THE DOSE

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Thames Valley Family Health Team's Drug Information Newsletter

Thames Valley Family Health Team

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In this issue:

FDA removes menopause therapy black box warnings[1]

The FDA has updated black-box warnings on menopause hormone therapy (MHT) to reflect evolving safety evidence and individualized care. Hesitation around MHT stemmed mainly from the 2002 Women's Health Initiative (WHI)[2] trial, but **newer safety data reinforces limitations of the WHI study** and informs current best practice with bioidentical hormone formulations.

	WHI Study (2002)[2]	Current evidence & guidelines[3,4]
Age at initiation	63 years old	<60 years old or within 10 years of last menstrual period
Hormone formulations	Conjugated equine estrogen + medroxyprogesterone acetate	**Bioidentical† estradiol + micronized progesterone**
Objective	Evaluate CV protection	Manage menopausal symptoms
CVD, cancer risk	Increased risk	**No increased risk***
Dosing approach	Fixed, higher dose estrogen	**Individualized** to patient needs

†Regulated and manufactured hormones that are duplicates of human hormones. See below[5]
*When used appropriately (i.e. progesterone opposition) and with bioidentical products.[3]

Removed black box warnings

× CVD risk
× Stroke risk
× Breast cancer risk
× Dementia risk
× "Lowest effective dose for shortest duration"

Unchanged labelling

⚠ Endometrial cancer risk with unopposed estrogen use in people with an intact uterus

New labeling

✓ Initiating MHT in those <60 years old or within 10 years of last menstrual period optimizes benefit-risk ratio

Written by: Nicoletta Carangounis, PharmD student

FAQs: menopause hormone therapy

Q: Do the above risks apply to local (vaginal) estrogen therapy?

A: No, these risks do not apply as local estrogen therapy has minimal systemic absorption. No progesterone is needed for patients using local estrogen only.

Q: What is a "bioidentical" hormone? Are these the custom compounds made in pharmacies?[5]

A: "Bioidentical" describes a hormone that is chemically identical to the human hormone, and can be manufactured in different ways:

1) Pharmaceutical-grade, regulated by Health Canada – **synthetic estradiol and micronized progesterone are recommended**, due to good safety and efficacy data.
2) Custom-compounded by pharmacies – **NOT RECOMMENDED** by Health Canada due to lack of regulation, presence of impurities, and lack of safety and efficacy data.

Micronized progesterone is only covered by ODB as Bijuva (combination with estradiol).

New non-hormonal therapies for vasomotor symptoms: boon or bust?

Two non-hormonal medications for vasomotor symptoms of menopause (VMS) were approved since 2024. What is their role in menopause management? How do they compare to current options?

Gold standard

MHT (menopausal hormone therapy) is **standard of care** in both **peri- and postmenopausal** women.[4,10]
Benefits include:
✓ VMS
✓ GSM
✓ Bone protection

Role of non-hormonal NK3 antagonist therapy

A **second-line option** for women with contraindications to hormone therapy or intolerances to multiple hormonal formulations.

- **Not studied in perimenopausal (i.e. still menstruating) women.**[6,7]
- Not studied in combination with any other menopause therapy.[6,7]
- Effective vs. placebo but no direct comparison to hormone therapy.
- **Benefits restricted to VMS only**. No benefit in genitourinary symptoms of menopause (GSM) nor for bone health.
- Costly, not covered: fezolinetant is $600+/90 days, elizanetant TBD.
- Frequent liver monitoring bloodwork with fezolinetant.

Prescribing considerations: bioidentical estrogen vs. NK3 receptor antagonists

	Bioidentical estrogen (with progesterone if intact uterus)	**NK3 receptor antagonists** (fezolinetant [Veozah], elizanetant [Lynkuet])
Mechanism	Supplement and stabilize fluctuating and declining estrogen levels.	Modulate activity in the hypothalamic thermoregulatory centre.[8,9]
Indication	**VMS and GSM from perimenopause† to postmenopause**, bone protection.	**Moderate to severe VMS** in **postmenopausal*** women.
Efficacy (at 12 weeks)	Baseline 10-13 hot flashes/day: ▪ Lower dose estradiol: 7-8 fewer ▪ Higher dose estradiol: 8-9 fewer ▪ Placebo: 3-6 fewer[10]	Baseline 11-14 hot flashes/day: ▪ Fezolinetant: 7 fewer[8] ▪ Elizanetant: 9 fewer[7] ▪ Both better than placebo
Monitoring	**Symptom-based. No bloodwork needed**. Routine breast cancer screening.	Fezolinetant: ALT, AST, ALP bilirubin at baseline and months 1, 2, 3, 6 and 9.[8]
Cost	Oral ~$150/90 days, transdermal ~$200-300/90 days. **ODB coverage for oral only**.[10]	No ODB. **Fezolinetant $600+/90 days**. Elizanetant cost TBA, not yet marketed.

*Menopause: lack of menstrual period ≥12 months. Postmenopause: any point beyond menopause.
†Perimenopause: presence of menopause-associated symptoms and/or menstrual cycle changes.

Test your knowledge: Menopause hormone therapy (MHT)

- When is pharmacotherapy for menopause indicated?
- What dose of progesterone should be prescribed for higher-dose systemic estrogen therapy?
- Where can you find one-page patient handouts on benefits and risks of MHT?

Need answers to these questions and more? Sign up for academic detailing on menopause!

CEP academic detailing updates

Physicians and NPs, sign up today for the newest topic: Menopause

Get evidence-based, easy to use resources and answers to your questions with a free 1-on-1 detailing visit, Mainpro+ accredited. Reach out to your TVFHT pharmacist or to CEP if you are not at a TVFHT site.

Many other topics are available, including pharmacotherapy for obesity and ADHD in adults.

New products on the market

Pylera® (bismuth, metronidazole, tetracycline capsules)[12]

A **combination product containing first-line medication choices** for *H. pylori* eradication.

Indication: *H. pylori* eradication in adults with *H. pylori* infection and active duodenal ulcer.

Dose: Three capsules PO QID for 10 days, each capsule contains bismuth subcitrate potassium 140 mg, metronidazole 125 mg and tetracycline 120 mg. Prescribe a PPI separately. Take after meals, swallow whole with 250 mL of water and remain upright for 30 minutes to prevent esophageal irritation from tetracycline.

Contraindications and precautions: Hypersensitivity to any of the components, pregnancy and lactation, paediatrics, renal or hepatic impairment.

Adverse effects: Same as the components. Bismuth: black stools, temporary darkening of the tongue. Metronidazole: metallic taste, interaction with alcohol. Tetracycline: photosensitivity, interaction with cations (separate administration by 2 hours).

Efficacy: The guideline-recommended duration of treatment is 14 days[13] but this product is packaged with capsules for a 10-day regimen only.

Place in therapy: An option with first-line medication choices **when minimizing pill burden or adherence is of high importance**. This antibiotic combination is more effective than amoxicillin + clarithromycin + PPI (HP-Pac and generics) but packaged for 10 days only which may increase risk of treatment failure. Prescribing the separate components for 14 days as per guidelines will likely maximize chances of *H. pylori* eradication and minimize treatment failure, re-treatment and additional antibiotic exposure.[13]

Cost: $150 per 10-day course. Not covered by public plans.

See The Dose January 2026, page 5 for an overview of *H. pylori* eradication regimens.

Anzupgo (delgocitinib 20 mg/g cream)[14]

Topical JAK inhibitor cream, a new option for **moderate to severe chronic hand eczema**. The lifetime prevalence of hand eczema is ~14.5%.[15]

Indication: Moderate to severe chronic hand eczema (CHE) in adults when topical corticosteroids are inadequate or inadvisable.[14]

Dose: Apply a thin layer to affected hands and wrists BID, approx. 12 hours apart. **Avoid applying other topical products 2 hours before and after use**. Discontinue when symptoms of CHE resolve and restart as needed for flares. Reassess if symptoms not improved by 12 weeks of treatment.[14]

Contraindications and precautions: Hypersensitivity to the components. Not authorized for paediatrics.

Pregnancy/lactation: Avoid use in pregnancy due to limited data. Only use in lactation if benefit outweighs risk to infant. Unknown if excreted in human milk. Avoid direct contact with nipple and surrounding area after applying.

Adverse effects: Most common were application site reactions (1.1%).

Efficacy: Phase III trials (n=960) included baseline 78% moderate CHE patients and 28% severe CHE. At 16 weeks, 24% on delgocitinib vs. 8.4% on vehicle cream achieved symptom-free CHE. Both physician- and patient-reported scales improved.[15,16]

Delgocitinib cream was more effective and safer than oral alitretinoin (indicated for severe CHE only) in a head-to-head phase 3 trial, n=513. At 12 weeks, a greater change in severity scale was observed with delgocitinib cream (-67.6) vs. oral alitretinoin (-51.5).[17] A change of 41 is considered a minimal clinical difference.[18]

Place in therapy: First-line treatment of CHE continues to be topical corticosteroids, but their use is limited due to safety concerns. Delgocitinib is a **possible topical second-line option with less adverse effects than systemic second-line options** oral alitretinoin (better efficacy, too) and oral immunosuppressants.[19] Use is limited by cost and access to specialist prescribers.

Cost: Each 60 g tube costs $600+. Not covered by public plans.

Rapid fire: quick updates for busy primary care providers

Vortioxetine now generic

Trintillex (vortioxetine) is a serotonin modulator and a first-line option for depression in adults.[20]

The generic is half the cost of brand name = cost savings if paying out of pocket. It is covered by ODB with no LU code.

Vortioxetine is an option for patients with SSRI intolerance with unique characteristics including:

- First-line for cognitive dysfunction in depression, stronger evidence than bupropion and duloxetine.[20]
- Lower rates of sexual side effects vs. SSRIs.[22]
- Long half-life (66 hours).[20,21]
- Take with food, GI side effects are common.

New ODB-covered option for Heterozygous Familial Hypercholesterolemia (HeFH)

Inclisiran (Leqvio) is one of three PCSK9 inhibitors available in Canada. It is indicated as an adjunct for familial and non-familial (adults with known ASCVD) hypercholesterolemia.[23]

Unlike the other PSCK9 inhibitors which are dosed SC every 2 weeks, inclisiran is dosed SC at months 0 and 3, then every 6 months.

Inclisiran is covered by ODB with LU code 732, exclusive to patients with HeFH. LU criteria are the same as evolocumab (Repatha) and alirocumab (Praluent): patients with above-target LDL despite high dose statin and ezetimibe for at least three months, or unable to tolerate two statins.

First biologic drug approval for COPD: dupilumab (Dupixent®)

Dupilumab was initially marketed for atopic dermatitis and asthma. A new indication is **add-on maintenance treatment in adults with COPD and elevated blood eosinophils** (≥300 cells/mcL in trials) on inhaler therapy with LAMA + LABA +/- ICS as appropriate.[24]

Dose 300 mg q2weeks, **cost $2000+/month. Not covered for COPD by ODB or NIHB**.

In two trials with 98% of patients on triple therapy (LABA + LAMA + ICS) and baseline two moderate or severe exacerbations in the previous year, dupilumab showed a **30% reduction in exacerbations/year vs. placebo** (0.8 vs. 1.2).[24]

New indication for Finerenone (Kerendia®): heart failure (HF) with LVEF ≥40%

Originally approved for diabetic kidney disease (DKD), finerenone is approved as an **adjunct to standard of care in heart failure with LVEF ≥40%** to reduce risk of CV death, hospitalization for heart failure (HHF), and urgent HF visits.[25]

Heart failure dosing is different than DKD. **For heart failure, the initial dose is 20 mg daily titrated to target dose 40 mg daily**. Dose adjust for renal impairment or if hyperkalemia occurs.[25]

Finerenone reduced the composite endpoint of CV death and total HF events (HHF + urgent HF visits) vs. placebo. **Benefit driven by reduction in total HF events**, RR 0.82 [0.71, 0.94], p=0.0062.[27,28]. **Event curves separated after one month**.

Practice tool spotlight: CKD Pathway

A 68-year old male with T2DM and HTN presents for a 3-month follow up. A1C and eGFR normal, but urinary ACR is high at 4.3 mmol/L. This is the first abnormal ACR for him. You can't remember when to retest ACR and if this requires a nephrologist referral.

What is it? CKD Pathway supports in diagnosing, managing, and referring patients with chronic kidney disease (CKD). It combines recommendations from Kidney Disease Improving Global Outcomes (KDIGO), Hypertension Canada, and Canadian Society of Nephrology.[11]

What does it provide? A clear flowchart for CKD management including cutoff points for diagnosis and referral. Defines the recommended frequency of retesting of eGFR and ACR. Elements can be expanded to show more information, including pearls like when eGFR may be unreliable.[11]

Bottom line: CKD pathway is a **clear, concise and interactive resource that is free to access online**.

After verifying with CKD pathway, you retest eGFR, ACR, and urinalysis in 2-4 weeks to confirm diagnosis.

Case: Cocktails to avoid ordering (ARNI + ARB, OAC + ASA in stable CAD)

This post-hospital discharge medication reconciliation and review ensured that inadvertent therapy duplications were corrected weeks before the patient saw the cardiologist.

As part of a routine hospital discharge program, nursing staff flagged a 73-year-old female for medication reconciliation due to med changes.

Medical conditions: New diagnoses in hospital include HFrEF (LVEF 20-25%), atrial fibrillation, pulmonary embolism. Known hypertension, dyslipidemia, stable angina, depression.

Allergies: ketorolac, amlodipine (peripheral edema).

Medication list on discharge:

1. ASA 81 mg daily (angina) – **still taking daily**
2. Apixaban 5 mg BID (a fib and PE) – **NEW**
3. Metoprolol 25 mg TID (a fib, HFrEF) – **NEW**
4. Sacubitril-valsartan 24/26 mg BID (HFrEF) – **NEW**, patient taking once daily only
5. Telmisartan 80 mg daily – **still taking daily**
6. Digoxin 0.125 mg daily (a fib) – **NEW**
7. Empagliflozin 25 mg daily (HFrEF) – **NEW**
8. Atorvastatin 10 mg daily (angina)
9. Nitro spray q5min PRN

1 Issues identified during med review

1. Apixaban and ASA: Patient is taking both. Days after hospital discharge (but before pharmacist assessment), patient presented to ER with rectal bleeding and was referred for investigations.
2. Sacubitril-valsartan: Patient was unintentionally taking once daily instead of twice daily.
3. Telmisartan: Patient continues to take despite being started on sacubitril-valsartan.

2 Pharmacist and physician collaboration

The patient was to follow up with the cardiologist but had no appointment booked. The pharmacist messaged the family physician with the following recommendations which were accepted:

1. Stop ASA and continue on apixaban alone, duplication may have contributed to rectal bleeding post-discharge.
2. Stop telmisartan and continue on valsartan alone.

3 Closed loop communication

That same day, the pharmacist called the patient back to provide instructions and notified the pharmacy of the discontinued medications.

Q: When is dual therapy with an anticoagulant and ASA appropriate?

- In patients with a fib and **stable CAD** (no ACS or revascularization in past year), **combining OAC and ASA is associated with increased risk of all-cause mortality, major bleeding, and no improved efficacy in stroke or MI prevention vs. OAC alone**.[27,28]
- In patients with a fib and recent PCI or ACS, refer to the 2023 CCS guideline update.[29]
- **Bottom line:** In most patients with a fib and stable CAD, OAC alone sufficiently protects against ischemic events, stroke and systemic embolism.[28]

Q: In patients taking an ACE inhibitor (ACEi) or ARB, how are they switched to an ARNI?

- Sacubitril-valsartan (Entresto) is an angiotensin receptor-neprilysin inhibitor (ARNI) indicated for patients with symptomatic heart failure.[30] Evidence shows reduced CV death, heart failure hospitalizations and symptoms vs. enalapril.[31,32]
- **Cannot be combined with an ACEi or ARB**. Initial dose 24.3-25.7 mg tab BID, titrated up as tolerated.[33] Monitor BP, heart rate, hypotension (can reduce diuretic dose if needed), SCr, and hyperkalemia.[33]

Switching from ACEi or ARB to ARNI (see pg. 14):[34]

- Stop ACEi → 36 hour washout → start ARNI
- Stop ARB → direct switch to ARNI next day

- **Bottom line**: Stop ACEi or ARB when starting ARNI.

References

1. Makary MA, Nguyen CP, Høeg TB, Tidmarsh GF. Updated Labeling for Menopausal Hormone Therapy. *JAMA*. 2026;335(2):117-118. doi:10.1001/jama.2025.22259
2. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA*. 2002;288(3):321-333. doi:10.1001/jama.288.3.321
3. Perpustakaan Negara Malaysia. Clinical practice guidelines: management of menopause in Malaysia [Internet]. Obstetrical and Gynaecological Society of Malaysia (OGSM); Malaysian Menopause Society (MMS); 2022. https://www.moh.gov.my/moh/resources/Penerbitan/CPG/Women%20Health/CPG_Management_of_Menopause_2022_e-version-1.pdf
4. Yuksel N, Evaniuk D, Huang L, Malhotra U, Blake J, Wolfman W, et al. Guideline No. 422a: Menopause: Vasomotor Symptoms, Prescription Therapeutic Agents, Complementary and Alternative Medicine, Nutrition, and Lifestyle. *J Obstet Gynaecol Can*. 2021 Oct 1;43(10):1188-1204.e1.
5. Bioidentical hormone therapy. Menopause & U. Accessed February 18, 2026. https://www.menopauseandu.ca/therapies/bioidentical-hormone-therapy/
6. Johnson KA, Martin N, Nappi RE, et al. Efficacy and Safety of Fezolinetant in Moderate to Severe Vasomotor Symptoms Associated With Menopause: A Phase 3 RCT. *J Clin Endocrinol Metab*. 2023;108(8):1981-1997. doi:10.1210/clinem/dgad058
7. Pinkerton JV, Simon JA, Joffe H, et al. Elinzanetant for the Treatment of Vasomotor Symptoms Associated With Menopause: OASIS 1 and 2 Randomized Clinical Trials. *JAMA*. Published online Aug 22, 2024. doi:10.1001/jama.2024.14618
8. Veozah product monograph. Astellas Pharma Canada Inc. Published Dec 2, 2024. Accessed February 18, 2026. https://pdf.hres.ca/dpd_pm/00077931.PDF
9. Lynkuet product monograph. Bayer Inc. Published Jul 23, 2025. Accessed February 18, 2026. https://pdf.hres.ca/dpd_pm/00081155.PDF
10. Menopause management. Centre for Effective Practice. Updated Oct 14, 2025. Accessed February 18, 2026. https://tools.cep.health/tool/menopause-management
11. Chronic Kidney Disease (CKD) Clinical Pathway. Updated Sept 23 2025. Accessed February 18, 2026. https://www.ckdpathway.ca/
12. Pylera product monograph. Laboratoires Juvisé Pharmaceuticals. Revised Aug 23, 2024. Accessed February 18, 2026. https://pdf.hres.ca/dpd_pm/00076786.PDF
13. Fallone CA, Chiba N, van Zanten SV, et al. The Toronto Consensus for the Treatment of Helicobacter pylori Infection in Adults. *Gastroenterology*. 2016;151(1):51-69.e14. doi:10.1053/j.gastro.2016.04.006
14. Anzupgo product monograph. Leo Pharma Inc. Updated Aug 25, 2025. Accessed February 18, 2026. https://pdf.hres.ca/dpd_pm/00081515.PDF
15. Molin S. Update on chronic hand eczema. *Canadian Dermatology Today*. 2024 Jun;5(2):24-27. https://canadiandermatologytoday.com/article/view/5-2-molin
16. Buhl T, Bauer A, Ehst BD, et al. Health-Related Quality of Life in Chronic Hand Eczema in a Phase 2b Trial of Delgocitinib Cream. *Dermatol Ther (Heidelb)*. 2025;15(5):1181-1193. doi:10.1007/s13555-025-01384-4
17. Giménez-Arnau AM, Pinter A, Sondermann W, et al. Efficacy and safety of topical delgocitinib cream versus oral alitretinoin capsules in adults with severe chronic hand eczema (DELTA FORCE): a 24-week, randomised, head-to-head, phase 3 trial. *Lancet*. 2025;405(10490):1676-1688. doi:10.1016/S0140-6736(25)00001-7
18. Oosterhaven JAF, Schuttelaar MLA. Responsiveness and interpretability of the Hand Eczema Severity Index. *Br J Dermatol*. 2020;182(4):932-939. doi:10.1111/bjd.18295
19. Reimbursement recommendation: Delgocitinib (Anzupgo). Canada's Drug Agency. *Can J. Health Tech*. 2025 Dec;5(12). Accessed February 18, 2026. https://www.cda-amc.ca/delgocitinib
20. Lam RW, Kennedy SH, Adams C, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) 2023 Update on Clinical Guidelines for Management of Major Depressive Disorder in Adults. *Can J Psychiatry*. 2024;69(9):641-687. doi:10.1177/07067437241245384
21. Vortioxetine product monograph. Apotex Inc. Updated Mar 7 2025. Accessed February 18, 2026. https://pdf.hres.ca/dpd_pm/00078813.PDF
22. Jensen B, Regier L, Soubolsky A. Depression: Antidepressant comparison chart. RxFiles. Published Jul 2025. https://www.rxfiles.ca/rxfiles/uploads/documents/books/charts.html
23. Leqvio product monograph. Novartis Pharmaceuticals Canada Inc. Revised Aug 19, 2024. Accessed February 18, 2026. https://pdf.hres.ca/dpd_pm/00076736.PDF
24. Dupixent product monograph. Sanofi-aventis Canada Inc. Updated Oct 27, 2025. Accessed February 18, 2026. https://pdf.hres.ca/dpd_pm/00082261.PDF
25. Kerendia product monograph. Bayer Inc. Updated Jan 19, 2026. Accessed February 18, 2026. https://pdf.hres.ca/dpd_pm/00083207.PDF
26. Solomon SD, McMurray JJV, Vaduganathan M, et al. Finerenone in Heart Failure with Mildly Reduced or Preserved Ejection Fraction. *N Engl J Med*. 2024;391(16):1475-1485. doi:10.1056/NEJMoa2407107
27. Yasuda S, Kaikita K, Akao M, et al. Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease. *N Engl J Med*. 2019;381(12):1103-1113. doi:10.1056/NEJMoa1904143
28. Andrade JG, Aguilar M, Atzema C, et al. The 2020 Canadian Cardiovascular Society/Canadian Heart Rhythm Society Comprehensive Guidelines for the Management of Atrial Fibrillation. *Can J Cardiol*. 2020;36(12):1847-1948. doi:10.1016/j.cjca.2020.09.001
29. Bainey KR, Marquis-Gravel G, Belley-Côté E, et al. Canadian Cardiovascular Society/Canadian Association of Interventional Cardiology 2023 Focused Update of the Guidelines for the Use of Antiplatelet Therapy. *Can J Cardiol*. 2024;40(2):160-181. doi:10.1016/j.cjca.2023.10.013
30. 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
31. McMurray JJ, Packer M, Desai AS, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. *N Engl J Med*. 2014;371(11):993-1004. doi:10.1056/NEJMoa1409077
32. Berg DD, Braunwald E, DeVore AD, et al. Efficacy and Safety of Sacubitril/Valsartan by Dose Level Achieved in the PIONEER-HF Trial. *JACC Heart Fail*. 2020;8(10):834-843. doi:10.1016/j.jchf.2020.06.008
33. Entresto product monograph. Novartis Pharmaceuticals Canada Inc. Revised Jul 13, 2021. Accessed February 18, 2026. https://pdf.hres.ca/dpd_pm/00062129.PDF
34. Is it heart failure and what should I do? Pocket guide. Canadian Cardiovascular Society, 2021. Available from: https://ccs.ca/pocket-guides/