolite, oseltamivir carboxylate, which inhibits viral neuraminidase, blocking release of progeny virions from infected cells and viral entry into uninfected cells.[4]

The effectiveness of oseltamivir has been highly debated due to criticisms of potential bias and incomplete data from the manufacturer, Roche.[5] In April 2014, the Cochrane review was updated based on full internal reports of oseltamivir and zanamivir trials including over 24000 patients and still found a modest benefit in patients with influenza-like illness and confirmed influenza virus infection. Dobson et al. conducted a separate meta-analysis by an independent research group, including all available data from randomized, double-masked, placebo-controlled adult trials (n=4328) and found that oseltamivir decreases duration of symptoms, reduces risks of lower respiratory tract complications and hospital admissions, but increases incidence of nausea and vomiting.[6] A Cochrane review of 2356 children, of which 1255 had laboratory-confirmed influenza, also found a modest benefit of oseltamivir treatment in duration of illness and incidence of acute otitis media, but increased nausea and vomiting.[7] Benefits of oseltamivir may be more pronounced in hospitalized children and decrease length of hospital stay[8], and may prevent hospitalization in high-risk patients.[9]

The Canadian Pediatric Society (CPS), Centres for Disease Control (CDC), and American Academy of Pediatrics (AAP) all recommend the use of oseltamivir to manage influenza illness, particularly in hospitalized children and those at high risk for complications. Although benefits are modest, oseltamivir is the best available antiviral for the treatment of influenza with a good overall safety profile other than increased nausea and vomiting.

An oseltamivir algorithm has been created to promote alignment with guidelines and optimize use of oseltamivir. Because rapid influenza diagnostic testing is available in BC Children's and Women's Hospital, our hospital's influenza protocol is a slightly conservative adaptation of available guidelines to treat with oseltamivir only in confirmed influenza-positive patients with risk factors for complications, limiting empiric oseltamivir use only for critically-ill patients or as guided by clinical judgment. When testing with nasopharyngeal wash or swab specimens is not feasible or rapid tests are not available, empiric therapy should be strongly considered to minimize treatment delay. No neuraminidase inhibitors are approved for children younger than one year of age in Canada, but oseltamivir was approved temporarily for use in this age group based on a favourable risk-to-benefit ratio during the 2009 H1N1 pandemic. Evidence and dosing studies exist for infants younger than one year of age,[10] and the Canadian Pediatric Society guidelines continue to recommend oseltamivir for this age group. Accordingly, the hospital's pediatric guidelines apply to patients from 2 weeks to 18 years of age.

The [BCCCH Pediatric Oseltamivir Algorithm](#) is available via [medworxx.com](#) and on page 9 of this newsletter.

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### **Use of Oseltamivir for Treatment of Influenza in Pregnant Women**

*Vanessa Paquette, BScPharm, PharmD  
Reviewed by Dr. Ashley Roberts, Infectious Diseases and Antimicrobial Stewardship*

Pregnant women and women up to four weeks postpartum are considered at high risk for influenza related complications. [1,2] Increased severity of illness, increased hospitalizations, and increased mortality have been observed particularly in women with influenza in their third trimester.[2,3] Influenza in pregnancy has also been associated with effects on the fetus including congenital abnormalities, low birth weight, preterm delivery, and fetal death.[1,4-6] (Continued...)

While annual influenza vaccination remains an important preventative measure for pregnant women, prompt use of oseltamivir is important for pregnant women with suspected or confirmed influenza.[1,7,8]

Oseltamivir may decrease severity and duration of symptoms, reduce the risk of lower respiratory tract complications, decrease hospital admissions and ICU admissions, and may also reduce mortality.[9-12] The greatest benefits are seen if oseltamivir is initiated within two days of symptom onset, however, may still be beneficial if started later.[12] Common adverse effects include nausea and vomiting.[10] Current data do not suggest any increased risk to the developing fetus if oseltamivir is taken during pregnancy.[13] Oseltamivir is considered the antiviral of choice for pregnant women for the treatment of influenza.[1,7,8]

Current influenza treatment guidelines from The Association of Medical Microbiology and Infectious Disease Canada (AMMI), Centers for Disease Control (CDC), and The Infectious Disease Society of America (IDSA), all recommend oseltamivir use for the treatment of suspected and confirmed influenza in the pregnant population.[1,7,8] An educational algorithm for the treatment of influenza in pregnant women has been created to align with these guidelines and with the existing policies and preprinted orders available at BC Women's Hospital.

The Women's Hospital Influenza [Policy](#), [PPO](#) and [algorithm](#) are available from [medworxx.com](http://medworxx.com); a copy of the algorithm is on page [10](#).

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## Updated Voriconazole Dosing and Therapeutic Drug Monitoring for Pediatric Patients

Karen Ng, BScPharm, PharmD, BCPS  
edited by Jennifer Kendrick, BScPharm, PharmD

Voriconazole is a broad-spectrum triazole antifungal considered first-line against invasive aspergillosis and a treatment option for other fungal infections. It exerts its antifungal effects by inhibition of ergosterol biosynthesis, a vital component of the fungi cellular membrane.[1] Both oral and intravenous dosage forms are available, with a variable oral bioavailability of 45 to 80% in young children and over 90% in those 12 years of age and older.[2,3] Voriconazole exhibits linear pharmacokinetics in children but nonlinear pharmacokinetics in adults due to saturable metabolism.

Significantly higher doses are warranted in younger children than in adults, due to accelerated metabolic clearance and higher capacity for elimination per kilogram of body weight.[4,5] A multi-centre prospective, open label study examining IV to PO dosage regimens found that children required higher than the previously recommended 7 mg/kg/dose PO Q12H oral dosage to achieve similar voriconazole exposure to adults.[6] Recently, a pharmacy resident conducted a retrospective review of BCCH oncology patients receiving voriconazole between January 2008 and September 2013 and found that our previous dosing recommendations were generally insufficient to reach target trough levels of 1 to 5.5 mg/L.[7] Only 5 of 15 patients reached the target trough range, and high inter- and intra-subject variability was observed.

The pros and cons of voriconazole therapeutic drug monitoring were reviewed in the Winter 2012 edition of the Pharmacy Informer. In summary, voriconazole serum trough levels observed in children are highly variable and are less likely to predict voriconazole exposure than in adults.[2,3,8] While a definitive relationship between voriconazole concentration and pharmacological response has not been clearly established, low concentrations of voriconazole are associated with a higher likelihood of therapeutic failures.[9] Since clinical effectiveness of voriconazole is difficult to assess, serum trough concentrations may be our best available surrogate for monitoring effectiveness over the generally long courses of therapy and are generally recommended in the literature.[10]

The dosing guidelines for voriconazole in children under 12 years of age at BCCH have been updated and the dose has been increased to 9 mg/kg/dose PO/IV Q12H. A loading dose for this age group is no longer necessary, and the same dosage is recommended whether given orally or intravenously. Dosing for adults and children 12 years of age and over remains unchanged. To standardize the monitoring at BCCH, weekly steady-state voriconazole serum trough concentrations are recommended. Steady state is achieved after a minimum of 4 days after starting or changing the dose of voriconazole. Levels should be drawn on Tuesday mornings as they are processed every Wednesday morning at St. Paul's Hospital. Once the patient is on a stable voriconazole dose and concentrations are consistently within the target range of 1 to 5.5 mg/L, decreasing frequency of therapeutic drug monitoring to once or twice monthly can be considered if there are no changes in clinical status or interacting medications.

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## Pharmacy Awareness Month March 2015

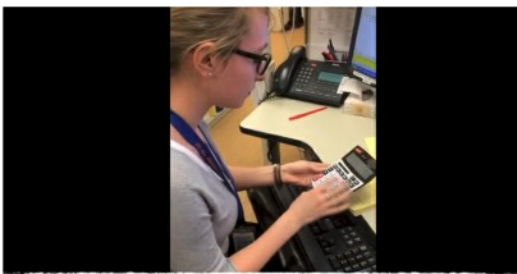
Come on down to Shaughnessy Cafeteria between 11:30 AM and 1 PM on Monday March 9th through Thursday March 12th to help us celebrate Pharmacy Awareness Month!

You can meet our team of dedicated hospital pharmacy staff: the pharmacists, pharmacy technicians and assistants who help make sure our patients receive treatment with safe and effective medications to help them get better.

We will feature our new video "Life of a Medication Order" that will take you inside the inner workings of our department, and how a written order turns into a dose of medication ready to be administered to your patient.

You can test your pharmacy knowledge with our fun fact trivia quiz, or play **name that dosage form** with the largest medication blister pack you have ever seen! There are giveaways of pens, lollipops, the coveted I ♥ PHARMACY buttons, and you can enter a draw to win great prizes like a copy of our BCCH drug dosing guidelines handbook, or even tickets to an upcoming Vancouver Whitecaps game.

The fun starts Monday March 9<sup>th</sup>, but if you can't wait, then check out the **Life of a Medication Order** video now available on YouTube at <http://bit.ly/PAM-video>



Pharmacist checks that dose ordered is appropriate

## Pharmacy Informer Editorial Board

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## Awards

*Karen Ng, BScPharm, PharmD, BCPS*

**Dan Rainkie, (Dr. Roxane Carr), and Dr. Mary Ensom** received the CSHP 2014 **Pharmacotherapy Best Practices Award** for their project/publication "Pediatric Assessment of Vancomycin Empiric Dosing (PAVED)".

**Dr. Mary Ensom** was awarded the **Class of 2014 Master Teacher Award** by the UBC Faculty of Pharmaceutical Sciences' graduating class.

**Dr. Mary Ensom** received the CSHP BC Branch's **Distinguished Service Award** for 2014, recognizing a member who has shown significant and extensive contribution to hospital pharmacy at the local, provincial and national level.

**Dr. Mary Ensom** was the recipient of the **Visionary Award** from the UBC Pharmaceutical Sciences Student Journal for 2013. She was also elected to a 3-year term as **Research Institute Trustee of the American College of Clinical Pharmacy (ACCP)**, a professional and scientific society of more than 14,000 members.

**Dr. Mary Ensom** was the distinguished recipient of the **Paul F. Parker Award** in 2013, awarded to a former resident of the University of Kentucky Pharmacy Residency Program or to an individual associated with the success of the program. This award recognizes those individuals who display sustained contribution to the profession in practice, teaching or research. The winner demonstrates supreme commitment to high ideals and excellence in their chosen field, leadership and innovation, and a passion to encourage the personal and professional growth of others.

**Dr. Eddie Kwan** was this year's recipient of the BC Women's Hospital NICU **Dr. Clive Meintjies Award of Excellence in Family Centered Care**. This award is presented annually by the NICU to honour the spirit and remarkable service of Dr Clive Meintjies and to recognize team members who exemplify leadership and family centered care.

**Dr. Roxane Carr** was awarded **Veteran Preceptor of the Year** of the Lower Mainland Pharmacy Services Residency Program Residency for 2013, recognizing her excellence in teaching, precepting, and mentoring residents.

**Sandra Yin** received the Lower Mainland Pharmacy Services Residency Program **Residency Impact Award** (2014), recognizing excellence in all aspects of professional development in the residency program.

## Editor's Corner

And...we're back! The Pharmacy Informer has resumed publishing after a 2 year hiatus, with new Editorial Board members and some great new ideas, including links to abstracts or free full text publications (when available) embedded and clickable right from inside the newsletter.

We would like to thank our previous editor Eva Cho and our previous editorial board members Sonia Jeffries, Kendra Sih, Dom Khoo and June Yee for their contributions.

Links in this document were verified as working at the time of publication, but these may change following publication, and this is beyond our control.

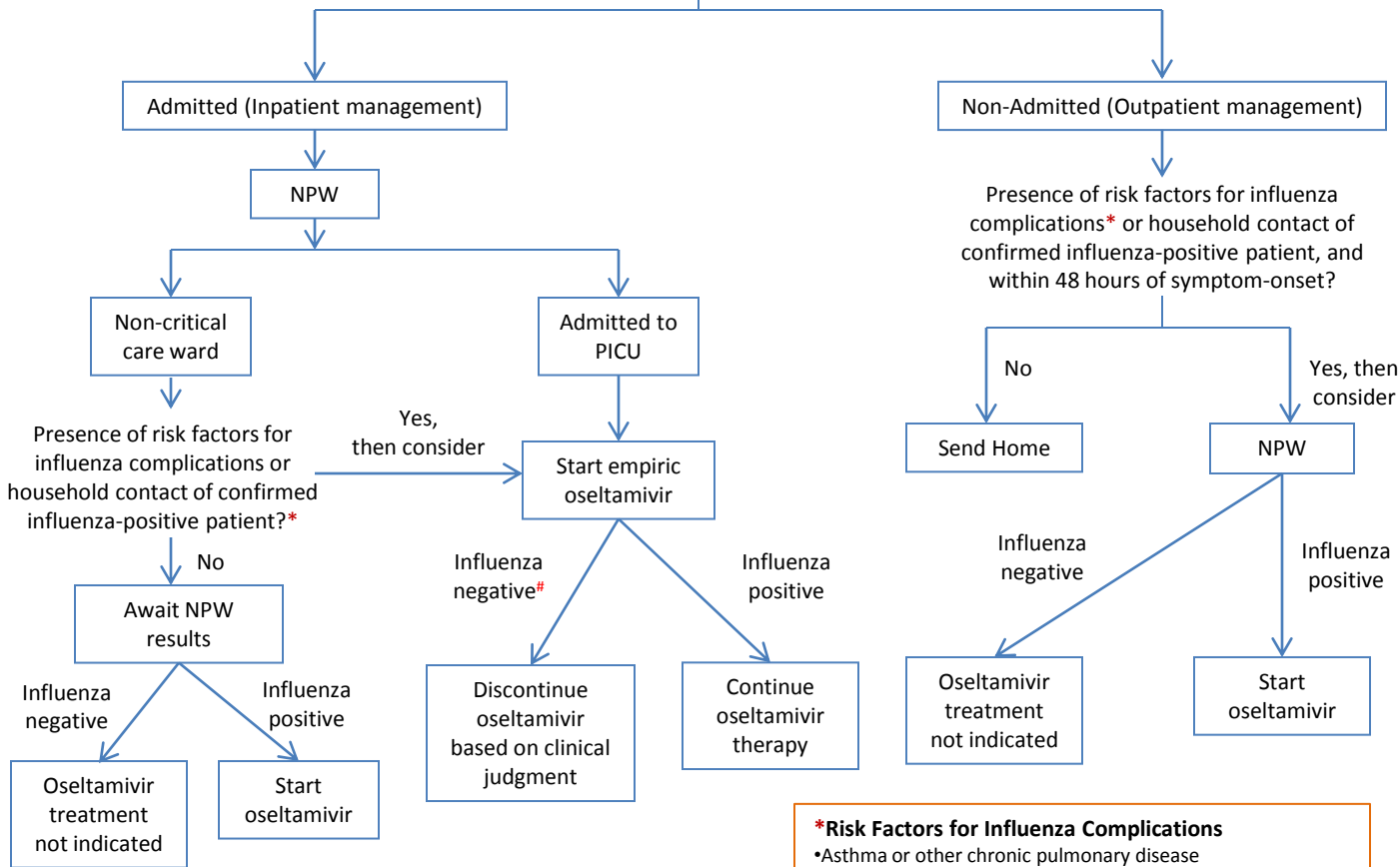
Please contact the Editors if you would like to be added to the distribution list. The Editorial Team welcomes comments and ideas, as well as letters to the Editor for publication in future editions.



# BCCH Algorithm For Oseltamivir Treatment of Influenza in Children and Youth (2 weeks to 18 years of age) for 2014-2015

Patients with influenza-like-illness (ILI) presenting to the Emergency Department

ILI is characterized by the abrupt onset of constitutional and respiratory signs and symptoms (e.g., fever, myalgia, headache, malaise, nonproductive cough, sore throat, and rhinitis)



**Note:**

- Greatest benefit is when oseltamivir is started within 48 hours of influenza illness onset, but may still be beneficial when administered >48 hours.
- \*Confirmation of a negative NPW requires a negative PCR for Influenza virus A and B.

**Oseltamivir dosing for treatment of influenza:**

Children <12 months: 3 mg/kg/dose PO twice daily x 5 days

Children ≥12 months to <13 years:

- ≤15 kg: 30 mg PO twice daily x 5 days
- >15 kg to ≤23 kg: 45 mg PO twice daily x 5 days
- >23 kg to ≤40 kg: 60 mg PO twice daily x 5 days
- >40 kg: 75 mg PO twice daily x 5 days

•Adolescents ≥13 years and adults: 75 mg PO twice daily x 5 days

**Dose interval and duration adjustment in renal impairment:**

Patients with GFR <30 mL/min: once daily x 5 days

Patients on PD/HD: once daily x 2 days

**\*Risk Factors for Influenza Complications**

- Asthma or other chronic pulmonary disease
- Cardiovascular disease
- Malignancy
- Immunosuppression or immunodeficiency
- First Nations, Inuit and Métis children and youth
- Diabetes mellitus and other metabolic diseases
- Hemoglobinopathies such as sickle cell disease
- Neurological disease or neurodevelopmental disorders that compromise handling of respiratory secretions
- Chronic renal insufficiency
- Chronic liver disease
- Children or youth who reside in homes or other chronic care facilities
- Individuals <18 years of age who are on chronic acetylsalicylic acid therapy
- Obesity with BMI ≥40 kg/m<sup>2</sup>, OR a BMI ≥3 z-scores above the mean for age and gender

(Age is not included in this list of risk factors to avoid over-testing of patients.)

**References:**

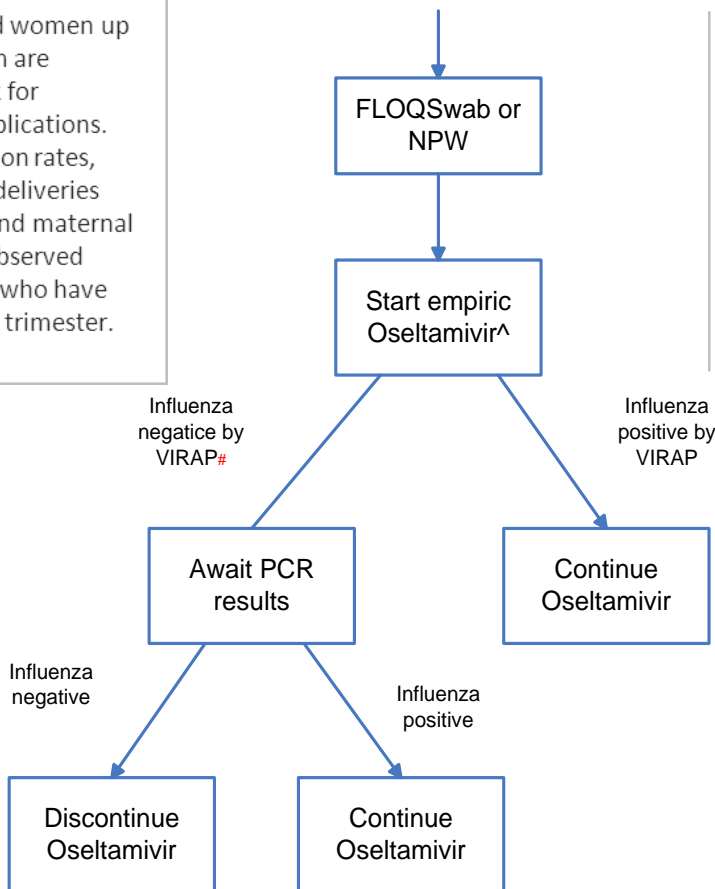
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Patients with influenza-like-illness (ILI)

\*Pregnant women and women up to 4 weeks postpartum are considered at high risk for influenza related complications. Increased hospitalization rates, stillbirths, premature deliveries and increased infant and maternal mortality have been observed particularly in women who have influenza in their third trimester.

ILI is characterized by:

- Fever and cough
- Fever and gastrointestinal symptoms (nausea, vomiting, diarrhea)
- Contact with anyone with flu like symptoms in the last 7 days PLUS
- Any of the following: muscle aches, joint pains, sore throat, extreme fatigue or weakness



^Pregnancy is NOT a contraindication to osetamivir use. Osetamivir is the preferred antiviral agent for the treatment of influenza in pregnant women. No adverse effects on the fetus have been observed.

To order antiviral therapy please refer to pre-printed orders **Treatment And Monitoring of Women with Influenza (WW.13.03C)**

**Note:**

- Osetamivir may reduce the duration of hospitalization, ICU admissions and mortality in hospitalized patients with influenza and reduce lower respiratory tract complications in outpatients
- Greatest benefit is when osetamivir is started within 48 hours of influenza illness onset, but may still be beneficial when administered >48 hours.
- #Confirmation of a negative FLOQSwab/NPW requires a negative PCR for influenza virus A and B.

**Osetamivir dosing for treatment of influenza:**

- All adults (including pregnant women): 75 mg po BID x 5 days

**Dose interval adjustment in renal impairment:**

- Patients with GFR 31 to 60 mL/min: 75 mg po once daily x 5 days OR 30 mg po BID x 5 days
- Patients with GFR ≤ 30 mL/min: 30 mg po once daily x 5 days

Please refer to **Fetal Maternal Newborn Policy Influenza Virus: Managing Women Presenting to BCW (WW.13.03A)** for further details.

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**Disclaimer Message**

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