SEPT 2026

THE DOSE

Thames Valley Family Health Team's Drug Information Newsletter

Thames Valley Family Health Team

Are you a healthcare provider outside of Thames Valley FHT? Sign up to receive emailed newsletters and Drug Info Blast updates here.
Would you like to share feedback or a topic suggestion for a future edition?
Email us at druginfo@thamesvalleyfht.ca

In this issue:

Done with dopamine agonists: RLS guidelines update

The 2025 updated guidelines for treatment of RLS (restless legs syndrome) include major changes since the 2012 guideline.[1]

- Regularly test iron studies. Give oral or IV iron for adults with ferritin <75 mcg/L (IV iron recommended if ferritin 75-100 mcg/L) or transferrin situation <20%, and children with ferritin <50 mcg/L.
  - Draw fasting labs, avoiding red meat and iron supplement 24 hours prior to blood draw.
  - Consider IV iron if no response to or cannot absorb oral iron.

Tip: Before adding medications, initial management of RLS addresses **exacerbating factors**: alcohol, caffeine, antihistaminic, serotonergic (SSRIs, tricyclic antidepressants, mirtazapine), and antidopaminergic (e.g. metoclopramide[3], first generation antipsychotics) medications and untreated obstructive sleep apnea. Physical activity is recommended.[1,2]

Pharmacological recommendations[1] Summary infographic

1. **First-line**: **Gabapentin or pregabalin** at the lowest effective doses. Drowsiness and dizziness are common dose-dependent adverse effects which can be limited by a slow titration.
2. **Last-line**: Opioids, based on one trial with oxycodone extended release. Not appropriate for many patients due to significant adverse effects including physical dependence and addiction.
3. **Conditional recommendation against** dopamine agonists (pramipexole, ropinirole, rotigotine, levodopa). **Long-term use can cause augmentation:** iatrogenic worsening of RLS, presenting as earlier symptom onset in the day or worsened symptoms despite dose increases. Risks of these medications include hypersexuality and problematic gambling and/or addictions.[2]

Important update: Generic semaglutide is here

Availability	The following products are currently on the market: • Apo-semaglutide, 0.25-0.5 mg pen and 1 mg pen • Dr. Reddy's semaglutide, 0.25-0.5 mg pen and 1 mg pen • Ozempic®, 0.25-0.5 mg pen and 1 mg pen
ODB coverage	All semaglutide injections are covered for type 2 diabetes only.
Cost (one pen = 4 weeks' supply)	• Both generics cost ~$100 per pen (both strengths) • Ozempic® costs ~$300 per pen (both strengths)
Financial assistance	For patients **paying out of pocket or with partial private coverage** Novo Nordisk may provide financial coverage. Inquire with the community pharmacy. This **does NOT apply** to those with ODB coverage.

Inventory varies at the pharmacy level. Patients should inquire with the community pharmacy about current stock, ordering and cost.

Note: Click counting remains off label and differs among brands.[4]

Should we still use Diclectin?

Diclectin = doxylamine 10 mg/vitamin B6 (pyridoxine) 10 mg

Written by Kate Sherrer, PharmD student

Diclectin is considered a first-line option in nausea and vomiting of pregnancy (NVP) despite evidence showing **only modest clinical benefit over placebo**.[5,6] In 2018, Dr. Nav Persaud reanalyzed the data submitted to Health Canada for Diclectin's approval and found that Diclectin did not meet the requirements for clinical benefit set out by the manufacturer.[7] Despite these concerns regarding efficacy, Diclectin is still recommended as a first-line option in NVP guidelines in Ontario (last updated in 2016) and prescribing rates have only decreased by 1.2% across Ontario.[5,8]

Pyridoxine

~$40 for 1000 x 25 mg tablets

- Two studies of pyridoxine vs. placebo showed a **reduction in NVP** by 1 point on visual analogue scale. No side effects were reported.[10]
- A Health Canada review found a possible link between pyridoxine-containing natural health products ≥10 mg/day and peripheral neuropathy, but insufficient evidence for prescription pyridoxine products.[11]

Why is Diclectin first line?

- Longstanding use in pregnancy[7]
- Strong reproductive safety[7]
- Only medication approved for NVP in Canada[9]

DIC-301 randomized controlled trial

Diclectin showed a statistically significant improvement in the pregnancy-unique quantification of emesis (PUQE) scores compared to placebo, but the benefit was small (less than one point) and **did not meet the criteria for clinical significance**.[6]

Dicletin

~$60 for 120 generic tablets

- Adding doxylamine to pyridoxine has no clear evidence of being more effective than pyridoxine alone.[10]
- In some small studies, adding doxylamine to pyridoxine showed a small increased risk of pyloric stenosis and childhood malignancies which was not shown in large cohort studies.[10]
- Doxylamine **increased drowsiness** compared to placebo.[12]

Bottom line: Diclectin is not more effective, costs more, and may have greater safety concerns than pyridoxine alone.[7,10,12]

What to use instead

- For **mild** symptoms: non-pharmacological measures such as ginger, dietary changes (smaller meals more frequently), stopping iron-containing multivitamin and switching to folic acid only, rest, maintaining oral hydration[5,12,13]
- For **moderate** symptoms: non-pharmacological measures plus pyridoxine 10mg QID (single-entity product)[10-13]
- If symptoms are not controlled or worsen: add H1 receptor antagonist (diphenhydramine 25-50mg q4-6h or dimenhydrinate 50-100mg q4-6h)[13]
- If **symptoms are not controlled** or worsen after addition of a H1 receptor antagonist: assess hydration and consider referral (can consider adding prochlorperazine 5-10 mg q 6-8h or ondansetron 4 mg q8h if dehydration is not a concern)[13]

Clinical pearls

- Pyridoxine is available as 25mg, 50mg, 100mg and 250mg tablets. For NVP, pyridoxine 10mg QID is recommended. Since a 10 mg tablet is not available, 12.5 mg (½ of a 25 mg tablet) QID is the closest practical dose.
- Most patients with NVP will experience **spontaneous resolution of symptoms by 16-20 weeks** of gestation regardless of treatment.[14]

CEP academic detailing updates

New topic: Psoriasis

Did you know that 80% of patients respond well to topicals that can be prescribed in primary care?

Book a 1-on-1 meeting to learn which topical treatments are recommended and covered! Accredited detailing visits are open to physicians and nurse practitioners. Reach out to your TVFHT pharmacist or to CEP if you are not at a TVFHT site

Menopause: Do you know what the MQ6 is? Learn an evidence-based approach to choosing the best treatment. Free online tool available here.

Pharmacotherapy for obesity: Which five medications have an indication for weight loss in Canada? This topic covers a framework for managing obesity. Free online tool available here.

New products on the market

See page 2 of The Dose Winter 2024 for a comparison of the CCS and PEER lipid guidelines.

Jatenzo (testosterone undecanoate capsules)[15]

158, 198 and 237 mg capsules

Drug delivery system bypasses first-pass liver metabolism via absorption in the lymphatic system to maximize oral bioavailability.

Indication: Testosterone (T) replacement therapy for male hypogonadism.

Dose: Initially 237 mg BID, **multiple dose adjustments based on repeat morning T levels**, up to max 396 BID. Take with food.

Contraindications: History of breast or prostate cancer, women, pregnancy.

Adverse effects: (3-5%): ↑ hematocrit, ↑ blood pressure (+4.9 mmHg systolic BP [SBP] vs. +0.2 mmHg SBP on topical T), ↓ HDL-C (dose related). No change in liver function tests.

Efficacy: Mean age 51, n = 166 treated with Jatenzo while 55 received topical T solution (unavailable in Canada). 87% in both groups achieved T levels within the normal range.[16]

Place in therapy: Alternative oral T option requiring dose adjustments based on repeat T levels. Achieves similar T but more ↑ hematocrit, ↑ BP (+4.9 mmHg) and ↓ HDL-C. No data compares Jatenzo to other oral T. Not studied in transgender or non-binary individuals.

Cost: $160-250/30 days. No ODB coverage. **Needs intervals for refills**.

Jornay PM (methylphenidate delayed- and extended-release)[17]

20, 40, 60, 80 and 100 mg caps

Pediatric stimulant given **daily in the evening** with an **8-10 hour delay until medication onset.**

Indication: ADHD in children aged 6 to 12 years.

Dose: 20 mg daily at 8 pm. Do not take in the morning. Can dose between 6:30-9:30 pm. Titrate to max 100 mg/day or 3.7 mg/kg/day. Capsules may be opened. With or without food; a high-fat meal at night can delay absorption.

Contraindications: Same as for all methylphenidate formulations, including risk of diversion and abuse. See monograph for full list. Anxiety and agitation are listed as contraindications.

Pregnancy/lactation: No safety data in pregnancy or lactation. Not indicated in adults. May lead to premature delivery, low birth weight. Passes into breast milk.

Adverse effects: Most frequent (>10%): insomnia, mood lability, headache, ↓ appetite, ↑ diastolic blood pressure, upper respiratory tract infection. No serious adverse events in the 6-week trial.[18]

Efficacy: 6-week open-label trial, n = 155 children aged 6-12 years (mean age 9.4). Mean dose 66 mg, most common dosing time 8 pm. Improvements in symptom scales seen in early morning, during the day, and in the evening.[18]

Place in therapy: The 8-10 hour delay before onset can help children with significant ADHD symptoms in the morning.

Cost: $150-200 per month[19]. No ODB coverage

Nilemdo (bempedoic acid 180 mg tablets)[20]

First-in-class lipid-lowering agent that inhibits cholesterol synthesis in the liver.

Indication: LDL-C reduction as adjunct to diet, statins, +/- ezetimibe and PCSK9 inhibitors, or if other therapies not tolerated as monotherapy. Prevention of cardiovascular (CV) events in adults at increased risk.

Dose: 180 mg daily with or without food. Max concomitant simvastatin dose 20 mg daily. No renal or hepatic dose adjustment. **May precipitate gout** - measure serum uric acid (urate) level at baseline and periodically during treatment.[20]

Contraindications and precautions: Pregnancy, lactation, simvastatin >40 mg daily (2x ↑ in simvastatin exposure). ↑ plasma concentrations of statins (~1.5x ↑ exposure), thus potential ↑ risk of myopathy.

Adverse effects: (<5%): anemia (4.6% vs. 1.9% in placebo), gout, ↑ AST, hyperuricemia (15% ↑ serum uric acid, resolved on stopping), pain in extremities. Muscle symptoms similar to placebo.[21]

Efficacy: n=13,970 statin-intolerant patients at high risk of CV disease. At 3.4 years, major adverse CV events lower than placebo (11.7% vs. 13.3%). **Primary prevention group had more benefit** than secondary prevention. Mean LDL-C lower than placebo by 0.76 mmol/L.[22]

Place in therapy: Non-statin option that ↓ MI and revascularization in primary prevention – stronger evidence than ezetimibe. Not as effective as statins for secondary prevention.

Cost: $160/30 days. No ODB coverage

Rapid fire: quick updates for busy primary care providers

PCOS is now PMOS[23]

Polyendocrine metabolic ovarian syndrome (PMOS) is the new name for polycystic ovary syndrome (PCOS).

Growing evidence shows that PMOS is a multisystem disorder that results in metabolic, reproductive, psychological, and dermatological disturbances. It is not solely a gynecological disorder. Weight management is also a common consideration in PMOS.

Diabetes Canada Metabolic Dysfunction-associated Steatotic Liver Disease (MASLD) update[25]

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the new name for nonalcoholic fatty liver disease (NAFLD). 70% of people with type 2 diabetes (T2DM) are affected by MASLD.

- Screen for MASLD-related liver fibrosis in all patients with prediabetes or T2DM with FIB-4 (Fibrosis-4 index) score [uninsured, $15]
- If FIB-4 <1.3, manage metabolic syndrome (diabetes and weight) in primary care. If FIB-4 score >1.3, consider referral.
- 5-10% **weight reduction recommended**, but >10% may help reverse liver fibrosis.
- Pioglitazone (EAP coverage only), SC **semaglutide and tirzepatide may reduce progression** of liver fibrosis.[25,26]

ODB coverage updates – Evolocumab (Repatha) for dyslipidemia and Libre 3[24]

Evolocumab has a new LU code 737 for adults with cardiovascular disease, **regardless of heterozygous familial hypercholesterolemia status**. Criteria include: acute coronary syndrome in past year, unable to meet cholesterol targets despite max statins and ezetimibe trial if LDL-C level 1.8 to 2.2 mmol/L.

FreeStyle Libre 3 sensors and readers are now covered for **any ODB recipients on insulin**, including type 1 and type 2 diabetes. Libre 2 and Dexcom G7 are also covered for patients on insulin. For a comparison of CGMs, see page 2 of The Dose August 2025.

Heart failure with nonreduced ejection fraction (HFnrEF) (LVEF >40%) guidelines[27]

HFnrEF encompasses heart failure with mildly reduced (LVEF 41-49%) or preserved (LVEF ≥50%) ejection fraction, as newer evidence shows their management is similar.

This simplified guideline recommends the following for reducing heart failure-associated hospitalizations:

1. **Two standard therapies** (1) **SGLT2-inhibitors** (dapagliflozin or empagliflozin) and (2) **mineralocorticoid receptor antagonists** (spironolactone, eplerenone, or finerenone*).
2. If LVEF >45% and BMI ≥30, evidence-based drugs with GLP-1 activity (semaglutide, tirzepatide)
3. If systolic BP ≥100 mHg and not at risk of symptomatic hypotension, ARNI (sacubitril-valsartan) or candesartan if not tolerated

*Finerenone has a new indication for HFnrEF. See page 4 of The Dose April 2026 for dosing tips.

Practice tool spotlight: Deprescribing.org algorithms[28]

Ethel is an 86-year-old with dementia. Her caregiver asks if medications can be reduced. She takes a statin and has no history of cardiovascular disease or stroke. You check the statin deprescribing algorithm.

What is it? Deprescribing.org is led by pharmacist researchers who create guidelines and tools to support deprescribing, with the goal of improving the well-being of older adults.

What does it provide? Evidence-based practical algorithms, and patient handouts. **Deprescribing algorithms include statins, proton pump inhibitors, antipsychotics, benzodiazepines**, and more. These ensure nothing is missed prior to deprescribing and are easily reviewed during an appointment.

How to access? Deprescribing.org algorithms are available online and free to access.

Bottom line:. Deprescribing.org distills evidence around complexities of deprescribing into practical, actionable recommendations. Patient values and autonomy are emphasized where evidence is lacking.

You share that in patients not at end-of-life, there may be an increased chance of cardiovascular events after stopping, but evidence is uncertain. Collectively it is decided for Ethel to remain on a statin.

References

1. Winkelman JW, Berkowski JA, DelRosso LM, et al. Treatment of restless legs syndrome and periodic limb movement disorder: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2025;21(1):137-152. doi:10.5664/jcsm.11390
2. Jensen B, Jin M, Regier L. Essential tremor (ET) and restless legs syndrome (RLS): Treatment options. *RxFiles Drug Comparison Charts* (15th Ed). July 2025. Available from: www.rxfiles.ca
3. Sieminski M, Zemojtel L. Acute Drug-Induced Symptoms of Restless Legs Syndrome in an Emergency Department. *J Clin Sleep Med*. 2019;15(5):779-780. Published 2019 May 15. doi:10.5664/jcsm.7774
4. Elliott T. Counting the clicks with semaglutide 4 mg pens. BC Diabetes. Updated Aug 26, 2026. Accessed Sept 2, 2026. Available at: https://www.bcdiabetes.ca/wp-content/uploads/bcdpdfs/counting-the-clicks-with-semaglutide-in-Canada.pdf
5. Campbell K, Rowe H, Azzam H, Lane CA. The management of nausea and vomiting of pregnancy. *J Obstet Gynaecol Can*. 2016;38(12):1127-1137. doi: 10.1016/j.jogc.2016.08.009
6. Persaud N, Meaney C, El-Emam K, Moineddin R, Thorpe K. Doxylamine-pyridoxine for nausea and vomiting of pregnancy randomized placebo controlled trial: prespecified analyses and reanalysis. *PLoS One*. 2018;13(1):e0189978. doi:10.1371/journal.pone.0189978
7. Crowe K. Morning sickness drug Diclectin doesn't work, confidential industry documents reviewed by doctor show. CBC News. January 17, 2018. Accessed May 20, 2026. https://www.cbc.ca/news/health/diclectin-pregnancy-nausea-vomiting-persaud-duchesnay-confidential-industry-documents-health-canada-1.4491300
8. Chaudhry S, Yazdani S, Chu C, Tharmarajah S, Persaud N, Tadrous M. Changes in doxylamine-pyridoxine dispensation in Ontario following media attention. *Can Fam Physician*. 2025;71(1):43-49. doi 10.46747/cfp.710143
9. Jansen LAW, Shaw V, Grooten IJ, Koot MH, Dean CR, Painter RC. Diagnosis and treatment of hyperemesis gravidarum. *CMAJ*. 2024;196(14):E477-E4485. doi 10.1503/cmaj.221502
10. Persaud N, Chin J, Walker M. Should doxylamine-pyridoxine be used for nausea and vomiting of pregnancy? *J Obstet Gynaecol Can*. 2014;36(4):343-348. doi 10.1016/S1701-2163(15)30611-3
11. Summary safety review - Vitamin B6 health products - Assessing the potential risk of peripheral Neuropathy. Health Canada. Updated Sept 2, 2026. Accessed Sept 2, 2026. https://dhpp.hpfb-dgpsa.ca/review-documents/resource/SSR1773147434487
12. HV Joffe. Summary review for regulatory action. Center for Drug Evaluation and Research. Jun 2012. Accessed Sept 2, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/021876Orig1s000SumR.pdf
13. Association of Ontario Midwives. Clinical treatment algorithm. Nausea and vomiting of pregnancy (NVP). Published October 2025. Accessed May 20, 2026. https://www.ontariomidwives.ca/sites/default/files/Clinical%20Topics/NVP%20Legal%20size%20-%20Oct%202025%20V5.pdf
14. Parker SE, Starr JR, Collett BR, Speltz ML, Werler MM. Nausea and vomiting during pregnancy and neurodevelopmental outcomes in offspring. *Paediatr Perinar Epidemiol*. 2014;28(6):527-535. doi 10.1111/ppe.12151
15. Jatenzo product monograph. Tolmar International Ltd. Dec 12, 2025. Accessed Sept 2, 2026. https://pdf.hres.ca/dpd_pm/00082762.PDF
16. Swerdloff RS, Dudley RE. A new oral testosterone undecanoate therapy comes of age for the treatment of hypogonadal men. *Ther Adv Urol*. 2020;12:1756287220937232. Published 2020 Jun 30. doi:10.1177/1756287220937232
17. Jornay PM product monograph. Knight Therapeutics Inc. Jan 14, 2026. Accessed Sept 2, 2026. https://pdf.hres.ca/dpd_pm/00083170.PDF
18. Childress AC, Cutler AJ, Marraffino A, et al. A Randomized, Double-Blind, Placebo-Controlled Study of HLD200, a Delayed-Release and Extended-Release Methylphenidate, in Children with Attention-Deficit/Hyperactivity Disorder: An Evaluation of Safety and Efficacy Throughout the Day and Across Settings. *J Child Adolesc Psychopharmacol*. 2020;30(1):2-14. doi:10.1089/cap.2019.0070
19. Pharmacotherapy for ADHD management. Centre for Effective Practice. Updated Jan 23, 2026. Accessed Sept 2, 2026. https://cep.health/clinical-products/adhd/
20. Nilemdo product monograph. HLS Therapeutics Inc. Nov 11, 2024. Accessed Sept 2, 2026. https://pdf.hres.ca/dpd_pm/00082429.PDF
21. Richter DJ. Bempedoic acid: mechanism, evidence, safety, and guideline role in 2025. European Society of Cardiology. Published Dec 2, 2025. Accessed Sept 2, 2026. Available from: https://www.escardio.org/communities/councils/cardiology-practice/education/cardiopractice/bempedoic-acid-mechanism-evidence-safety-and-guideline-role-in-2025/
22. Nissen SE, Lincoff AM, Brennan D, et al. Bempedoic Acid and Cardiovascular Outcomes in Statin-Intolerant Patients. *N Engl J Med*. 2023;388(15):1353-1364. doi:10.1056/NEJMoa2215024
23. Teede HJ, Khomami MB, Morman R, et al. Polyendocrine metabolic ovarian syndrome, the new name for polycystic ovary syndrome: a multistep global consensus process. *Lancet*. 2026;407(10545):2329-2339. doi:10.1016/S0140-6736(26)00717-8
24. ODB Formulary Search. Accessed Sept 2, 2026. Available from: https://www.formulary.health.gov.on.ca/formulary/
25. Diabetes Canada Clinical Practice Guidelines Expert Working Group:, Kim J, Bajaj HS, Ramji A, Bemeur C, Sebastiani G. Diabetes and Metabolic Dysfunction-associated Steatotic Liver Disease in Adults: A Clinical Practice Guideline. *Can J Diabetes*. 2025;49(4):222-236. doi:10.1016/j.jcjd.2025.04.003
26. Loomba R, Hartman ML, Lawitz EJ, et al. Tirzepatide for Metabolic Dysfunction-Associated Steatohepatitis with Liver Fibrosis. *N Engl J Med*. 2024;391(4):299-310. doi:10.1056/NEJMoa2401943
27. Virani S, Zieroth S, Aleksova N, et al. Canadian Cardiovascular Society/Canadian Heart Failure Society 2025 Guideline Update for Pharmacologic Management of Heart Failure With Nonreduced Ejection Fraction (LVEF > 40%). *Can J Cardiol*. 2025;41(10):1857-1874. doi:10.1016/j.cjca.2025.07.027
28. Deprescribing guidelines and algorithms. Deprescribing.org. Accessed Sept 2 2026. Available from: https://deprescribing.org/resources/deprescribing-guidelines-algorithms/