SPRING/SUMMER 2024

THE DOSE

Thames Valley Family Health Team

Thames Valley Family Health Team Pharmacists' Quarterly Drug Information Newsletter

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Have feedback or a topic you would like to see in a future issue? Email us at druginfo@thamesvalleyfht.ca

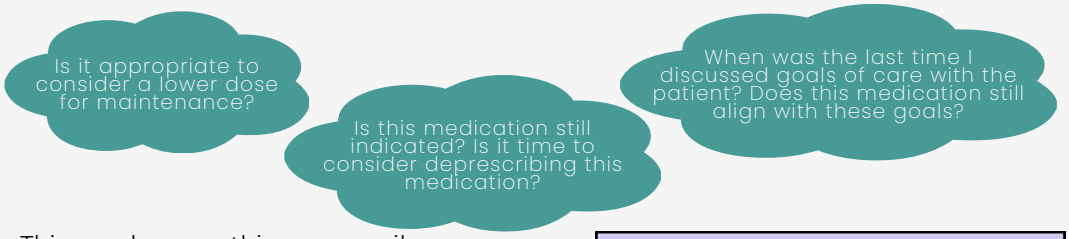
In this issue:

Finding the silver lining in drug shortages

Thank you to one of our TVFHT physicians who shared this CFP article which inspired this topic.

Drug shortages have been a growing issue in recent years. As we are all aware, managing shortages takes significant effort from pharmacists and prescribers, and can feel overwhelming, particularly when a commonly used drug becomes short. Receiving a message requesting that an alternative be prescribed can feel frustrating, particularly as those in the primary care office often do not have all the information about the availability of alternatives.

How often do we consider that perhaps an alternative may not be needed? Receiving a message about a drug shortage could also inspire us to consider other opportunities, such as:



This may be something a prescriber chooses to call the patient in to discuss, or it may be a reason they refer the patient to the FHT pharmacist or the patient's community pharmacist for a medication review.

If the treatment is appropriate to continue, two helpful websites are:

Drug Shortages Canada
Look up status updates on shortages of individual products, estimated dates of return if available

MedSask Drug Shortages
(SK drug information service) Contains information on availability of products experiencing shortages, suggestions for alternatives

In case you missed it: Lifelabs updates eGFR calculation

Effective April 2024, LifeLabs is now reporting eGFR using an updated calculation based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2021 equation (previously used the 2009 equation). Most notably this calculation removes a race-based element to the calculation. The full announcement and details can be found here.

What you should know:

- The equation is only validated in ages 18 and over, eGFR will not be reported with creatinine results in younger patients
- True GFR is not reliably predicted by eGFR in vegetarians, amputees, those at extremes of weight, muscle mass or age; and those taking some medications including trimethoprim, ciprofloxacin and fenofibrate
- eGFR is only an estimate - 80-90% of values fall within 30% of measured GFR. Serialized eGFR measurements and monitoring for albuminuria can be useful to provide more clinical context

A website that can be used to compare the different methods of calculating eGFR can be found here

Surgery? Pregnancy? What to do about GLP-1 agonists

As GLP-1 agonists remain popular agents for diabetes management and weight loss, new cautions and guidance have emerged about the risks associated with their use in special circumstances. For elective surgery, there has been an observed increase in risk of aspiration during anesthesia among patients using GLP-1s, and there are two guidance documents with differing opinions on how this should be managed.

All GLP-1 agonists are contraindicated in pregnancy and should be discontinued in the event of an unplanned pregnancy. For patients planning a pregnancy, the product monographs recommend varying wash-out periods.

There has also been reports of higher rates of unplanned pregnancies in women with PCOS who have had fertility improve after losing weight while taking a GLP-1 agonist. Epidemiologic data suggests there is a 21% relative increased risk of NICU admission among newborns whose mother took a GLP-1 agonist for weight loss in the 90 days prior to conceiving than those whose mother did not take any weight loss drug. Consider contraceptive counselling all patients of childbearing age who are not planning a pregnancy and are being prescribed a GLP-1 agonist.

Consultation with endocrinology for guidance on how to manage the patient's blood sugar while the GLP-1 agonist is being held is recommended by all guidance literature on this topic, if the patient is using the agent for diabetes management.

<table>
<tr><th></th><th>Liraglutide</th><th>Lixisenatide*</th><th>Dulaglutide</th><th>Semaglutide</th><th>Tirzepatide</th></tr>
<tr><td rowspan="3">Elective surgery planning</td><td colspan="2">American Society of Anesthesiologists: Hold the dose on the day of surgery</td><td colspan="3">American Society of Anesthesiologists: Hold a week prior to surgery</td></tr>
<tr><td colspan="5">Canadian Journal of Anesthesiology editorial: hold for 3 half-lives</td></tr>
<tr><td>t ½ = 13h</td><td>t ½ = 3h</td><td>t ½ = 5 d</td><td>t ½ = 7 d</td><td>t ½ = 5 d</td></tr>
<tr><td>Prenatal planning</td><td colspan="2">Discontinue if planning pregnancy, no specific timeframe suggested</td><td>Discontinue at least 1 month prior to a planned pregnancy</td><td>Discontinue at least 2 months prior to a planned pregnancy</td><td>Discontinue at least 1 month prior to planned pregnancy
Risk of unplanned pregnancy in patients using oral contraceptives in the 4 weeks after initiation and each dose escalation.</td></tr>
</table>

*the lixisenatide solo product (Adlyxine®) has been discontinued in Canada. Lixisenatide is only available in combination with insulin glargine in the product Soliqua®. There may be added considerations to holding Soliqua® given the patient would also be holding their basal insulin

Practice tool spotlight: Bugs and Drugs 2.0

What is it? Bugs and Drugs is a reference that provides information about general empiric antibiotic use and treatment of patients with infectious diseases
What we like about it This is a comprehensive Canadian reference that is available ***free of charge*** on the web and as a mobile app. It is supported by Alberta Health Services, Alberta Health, the BC Ministry of Health, and the Do Bugs Need Drugs?® program. The recommendations are based on literature review and consultation with specialist experts
Bottom line Bugs and Drugs 2.0 is an excellent antimicrobial reference to supplement local antibiogram data

Website **Apple App Store** **Google Play**

New drugs that have caught our attention

Quviviq® (daridorexant, 50mg tablets)

This second dual orexin receptor antagonist joins lemborexant (Dayvigo®) on the market approved for treatment of insomnia. Daridorexant has a shorter half life (8 hours) compared to lemborexant (17-19 hours) which may contribute to why it had less reported fatigue and somnolence when individual placebo-controlled trials were compared (these drugs have not been studied head-to-head).

The magnitude of effect may be small. In two placebo-controlled trials, patients treated with 50mg daily for 3 months experienced an average increase in sleep duration of 35-29 minutes, compared to 11-23 minutes with placebo (EMA review).

Cost: ~$95/30 tabs

Ryaltris® nasal spray (olopatadine/mometasone, 665/25 mcg/act)

Ryaltris is a second option for combination antihistamine/intranasal corticosteroid (INCS) indicated for moderate-severe seasonal allergic rhinitis and associated ocular symptoms (the other is Dymista®, fluticasone/azelastine). The two have not been compared head-to-head. Consider these products when INCS alone does not control symptoms, or when rapid onset of effect (sooner than 2 weeks) is desired. See The Dose S/S 2023 for more information about allergic rhinitis

Dosing for aged 12 and older is 2 sprays in each nostril twice daily. For children 6-11 years old use 1 spray in each nostril twice daily

Cost: ~$80/bottle (240 doses)

Awiqli® (insulin icodec, 700 units/mL)

This much anticipated insulin has a half-life of 7 days, independent of dose, making it suitable for **once-weekly injection**. This may have potential applications for patients with physical or cognitive limitations that make daily insulin injections difficult. The FlexTouch pen administers doses in 10 unit increments, with starting dose of 70 units once weekly.

In the ONWARDS trials, insulin icodec was found to be non-inferior to insulin degludec and glargine, but did not offer additional A1c lowering. There was a non-significant increased risk of severe hypoglycemia. CADTH has reviewed and provided feedback here.

Status: expected to be available July 1
Cost: expected to be $1300/year or more, depending on dose, comparable to Tresiba

Rapid fire: quick updates for busy primary care providers

Paxlovid® evidence and coverage

Recently reported EPIC-SR data found no significant difference in time to alleviation of COVID-19 symptoms between patients who received nirmatrelvir-ritonavir (Paxlovid®) and placebo

Government stock of Paxlovid® has mostly expired. Treatment now must be paid for out of pocket or processed through insurance. Cost is approx. $1300 plus pharmacy fees and markup. Coverage by private plans is still being negotiated, according to Pfizer.

As of May 17, 2024 ODB will cover Paxlovid® with a LU code for eligible patients.

Wegovy® now available

Wegovy® (semaglutide) is now available as an approved treatment for weight management in patients with BMI ≥ 30m2 or ≥ 27m2 with at least one weight-related comorbidity.

Not covered by ODB, the out of pocket cost is $~450 per month, at all doses.

Five FlexTouch pens are available, each marked with only one of the titration doses (0.25mg, 0.5mg, 1.0mg, 1.7mg, 2.4mg). Each dispenses 4 weekly doses. Validity of the "click method" of alternative dosing has not been established as a cost saving method for Wegovy®, as is used with Ozempic®.

Updated CANMAT 2023 guidelines for major depressive disorder in adults

This guideline update focuses on evidence from systematic reviews and meta-analyses published since the last publication (Jan 2015-May 2023).

Among other updates, visuals are now included (tables 3.4, 3.5) to help compare the tolerability of antidepressant drugs. There are also sections on digital health interventions and measurement-based care.

Depo Provera® mixed lots and expiries

Recent shipments of Depo Provera® injections have contained different expiries on the packaging. This is because the needle and syringe are produced at different times and are assigned different expiries.

Guidance from the manufacturer's medical info department suggests that the shorter of the two expiry dates is the one that should be followed.

Something's fishy: sustainability of omega-3 supplements

Omega-3 supplements from fish oil, including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Recent meta-analyses and systematic reviews (1-3) have found minimal positive impact on the prevention of cardiovascular disease and mortality than we once expected with omega-3 supplements. They have also identified risks, such as atrial fibrillation. This evidence may lead to you to recommend these supplements less often to your patients, particularly if they are on a statin.

Another reason we may look at use of omega-3 supplements more critically are the sustainability and ethical considerations around the sources of fish used. Experts warn that overfishing of small fish like anchoveta for omega supplements may disrupt the ocean ecosystems. The carbon footprint of processing the fish and extracting the oils is also predicted to be much higher carbon burden than catching and eating the fish (4). More sustainable products are vegan alternatives, which source omega-3s from plant or bacteria sources.

Lastly, stability of the products, which are often shipped from overseas over long periods of time in uncontrolled conditions is a concern. Oxidization of the fish oils in omega-3 products, leads to production of oxidization products whose toxicological effects are not well studied and contribute to rancid product smells (5).

Consider rethinking when you recommend omega-3 supplements based on available evidence, and what products you recommend if you do.

CEP academic detailing updates

COPD VISITS: Do you have questions about the role of triple therapy for COPD? Or about the differences between recommendations in the recent COPD guidelines? Are you interested in knowing the features and differences between the available inhaler devices, or have other questions about COPD?

Accredited COPD learning visits are still ongoing for physicians and nurse practitioners. Reach out to your TVFHT pharmacist if you are interested, or to CEP if you are not at a TVFHT site

DIABETES HANDOUTS: CEP has updated their GLP-1 patient handout, SGLT2i patient handout and the non-insulin drug pearls document, all available here in the additional resources section.

MENTAL HEALTH RESOURCES: Woebot and Wellness Together Canada are no longer available. Please consult the online tool. The section on "Resources for patients and caregivers" for a list of available free resources

New nicotine replacement you may not have heard about

Nicotine pouches are relatively new to the market. In Canada, the only approved pouch goes by the name of Zonnic® (in the United States the product name is Zyn®). These pouches contain 4mg of nicotine and artificial flavours like mint, berry frost or tropic breeze. They do not contain tobacco. Intended to be used as nicotine replacement therapy used only for smoking cessation, the pouches are placed between the gum and upper lip and left there for up to an hour to curb cravings for cigarettes. The maximum recommended dose is 15 pouches per day.

You may have heard about Zonnic® nicotine pouches in the media, as there have been concerns about the accessibility, marketing and flavouring being dangerously appealing to youth who do not smoke, mirroring the trendiness of flavoured e-cigarettes.

There has also been a public advisory regarding the sale of unauthorized products. The B.C. government has moved sales of nicotine pouches behind the counter in pharmacies, where counselling on safety and appropriate use can be provided, but in all other provinces Zonnic® remains widely available at convenience stores.

Beyond cigarettes: talking about vaping cessation

This contribution was written by Sapna Karwal, PharmD Candidate from the University of Waterloo

E-cigarette, or vaping products can be used to deliver cannabis, nicotine, flavourings, chemicals, and other substances. They are known by many different names and come in the form of many devices. Some common names include(1):

- E-cigs
- Vapes
- Vape pens, dab pens, and dab rigs
- Tanks
- Mods
- Pod-mods
- Electronic Nicotine Delivery Systems (ENDS)

The use of e-cigarettes has increased considerably in the last 10 years, with 18.2% of Canadians aged 15 years and older reporting vaping at least once(2). Among people who use e-cigarettes, most individuals use primarily nicotine products, and the use is highest among those aged 20-24 years old. The prevalence of using e-cigarettes is higher in men than women (2).

While vaping is less harmful than smoking, since the user inhales vapor instead of smoke, vaping is not harmless (3). There are several adverse effects associated with vaping, including throat and mouth irritation, headache, cough, and nausea. Longitudinal studies are required to delineate the long-term risks of vaping on developing cardiovascular, respiratory, and other diseases (3).

There is currently a lack of evidence-based clinical practice guidelines that can be used to help youth and adults quit vaping (4). As such, the Centre for Addiction and Mental Health (CAMH) has developed a Vaping Cessation Guidance Resource (5) to help healthcare providers to support their patients who want to quit vaping. The recommendations are based on evidence and expertise currently available. However, it is important to note that as more evidence emerges for vaping cessation, the recommendations may be updated accordingly.

Image source: Department of Health and Human Services Nevada Division of Public and Behavioral Health

Many of the recommendations are adapted from the current practice employed for tobacco cessation:

- The nicotine in the vaping products causes the physical addiction, similar to cigarettes. Therefore, pharmacotherapy targeting the nicotine receptors, such as varenicline, NRT and cytisine (Craav®) as well as agents that increase dopamine such as bupropion can be used for vaping cessation (5,6).
- There has been limited study on the use of pharmacotherapy for vaping cessation; it is considered off-label.
- The doses recommended by expert opinion are the same as the doses used for cigarette cessation. For NRT, the dose should be selected based on the amount of nicotine being vaped (pods or mL of juice per day x concentration of juice = amount of nicotine), or start with on-demand short-acting NRT and after a few days convert some NRT to the patch based on the amount of short acting NRT that was used (6).
  - e.g. Patient shares that they vape one STLTH vape pod every week (7 days.) These pods are 10mL and contain 20mg/mL of nicotine
    - 10mL x 20mg/mL = 200mg nicotine / 7 days (divide by 7 to obtain daily dose) = 28mg nicotine per day
    - You may suggest the 21mg patch + a short-acting NRT (gum, inhaler etc.) for as-needed use for cravings

Further resources for both patients and healthcare providers can be found at CAMH – Nicotine Dependence Clinic.

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