Thames Valley
Family Health Team

THE DOSE- Fall 2022

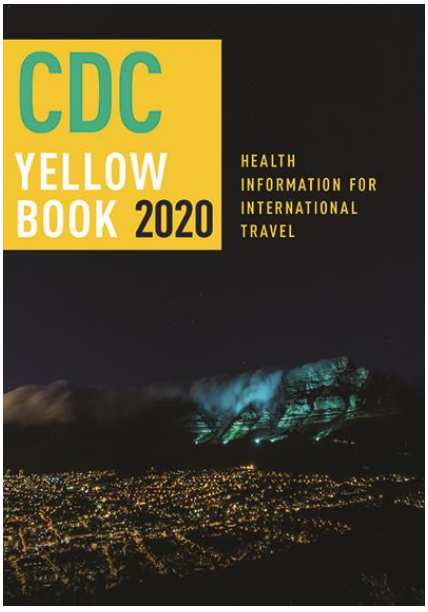
In this issue:

We're Back! After a short hiatus, TVFHT's drug information newsletter has returned!
Have a topic you'd like to see covered in a future issue? Email Jenny at jenny.reid@thamesvalleyfht.ca

Managing Travel Medicine Requests

As patients return to travel, you may see an increase in requests for travel medicine advice. There are several resources that can be helpful in advising these patients.

- Health Canada Travel Advisories by Country
  - Canadian resource, listing travel information by country. Not specific to travel medicine only (also includes other risks, alerts, entry and exit requirements, legal considerations, consular information, etc)
- CDC Traveler's Health By Destination
  - Health specific recommendations by country for precautions and vaccinations, more concise than Health Canada. Information is sourced from the CDC Yellow Book, a US-based resource.
- CDC Yellow Book
  - Comprehensive travel medicine reference published by the United States CDC. Provides, among other things, region-specific malaria prophylaxis suggestions, recommendations for advising specific populations (pregnancy, immunocompromised etc), clinician tools and resources



Basic travel medicine advice can be provided in Primary Care. For destinations with greater risk, or with Yellow Fever vaccination requirements, consider referring to a Travel Medicine clinic (additional costs incurred to the patient). For tips on managing interrupted vaccination series, keep on reading!

Immunization Catch Up

Continue to assist patients to complete their routine and travel immunization series which may have been delayed throughout COVID.

- Consult the Publicly Funded Immunization Schedules for Ontario document which contains the recommended intervals between routine immunizations for those patients who have gotten off track. This document lists both the minimum interval between doses as well as the recommended age and interval at which immunizations should be given—adhering preferentially to the recommended intervals where possible will provide optimal protection.
- Consider running EMR queries or using reminders to capture older adult patients who have not yet received pneumococcal or herpes zoster vaccinations, or to query for patients who started vaccinations series but they remain incomplete. Reach out to FHT pharmacists for assistance if needed.

Most vaccination series do not need to be restarted if they are interrupted!

- Do not restart vaccination series regardless of the time that has passed between doses (exceptions to this include the rabies and cholera/travelers' diarrhea vaccination series). Most importantly, remind patients that multi-dose series need to be completed for the final antibody concentrations and maximum protection to be achieved.

Academic Detailing Update: Heart Failure

- ***Something new:*** the NT-ProBNP blood test is newly funded by OHIP and can be a helpful diagnostic tool in the investigation of suspected heart failure, especially in those with shortness of breath NYD.
- ***Something you may or may not know already:*** new guidelines have been released in Canada recently which recommend quadruple therapy – a combination of four classes of medications which together can reduce mortality and hospitalizations due to heart failure (in other words, add years to your patients' lives, and improve their quality of life by avoiding hospital)
- ***Something that may surprise you:*** initiating quadruple therapy for HF-rEF can be approached differently than initiation of other medications. In this case, there can be benefits to starting meds in tandem rather than sequentially, in terms of improving tolerability and time to benefit.

Talk to your FHT Pharmacist today to schedule a visit to discuss these pearls and more!

Update on Pediatric Antipyretic Drug Shortages

Pediatric antipyretics (children's and infant's acetaminophen and ibuprofen products, including stock bottle sizes) remain to be available in intermittent and limited supply. This is expected to continue to the new year. This issue is being largely attributed to increased demand due to unseasonably higher than usual rates of pediatric respiratory illnesses over the summer, and supply chain issues. Pharmacies have been advised to place temporary limits on purchases to ensure better availability of these medications (Canadian Pharmacists Association communication August 29, 2022).

Refer to TVFHTs guidance document to help direct parents with dosing using dosage forms they may be less familiar with (e.g. adult tablets or chewables).

Minor Ailments Prescribing by Pharmacists – coming January 2023

Regulatory amendments have been approved to allow for pharmacists to prescribe treatment for minor ailments, effective January 1, 2023. Pharmacists who have completed a mandatory educational component will be permitted to initiate treatment from an established list of drugs for the following conditions:

- Allergic rhinitis
- Candidal stomatitis (oral thrush)
- Conjunctivitis (bacterial, allergic and viral)
- Dermatitis (atopic, eczema, allergic and contact)
- Dysmenorrhea
- Gastroesophageal reflux disease (GERD)
- Hemorrhoids
- Herpes labialis (cold sores)
- Impetigo
- Insect bites and urticaria (hives)
- Tick bites, post-exposure prophylaxis to prevent Lyme disease
- Musculoskeletal sprains and strains
- Urinary tract infections (uncomplicated)

More details of how this program will be rolled out to the public are expected in the coming months.

New Progestin-Only Pill: Slynd® (drospirenone)

Slynd®(drospirenone)	
Indication	Contraception for adolescent and adult women
Dosing	Provided in 28-day packages as 24 days of 4mg drospirenone active tablets followed by 4 days of inactive tablets, to be taken one tablet every 24 hours
Dose adjustment	Switching from another contraceptive to Slynd®: - Start the first pill of Slynd® the day the next oral contraceptive pack was to be started - Start on the day the next depo injection was to be given - Start on the day the next patch or ring would have been applied/inserted - Start on the day of removal of IUD/implant
Missed doses	If one active tablet is missed, (up to 24 hours late) take it as soon as possible. Backup contraception not recommended by the manufacturer. *N.B. Evidence supporting this recommendation is limited If two or more active tablets are missed, take the last missed tablet as soon as possible and continue until the pack is finished. Use additional non-hormonal contraception as backup for the 7 days after having missed a tablet
Contraindications/Precautions	Contraindicated in women with hypersensitivity to drospirenone or any non-medicinal ingredient in the formulation (see monograph for list). Contraindicated in women with the following conditions: - Renal impairment - Adrenal insufficiency - Presence or history of cervical cancer or progestin sensitive cancers - Liver tumors or hepatic impairment - Undiagnosed abnormal uterine bleeding Hyperkalemia: drospirenone is contraindicated in women with conditions that predispose to hyperkalemia. Women using treatments or drugs that can increase serum potassium or who are taking chronic medications that are strong CYP3A4 inhibitors should have serum potassium checked prior to starting drospirenone and again during the first cycle

Pregnancy/ Breastfeeding/Special populations	Should not be used in pregnancy Negligible amounts of drospirenone are excreted in breast milk. No adverse effects found on milk production or health, growth or development of a breast fed infant with the use of progestin-only pills.
Adverse Reactions	Most common: unscheduled bleeding (61.4% in first cycle, 40.3% by cycle 13), acne (3.8%), metrorrhagia (2.8%), headache (2.7%), breast pain (2.2%) Other: hyperkalemia
Drug interactions	Avoid giving Slynd® with CYP 3A4 inducers (e.g. topiramate, carbamazepine) as they may reduce efficacy Taking Slynd® concurrently with CYP 3A4 inhibitors may increase the exposure to drosperinone and may increase the risk of hyperkalemia and other adverse effects Monitor potassium in patients taking other medications causing increases in serum potassium (e.g. ACEIs, ARBs, NSAIDs etc)
Efficacy	In a pooled analysis of 2 single-arm trials that included a total of 1571 women 18-45 years old who took drospirenone over nine (trial 2) or thirteen (trial 1) 28-day cycles, the Pearl index (number of pregnancies per 100 woman-years) was 0.7258. Has not been studied head-to-head against norethindrone.
Place in therapy	For patients who require a progestin-only contraceptive, after considering levonorgestrel-releasing intrauterine system or progestin implant, as they are more effective as contraceptives. For patients who require a progestin-only contraceptive for whom IUS or implant are not appropriate, and who have difficulty adhering to taking norethindrone (Micronor®/Movisse®/Jencycla®) within 3 hours of their scheduled dose.
Cost/coverage	Not covered by ODB $29 for 28 days

PREVNAR 20®

Now available in Canada, PREVNAR 20® is a new 20-valent pneumococcal conjugate vaccine (PCV20) approved for use in adults 18 years and older. The new vaccine includes the 13 serotypes which are included in PREVNAR 13® (PCV13), as well as polysaccharide conjugates for seven additional serotypes known to cause invasive pneumococcal disease and have been associated with higher fatality, antibiotic resistance and/or meningitis (8, 10A, 11A, 12F, 15B, 22F and 33F).

PREVNAR 20® is approved for use in Canada, but its place in therapy has not been recommended by NACI, nor is it publicly funded at this time by public health or ODB. The approximate retail cost of PREVNAR 20 is $140-150, depending on individual pharmacy fees.

The American CDC Advisory Committee on Immunization Practices (ACIP) currently recommends the following:

- *Adults 65 years of age or older who have not previously received a pneumococcal conjugate vaccine or whose previous vaccination history is unknown should receive a pneumococcal conjugate vaccine (either PCV20 or PCV15). If PCV15 is used, this should be followed by a dose of PPSV23.*
- *Adults aged 19 years of age or older with certain underlying medical conditions or other risk factors1 who have not previously received a pneumococcal conjugate vaccine or whose previous vaccination history is unknown should receive a pneumococcal conjugate vaccine (either PCV20 or PCV15). If PCV15 is used, this should be followed by a dose of PPSV*23.

The most common adverse effects found in the clinical trials included pain at the injection site, muscle pain, fatigue, headache, and joint pain.

If a patient has already received a series containing PCV13 and PPSV23 it is not considered necessary to re-vaccinate with PCV20. Patients who have already started and received PCV13 should complete their series with PPSV23.

Seeing Red: new OTC treatment for red eye

Lumify® (brimonidine 0.025% opthamic solution) is the first OTC brimonidine drop. Different from prescription-strength Alphagan (brimonidine 0.15%) used for glaucoma, Lumify is approved and marketed for the treatment of red eye.

How does Lumify® differ from other OTC red eye remedies? While there is no evidence to say OTC brimonidine is more effective than standard OTC ocular decongestants such as tetrahydrazoline (Visine® Original), based on the Phase 3 trials, it appears to have low rates of rebound redness and no reports of tolerance (tachyphylaxis). There is a significant cost difference, around $20 for 7.5mL bottle of Lumify®, compared to $4 for other OTC drops used to relieve redness.

Did you know?

Ocular decongestants are known to potentially cause rebound redness after 3 days of use

How is Lumify® used? 1 drop every 6-8 hours (maximum of 4 drops per day). Adverse effects are generally mild, including pain at the instillation site, itching or foreign body sensation. In the Phase 3 trials, changes in intraocular pressure were not observed. Patients who use contact lenses should wait at least 15 minutes before inserting lenses. Patients who use other eye drops should wait at least 5 minutes between instilling different drops.

Other helpful tips for managing ocular redness: remind patients that trigger (smoke, allergens etc) avoidance and artificial tears can be effective tools for managing red eye. Counsel patients to seek further evaluation by an optometrist if redness persists beyond 3 days of use.

Bottom line: *when advising patients on treatment for red eye, first consider modifiable triggers. If a patient has a history of rebound redness with ocular decongestants, consider Lumify® preferentially. Otherwise the options are equally efficacious. Any issue that persists beyond 3 days should be evaluated further*

Vulvovaginal Symptoms Due to Menopause: Navigating Newer Third-Line Treatments

Vulvovaginal complaints (e.g. burning, dyspareunia) post-menopause are due to vulovaginal atrophy caused by estrogen loss. These symptoms are common among post-menopausal women (estimated between 39-47% in some surveys), but it is believed that up to 70% of women who experience them do not discuss them with their primary care provider.

Ask patients who are in the menopausal transition or who are post-menopausal about genitourinary symptoms and use the reported symptoms they are experiencing to guide individualized treatment.

First-line treatment of vaginal dryness or dyspareunia is non-hormonal moisturizers and lubricants. Lubricants such as K-Y® jelly can be used as needed prior to intercourse. Moisturizers such as Replens® and Gynatrof® require regular use for best effect—daily or two to three times weekly.

Second-line consider vaginal estrogen therapy, such as cream (Premarin®, Estragyn®), ring (Estring®) or tablet (Vagifem®), titrated to the minimal dose to improve symptoms. These treatments usually are well-tolerated and typically have minor adverse effects such as local irritation, itching or bleeding. This method of dosing is expected to have lower systemic absorption and as such an opposing progestin is not required in most cases, though RCT data beyond 1 year of treatment is not available. There is not long-term RCT data on the safety of topical low-dose vaginal estrogens, though long-term observational data suggests there is no increased risk of breast or endometrial cancer, heart disease, VTE or stroke. NAMS recommends local therapy over systemic therapy for patients who are only presenting with vulvovaginal symptoms.

Third-line treatments (these are the newer agents!) for patients whose symptoms persist despite trials of the above include prasterone and ospemifene.

Prasterone (DHEA) (Intrarose® vaginal insert) is approved for the treatment of dyspareunia associated with menopause.

Mechanism of Action	Inactive steroid (DHEA) converted to estrogens and/or androgens. Exact mechanism of action for vulvovaginal atrophy/dyspareunia is unknown
Evidence	There is less evidence of safety and efficacy of vaginal prasterone compared to local estrogen therapy, and the two have not been studied head-to-head. It is associated with increases in serum levels of testosterone and estrone. In one study, prasterone was found to improve total Female Sexual Function Index (FSFI) scores by 41.3% compared to placebo (p=0.0006).
Contraindications and Cautions	Patients with undiagnosed vaginal bleeding are contraindicated from using prasterone. Prasterone should be used with caution in patients with a history of estrogen-sensitve cancers, given the rise in serum estrone with use.
Dosing	6.5mg vaginal suppository inserted once daily at bedtime No dose adjustment in renal or hepatic impairment have been recommended by the manufacturer.
Interactions	No known significant interactions
Adverse Effects	Vaginal discharge (6-14%), abnormal pap smear (2%)
Place in Therapy	For patients without contraindications to hormonal therapy but who prefer to avoid estrogens, or who have failed using estrogens. Patients who prefer a local method of drug delivery over an oral medication.
Cost	$532/year as reported to CADTH by the manufacturer, not covered by ODB

Ospemifene (Osphena® oral tablet) is approved for the treatment of moderate to severe dyspareunia and/or vaginal dryness caused by vulvovaginal atrophy in menopausal patients.

Mechanism of Action	Ospemifene is a selective estrogen receptor modulator (SERM) which through binding to estrogen receptors through the body leads to activation of some estrogenic pathways and blockade of others.
Evidence	In an RCT investigating the effect on moderate to severe dyspareunia over 12 weeks of treatment in women aged 40-80 years, ospemifene 60mg daily was found to increase the number of participants who reported “no vaginal pain” (38.3% vs 29.5%) and increase the number of patients who saw a 2-3 point improvement in vaginal pain severity rating scores (55.7% vs 41.8%). Investigators also reported a reduced number of participants who reported the need to use lubricants at the end of the trial.
Contraindications and Cautions	Ospemifene is contraindicated in patients with a known hypersensitivity, undiagnosed abnormal vaginal bleeding, current or history of DVT or PE, active or history of arterial thromboembolic disease (e.g. MI, stroke), estrogen-dependent cancers, or who are or may become pregnant.
Dosing	60 mg orally once daily No dose adjustment in renal impairment or mild-moderate hepatic impairment. Not studied in severe hepatic impairment.
Interactions	Major substrate of CYP 3A4, avoid with 3A4 inhibitors (e.g. fluconazole), do not combine with other SERMs or estrogen products
Adverse Effects	Hot flushes (7-12% - in trials hot flushes typically resolved by 6 months of treatment and infrequently (<1%) led to discontinuation), headache (3%), vaginal discharge (4-6%), endometrial hyperplasia (10%), muscle spasm (2-5%), potential undefined risk of thrombosis
Place in Therapy	For patients with symptomatic vulvovaginal atrophy not relieved by non-pharmacological options who cannot or prefer not to use a vaginal product.
Cost	$567/year as reported to CADTH by the manufacturer, not covered by ODB

Testosterone as a gel applied vaginally has been proposed as a treatment for genitourinary symptoms of menopause in patients who also have reduced sexual desire, however there is very little data regarding efficacy and safety, and it is not an approved indication in Canada or the US.

Drug Information Tool Spotlight: CredibleMeds

CredibleMeds is an online reference that categorizes the risk of torsades de pointes (TdP) associated with drugs that are known to prolong the QT interval. This tool can help inform clinical decision making and evaluation of individual risk to the patient when combined with patient context.

Known Risk of TdP - These drugs prolong the QT interval **AND** are clearly associated with a known risk of TdP, even when taken as recommended.

Possible Risk of TdP - These drugs can cause QT prolongation **BUT** currently lack evidence for a risk of TdP when taken as recommended.

Conditional Risk of TdP - These drugs are associated with TdP **BUT** only under certain conditions of their use (e.g. excessive dose, in patients with conditions such as hypokalemia, or when taken with interacting drugs) **OR** by creating conditions that facilitate or induce TdP (e.g. by inhibiting metabolism of a QT-prolonging drug or by causing an electrolyte disturbance that induces TdP).

Drugs to Avoid in Congenital Long QT Syndrome (cLQTS) - These drugs pose a high risk of TdP for patients with cLQTS and include all those in the above three categories (KR, PR & CR) **PLUS** additional drugs that do not prolong the QT interval per se but which have a Special Risk (SR) because of their other actions.

Some of their tools:

- QT drugs list: search by drug name for the risk associated with that medication
- List of drugs to avoid in congenital long QT syndrome
- Therapeutic Options not on the QTdrugs List (search by condition for drugs with lower risk of TdP)

www.crediblemeds.org

Identifying TdP risk of individual medications is just the first step in critically evaluating a QT-prolonging medication or interaction. Consider following these additional steps as part of your process (from Pharmacists Letter, August 2022):

Assess Drug Risk

- Assess individual drug risks of TdP (can search individually on CredibleMeds)
- Consider interactions which could increase risk
- Consider if there are alternatives which have less risk (CredibleMeds)

Assess Patient Risk

- Does the patient have long QT syndrome or previous episode(s) of TdP?
- Does the patient have additional risk factors for developing TdP (cardiac disease, history of MI, family history of TdP, impaired renal or hepatic function, untreated thyroid disease, low electrolytes (K+, Mg2+, Ca2+), bradycardia, female sex, age >65)?

Manage Risk

- Follow the "Drugs to Avoid in Long QT syndrome" if patient has LQTS or previous TdP (CredibleMeds)
- Correct electrolytes, adjust current meds to manage bradycardia if applicable
- Dose QT prolonging medications appropriately using the lowest effective dose, adjusting for renal or hepatic function
- Manage interactions, avoid multiple QT prolonging medications or drugs that affect levels of QT prolonging medications
- Monitor ECG - at baseline and steady state after initiating a QT prolonging medication
- Educate the patient to self-monitor for symptoms such as pre-syncope, syncope, palipiatations and to report them

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