Don't Sweat It: Consulting RxFiles for Menopause Management

FMF
Family Medicine Forum
Forum en médecine familiale

THE COLLEGE OF FAMILY PHYSICIANS OF CANADA
LE COLLÈGE DES MÉDECINS DE FAMILLE DU CANADA

Taisa Trischuk, BSP, PharmD
Debbie Bunka, BScPharm

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Presenter: Taisa Trischuk

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- **Other:**

  None

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Presenter: Debbie Bunka

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SHARING PERSPECTIVES on MENOPAUSE MANAGEMENT

Rx FILES

Menopause

Updated July 2025

Did you know?

- If higher doses of estrogen are needed to control vasomotor symptoms, higher doses of progestogen are required to **adequately protect the uterus from endometrial cancer** (in women who have not had a hysterectomy). See page 3 for doses (e.g. **ESTRACE** 2mg daily pairs with medroxyprogesterone 5mg daily). **Low dose vaginal estrogen does not require a progestogen.**
- The **levonorgestrel IUD MIRENA** has data for 5 years of endometrial protection (off-label).[6,7] Candidates include those who require contraception, do not tolerate an oral progestogen, prefer the convenience, or have perimenopausal heavy menstrual bleeding. It can be used for patients on any estrogen dose.
- Vaginal estrogen is minimally absorbed at commercially available low doses. **Vaginal estrogen does not appear to increase the risks of harms such as breast cancer, endometrial cancer, or cardiovascular disease.**[11] Therapy can be continued for as long as benefit is perceived by the patient.[10] See page 7 for more info.
- **The buttocks** is a preferred application site for an estradiol transdermal patch due to ↑ privacy & ↓ skin irritation.[5]
- Although less effective than hormones, **select SSRIs and SNRIs** have shown benefit for treating vasomotor symptoms (see page 4). **The dose needed is typically lower** than for anxiety or depression (& higher doses are often no more effective).

TABLE OF CONTENTS

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90% of women enter menopause between the ages of 45 to 56 years.[8]
50% of women believe that menopause is still a taboo subject (and awareness of the full spectrum of symptoms – such as urinary tract infections – is low).[9]

Who is a candidate for systemic menopausal hormone therapy (MHT)?

Women (40+ yrs) who used hormone therapy in **1999**.[USA,4] **~22%**

WHI trial published in 2002 on potential benefits & harms of hormones

Women (40+ yrs) who used hormone therapy in **2010**.[USA,4] **~5%**

Systemic hormone therapy is **very effective** for treating vasomotor symptoms (e.g. ↓ hot flashes by 70-95%);[12] however, there are potential harms.[13] Canadian 2021 guidelines recommend hormone therapy as first line for women under the age of 60 or within 10 years of their last menstrual period (if no contraindications).[1] The back page of this newsletter helps weigh the benefits and risks of treatment.

Estrogens & Progestogens: Individualizing Systemic Therapy

- Starting at a low initial estrogen dose has fewer side effects and can ↓ cost, but may take 4-6 weeks to show benefit.[1] If severe symptoms, starting at a moderate dose can be an option for faster benefit (e.g. 2-4 weeks);[1] after treatment success, attempt to **find the lowest effective dose to reduce the risk of harm.**[14]
- **Continuous dosing** of a progestogen is generally preferred in women who have had at least 12 months of amenorrhea. **Cyclic dosing** (12-14 days/month) may be preferred during the menopause transition (to reduce breakthrough bleeding).
- **Combination products** (estrogen + progestogen) are useful to ↑ adherence, but can limit dose flexibility.
- **Micronized progesterone** PROMETRIUM can be sedating, which is desirable for some, but problematic to others. Patients should usually take it at bedtime.

Turn to page 3 for more

HORMONE THERAPY FACTS

Ask about vaginal health in women aged 45+ years.

Women who have genitourinary menopause symptoms:[1] **~50%**

Women who ask a healthcare provider for help with these symptoms:[3] **~25%**

At least half of patients do not realize that genitourinary symptoms of menopause (such as vaginal dryness, pain during sex, or recurrent UTIs) are treatable/preventable.[3] Normalize asking about vaginal health; one opportunity is when someone aged 45+ years is being screened with a Pap test. For treatment options, see page 3.

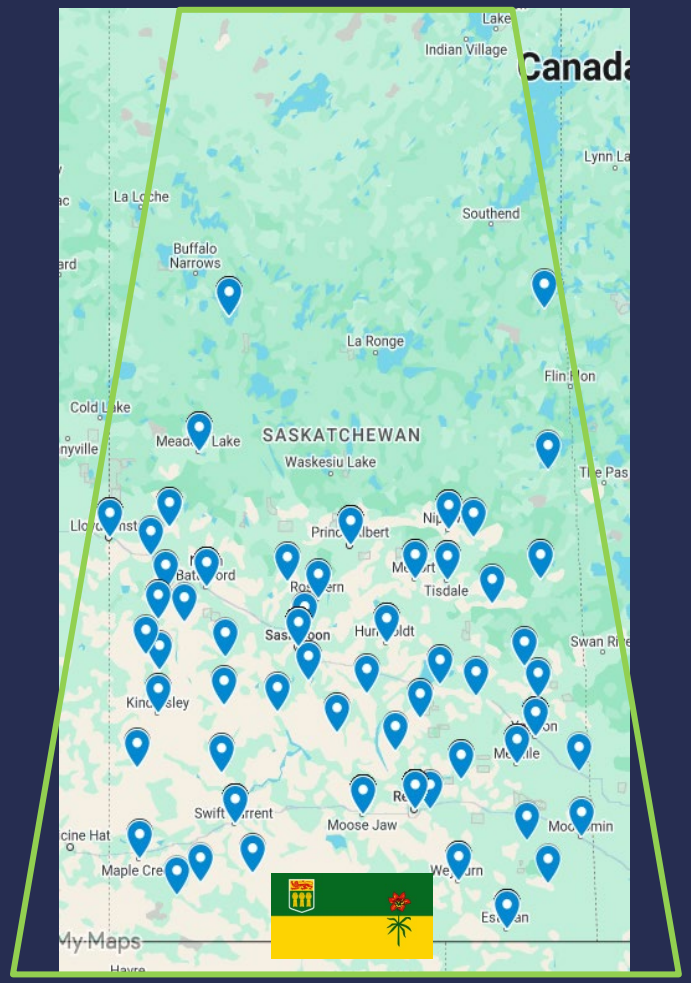
MHT=menopause hormone therapy **UTI**=urinary tract infection **WHI**=Women's Health Initiative

References and newsletter available @ www.rxfiles.ca/menopause

References available:

www.RxFiles.ca/menopause

MENOPAUSE: ACADEMIC DETAILING VISITS



SK Health Care Providers Detailed [Nov 2023 – Feb 2025] 1,154	
Family Physicians	466
Medical Residents	139
Nurse Practitioners	175
Pharmacists	252
Nurses	31
Students	19
Other	72

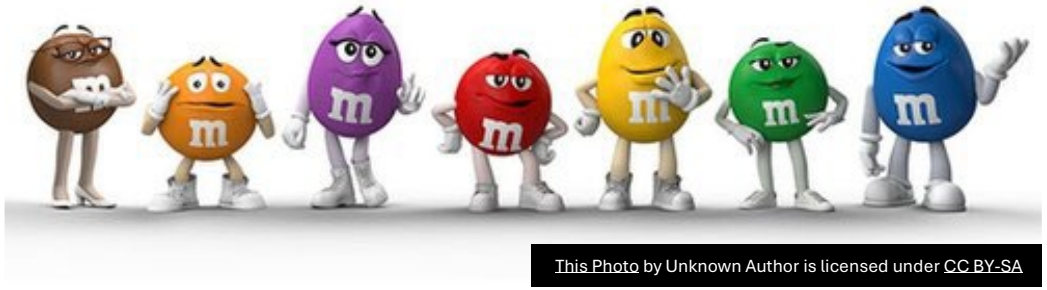
LEARNING OBJECTIVES

Through case-based discussions:

- **Individualize** systemic menopause hormone therapy regimens and utilize **non-hormonal therapy** options when appropriate.
- Discuss a personalized approach when choosing treatment options for **genitourinary syndrome of menopause**.
- Examine available evidence to address patient questions around **symptom management and treatment expectations** during the menopause transition.

Case 1: Non-Hormonal

Did someone say KNDy?



Non-Hormonal Therapy for VMS Control

PAGE 4: RxFiles Menopause Newsletter: www.rxfiles.ca/menopause

	Generic Name; TRADE Name	Dosing for VMS	$/30d	Adverse Events AE Drug Interactions DI	Efficacy for VMS vs placebo ↓ VMS 20-50%
NK3 θ	**Fezolinetant VEOZAH** ✗ ⊗ New: elinzanetant **LYNKUET** ✗ ⊗	45mg po daily	$210	AE: abd pain, diarrhea, back pain, insomnia. DI: CYP1A2.	**↓ 61-64%**: hot flash frequency. Onset within 1 wk, majority of effect at week 6. SKYLIGHT 1 & 2
SSRI	**Paroxetine PAXIL, g** **USA**: 7.5mg cap HS **BRISDELLE**	10-20mg po daily	$20	See Rxfiles: Antidepressants, pg 191 • AE: nausea, HA, drowsiness, dizziness, dry mouth, ↓ libido, (SNRI ↑ AE vs SSRI). • DI: paroxetine & fluoxetine: ↓ tamoxifen levels due to CYP2D6 inhibition (contraindicated).	SSRI/SNRI **↓ 27-65%:** composite of hot flash severity & frequency.[4,28] Often onset in days (vs weeks for depression).[31]
SSRI	**Citalopram CELEXA, g**	10-20mg po daily	$14		
SSRI	**Escitalopram CIPRALEX, g**	10-20mg po daily; See comments.	$20		
SNRI	**Venlafaxine EFFEXOR XR, g**	37.5-75mg po daily	$15		
SNRI	**Desvenlafaxine PRISTIQ ER, g** ✗ ⊗	100-150mg po daily	$92		
Gabapentinoid	**Gabapentin NEURONTIN, g**	Initiate 100-300mg HS, ↑ 100mg q3-4 days up to 900mg HS.[SOGC'21]	$13-15	See RxFiles: Seizures, pg 171 • AE: dizziness, drowsiness. • DI: ↑ risk of respiratory depression with opioids.[42]	Gabapentin **↓ 45-71%:** hot flash frequency;[34,35] onset within 1 week.[35]
Gabapentinoid	**Pregabalin LYRICA, g**	150-300mg po HS	$24		
Other	**Oxybutynin DITROPAN, g**	2.5-5mg po BID	$14	• AE: dry mouth 52%,[39] GI upset, constipation, blurred vision.	**↓ 60-77%:** hot flash frequency, onset ~1 wk.[40]

Clonidine, g: 0.025-0.05mg po BID; $15 Not generally recommended due to AE (e.g. dizziness, hypotension, sedation) & less effective than other non-hormonal options: **↓ VMS 20-40%;**[4,28,38, SOGC'21, NAMS'23] Discontinue slowly to avoid withdrawal symptoms.

CASE 1

- *My patient is requesting a trial of a medication for hot flashes that she read about on a breast cancer survivor forum.*

- *Can you help me to figure this out? Is it available in Canada?*

- *If so, do you recommend I taper off her SNRI before starting this? Or can she use both therapies?*

CASE 1 continued…

55-year-old cancer survivor: 2019 invasive ductal breast ca, ER/PR positive, bilateral mastectomy & total reconstruction

- plans to continue letrozole 2.5mg once daily until 2029

- Jan 2020: experiencing 20 to 30 bothersome hot flashes per day; initiated on gabapentin 200mg HS
- Oct 2020: switched to venlafaxine 37.5mg daily
- Dec 2021: dose increased to 75mg daily
- Feb 2024: dose increased to 112.5mg daily
- Mar 2025: having 8 – 12 hot flashes per day; patient requesting new medication

Neurokinin Receptor Antagonists

- Fezolinetant VEOZAH

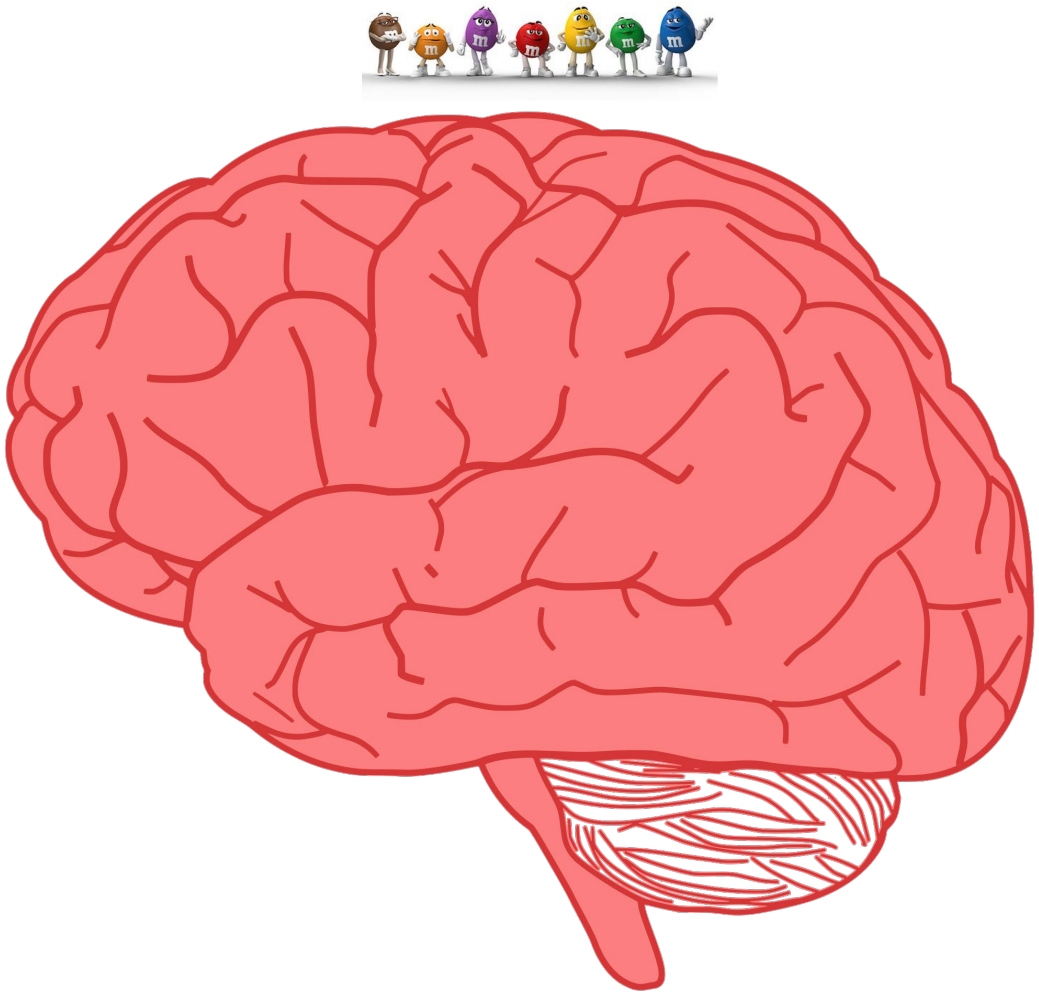
- Marketed in Canada as of March 2025 (available to Rx)
- Usual dose: 45mg tablet taken once daily
- Est cost for 30d supply: $210

- Elinzanetant LYNKUET

- Marketed in Canada as of July 2025 (not yet available)
- Usual dose: 120mg (2x60mg caps) taken once daily at bedtime
- Est cost: unknown

KNDy Neurons & NKR Antagonists … what we think we know about the mechanism of action

- KNDy neurons are in the hypothalamus – play a role in regulating body temperature
- KNDy neurons are influenced by estrogen levels
- As estrogen levels decline in menopause, KNDy neurons become more active and elevate neurokinin B levels, which can disrupt the body's temperature regulation system
- NKR (neurokinin receptor) antagonists block the action of neurokinin B at its receptor, thus reducing the activity of KNDy neurons and alleviating hot flashes



Can you use fezolinetant in combination with venlafaxine? Yes.

- All trials thus far have assessed fezolinetant alone vs placebo
  - **VENT** trial – recruitment phase; protocol states patients stable on SSRI/SNRI can remain on this therapy throughout the study
- Work via different mechanisms
  - ? synergistic benefit for VMS
  - ? additive side effects / safety concerns
- No known pharmacokinetic interactions identified for her med list
  - be aware that significant DI's do exist between fezolinetant and strong CYP1A2 inhibitors (e.g. fluvoxamine); use is contraindicated

Should you use fezolinetant in combination with venlafaxine? It depends.

- Consider: efficacy & safety data lacking for combo, pill burden / cost
- Consider: patient may rely on SNRI for other benefits like mood / pain

- Fezolinetant: onset of effect in first week; majority of effect by week 6
- Recommend to taper off SNRI once fezolinetant is established
  - Goal: find lowest effective dose of SNRI or stop SNRI if no additional benefit with combo

What do we know about using fezolinetant in breast cancer survivors using endocrine therapy?

- Evidence free zone
- No available data yet reporting efficacy or safety specifically in breast cancer survivors
- Clinical trials are underway:
  - **e.g. HIGHLIGHT 1 (Phase III)**: randomized, placebo-controlled trial enrolling ~540 women with stage 0–3 hormone receptor-positive breast cancer on adjuvant endocrine therapy, duration: 52 weeks

Health Canada Veozah. https://pdf.hres.ca/dpd_pm/00077931.PDF
HIGHLIGHT 1: https://clinicaltrials.gov/study/NCT06440967
OASIS 4 trial (elinzanetant).DOI:10.1200/JCO.2025.43.16_suppl.508

How effective is fezolinetant?

SKYLIGHT 1 & 2:
Randomized to fezolinetant 30 or 45mg daily vs placebo (n=1022)

What is the average decrease in frequency of moderate to severe hot flashes after 12 weeks of fezolinetant?[3-6]

Participants in clinical trials	▪ postmenopausal and healthy but experiencing ≥ 7 moderate to severe hot flashes per day, ages 40-65 ▪ without a history of breast or gynecologic cancer or a chronic condition such as cardiovascular disease

# hot flashes per day	baseline **11**	placebo **4 fewer**	fezolinetant 45 mg **7 fewer**

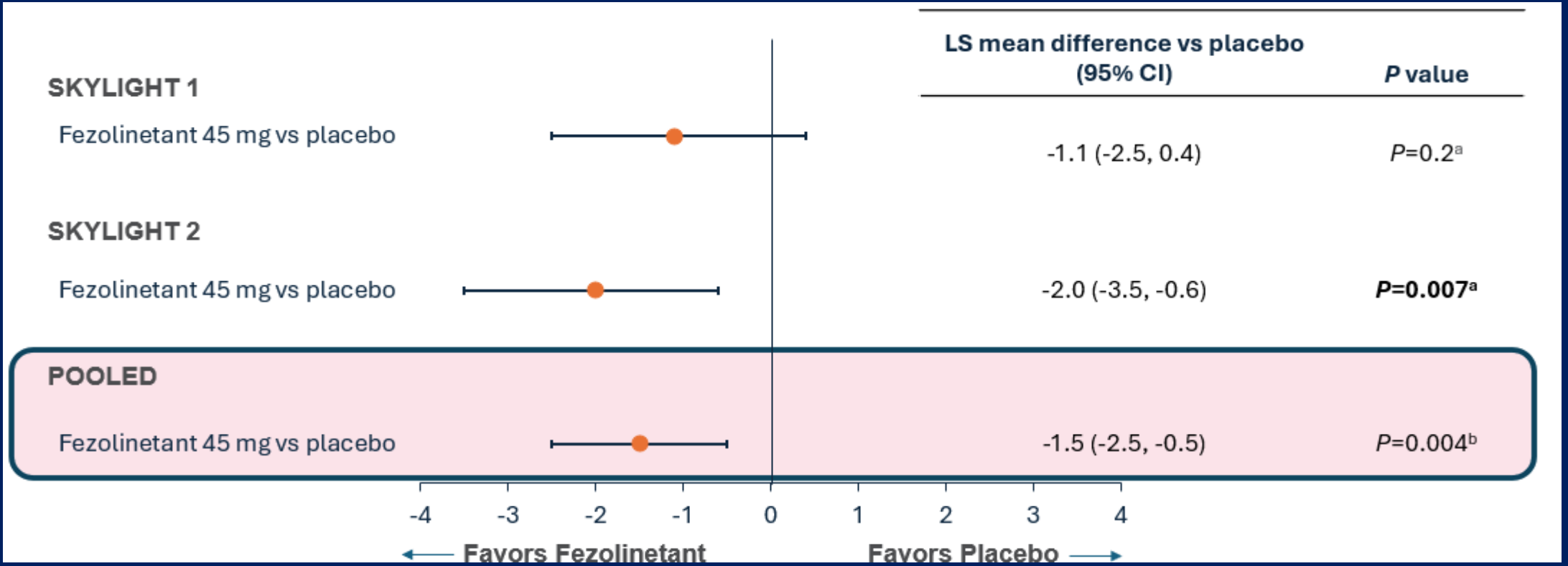
What proportion of participants are moderately or much better?[3]

placebo	fezolinetant 45 mg
~40%	~70%, NNT ~3

BC Provincial Academic Detailing 2025: Medications for Menopause VMS and GSM
Lederman S et al. **SKYLIGHT 1**. *Lancet* 2023. PMID:36924778
Johnson K et al. **SKYLIGHT 2**. *J Clin Endocrinol Metab* 2023. PMID:36734148

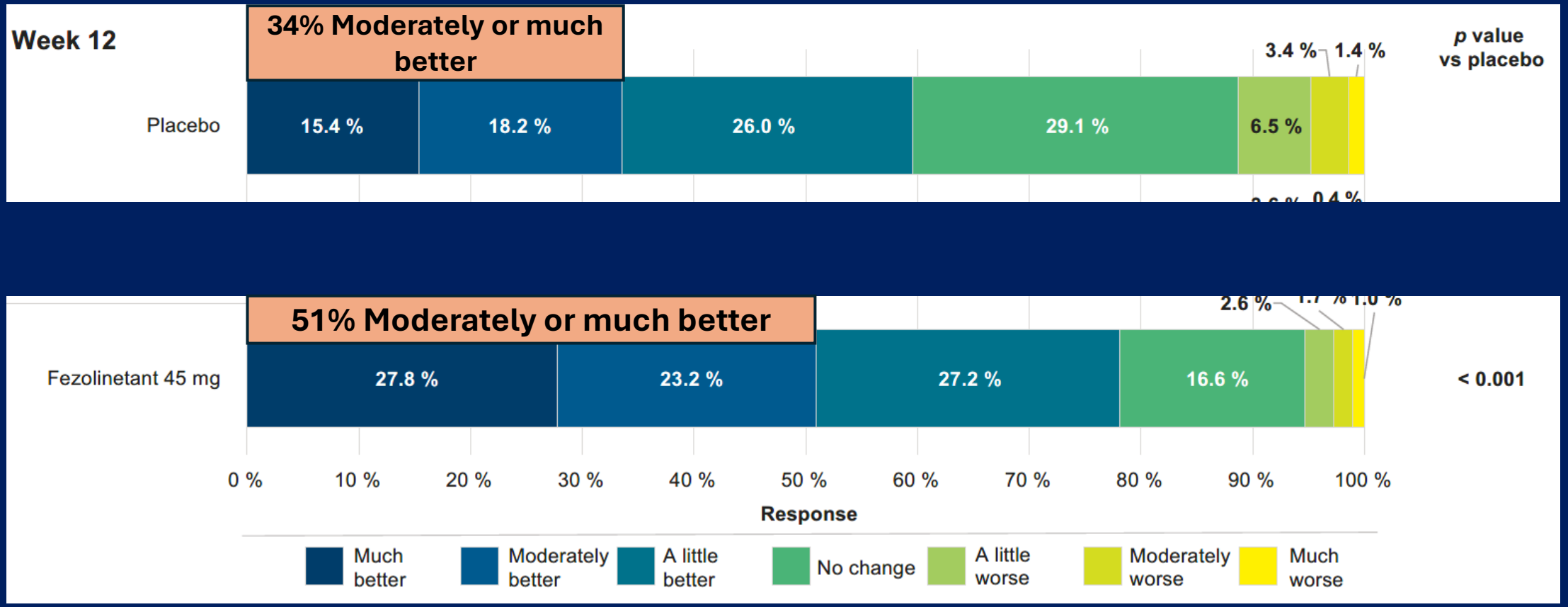
Will fezolinetant help with sleep? It may.

SKYLIGHT 1 & 2 Pooled Data at Week 12: **PROMIS SD SF 8b** (Patient-Reported Outcomes Measurement Information System Sleep Disturbance – Short Form 8b)



Shapiro C M M, et al. Effect of fezolinetant on sleep disturbance and impairment during treatment of vasomotor symptoms due to menopause. Maturitas. 2024 Aug;186:107999.

SKYLIGHT 1 & 2 Pooled Data: Patient Global Impression of Change in Sleep Disturbance



Shapiro C M M, et al. Effect of fezolinetant on sleep disturbance and impairment during treatment of vasomotor symptoms due to menopause. Maturitas. 2024 Aug;186:107999.

Is it well-tolerated?

Usual side effects?

Treatment discontinuation due to adverse effects:

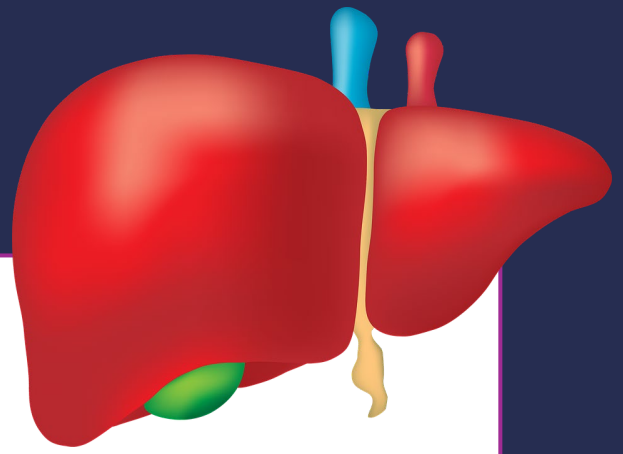
- similar between 45mg dose and placebo (<5% of participants)[SKYLIGHT-4]

Adverse effects: product monograph

- abdominal pain & diarrhea
- back pain
- insomnia

Health Canada Prescribing Information Veozah. https://pdf.hres.ca/dpd_pm/00077931.PDF
US FDA Review 2023 Veozah. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2023/216578Orig1s000MedR.pdf

Specific liver monitoring instructions



<u>Baseline bloodwork</u>: serum ALT, AST, ALP, and bilirubin (total and direct)

Do not start fezolinetant	ALT or AST or total bilirubin is ≥2x ULN
Proceed with caution	ALT or AST is between >1.5x ULN

<u>Monitoring</u>: monthly for first 3 months, then at 6 months and at 9 months

Discontinue fezolinetant	ALT or AST >5x ULN, <u>OR</u> ALT or AST >3x ULN and total bilirubin >2x ULN
Increase monitoring frequency until resolution	ALT or AST is >3x ULN

Counsel patients to report new onset fatigue, decreased appetite, nausea, vomiting, pruritus, jaundice, pale feces, dark urine or abdominal pain.[FDA, EMA]

- <u>Discontinue fezolinetant immediately</u>; elevated LFTs and/or symptoms of liver injury are generally reversible after discontinuation of fezolinetant.

VEOZAH® (fezolinetant) Product Monograph. Astellas Pharma Canada Inc. Dec. 2, 2024; US FDA Drug Safety Communication. Veozah. Dec 2024; European Medical Agency (EMA) Drug Safety Communication. Veozah. Dec 2024. https://www.ncbi.nlm.nih.gov/books/NBK608428/

CASE 1: revisited...

- Baseline bloodwork normal
- Started fezolinetant 45mg once daily in June 2025
- Patient remained on venlafaxine 112.5mg once daily
- Aug 2025: phone follow-up with pharmacist
  - Patient is very pleased with her response to therapy; down to 3 or 4 hot flashes/day
    - *“I am able to wear long-sleeved shirts again without overheating”*
    - *“My husband is thrilled to not have the fan blowing full blast at night”*
    - *“I’m sleeping well again”*
  - Discussed plan to taper venlafaxine dose over 4 weeks
  - No side effects noted
  - Plan in place to continue LFT monitoring

CASE 1: continued...

- Sept 2025: in-person appt with physician
  - venlafaxine taper did not go as planned
  - in clinic to discuss ongoing vaginal discomfort that has progressively been getting worse (dryness, pain with intercourse)
  - physical assessment confirmed GSM and ruled out other causes

Genitourinary Symptoms of Menopause

- Non-hormonal options are first-line.
- Discuss lubrication for love-making and moisturizers for maintenance.
- Some patients may prefer the viscosity of one agent over another; however, all considered equivalent.

Generic / TRADE	Usual (Equivalent) Dose	Cost/30d
Vaginal Moisturizer OTC ✗ ⊗ *many, examples include: REPLENS gel $16; GYNATROF gel $29; REPAGYN ovule $37	Apply vaginally HS 2-3x/ week	$16-37 [10 applications]
Vaginal Lubricant OTC ✗ ⊗ e.g. KY JELLY gel $8	Apply vaginally PRN before sex	$5-10/tube

Can vaginal estrogen be utilized in women with a history of breast cancer?

- International guidelines support offering women low-dose vaginal estrogen (preferentially vaginal tablets, soft gels, or rings over vaginal creams).
- Systematic review / meta-analysis[2025] of observational studies in breast cancer survivors with GSM, users of vaginal estrogen:
  - **no increased risk of breast cancer recurrence** (OR: 0.48, 95% CI 0.23-0.98)
  - **no increased risk of overall mortality** (OR: 0.46, 95% CI 0.42-0.49)
- For individuals taking an aromatase inhibitor, decisions should involve consultation with oncology.

Beste ME, et al. Am J Obstet Gynecol. 2025 Mar;232(3):262-270.e1. PMID: 39521301.

Vaginal Estrogen (low-dose)

CREAM	**Conjugated equine estrogen PREMARIN** 0.625mg/g vaginal cream (rose-scented)	0.5-2g vaginally HS x 2 weeks, then ↓ to 1-3x per week	$10 ($34/30g)
	Estrone ESTRAGYN 1mg/g vaginal cream (unscented)	0.5-2g vaginally HS x 2 weeks, then ↓ to 1-3x per week	$10 ($48/45g)
RING	**Estradiol-17β ESTRING** 2mg vaginal ring (releases 7.5mcg/day) Note: USA **FEMRING** releases 50-100mcg/day for VMS	Insert 1 ring vaginally q 90days	$32 ($96 up front)
TAB	**Estradiol-17β VAGIFEM** 10mcg vag tab	1 tab vaginally HS x 2 weeks, then ↓ to 1-3x per week	$30-70
	Estradiol-17β IMVEXXY 4, 10mcg softgel		$27-58

PRACTICE POINT

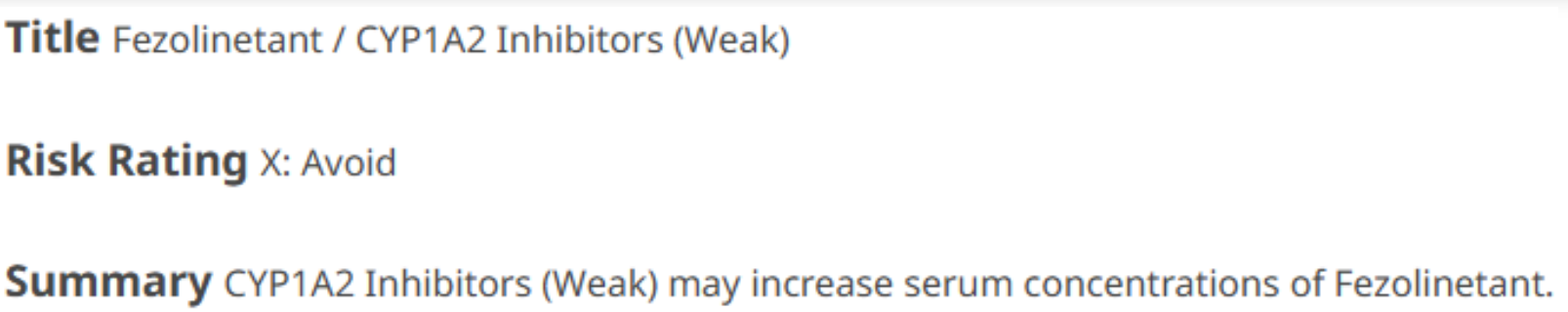
Vaginal estrogen can be used together with systemic estrogen in women who have both VMS and GSM.

Canadian Family Physician Article (RxFiles 2024): How to help patients navigate GSM

RxFiles Menopause Newsletter pg 3 & 6: MHT Drug Comparison Chart & Efficacy and Safety of MHT

Can you use fezolinetant in combination with vaginal estrogen? Yes.

Drug interaction checker: (UpToDate LexiDrug)



Overall, systemic absorption is minimal with any low-dose vaginal preparation when used according to directions and generally remained in the normal post-menopausal range.[NAMS'20]

Therefore, this is not a clinically important drug interaction.

RxFiles Menopause Newsletter pg 7: Menopause FAQs

The NAMS 2020 GSM Position Statement Editorial Panel. Menopause 2020;27:976-92.

Case 2: Menopause Hormone Therapy

MHT - Systemic

CASE 2

- *44 year-old woman, with an intact uterus, who has been having consistent night sweats over the past few months.*
- *Her primary complaints are drenching bed sheets 4 to 5 nights a week, sleep disruption, increasing inattention (brain fog), ++ irritability with husband and teenagers.*
- *I am likely going to prescribe therapy, but I am hopeful you could meet with her first to discuss best options and provide your recommendation, as she is quite concerned about hormonal risks.*

CASE 2

- Mostly consistent periods; manageable flow
- Using venlafaxine 112.5mg daily x 8 years for mood
- 20-year history of smoking ½ ppd; quit 2019, recently restarted vaping nicotine

- Family hx: no breast cancer, no endometrial cancer, two grandparents with stroke history; her sister (2 years older) experienced a DVT suspected due to CHC

- Husband had a vasectomy 12 years ago

Who is a candidate for systemic MHT?

✓ Consider MHT

- Age <60yrs or <10yrs since LMP and low risk (no cautions or contraindications)

✕ MHT Contraindicated

- Unexplained vaginal bleeding
- Acute liver disease
- Clotting disorder (e.g. factor V Leiden)
- Hx of CHD (CAD, stroke, TIA, unprovoked VTE, PAD) or at high-risk of CHD*
- Personal hx of estrogen-dependent CA (breast, endometrial, ovarian) or at high-risk of breast CA**
- Moderate risk of CHD*/breast CA** and age ≥60yrs and ≥10yrs since LMP

RxFiles Menopause Newsletter pg 1 & 2: Cover page and Menopause Overview

Who is a candidate for systemic MHT?

? MHT Cautioned	
• Moderate risk of CHD* and/or CV risk factors (smoking, HTN, DM, dyslipidemia, obesity) in ♀ age <60yrs or <10yrs since LMP • Migraine with aura • Hx of gallstones	**Consider transdermal estrogen.** *Expert opinion. Observational data suggest transdermal may ↓ risk of VTE (RR 0.61; 0.53-0.71), stroke (RR 0.81; 0.68-0.97) and gallstones (RR 0.79; 0.74-0.84) vs oral estrogen.* NAMS '22, 20-22
• Moderate risk of breast CA** in ♀ age <60yrs or <10yrs since LMP	**Consider non-hormonal tx.** *MHT 2nd line after individualized risk assessment.* Expert opinion. NAMS '22, 69, 70
• Age ≥60yrs and ≥10yrs since LMP	**Consider non-hormonal tx.** *MHT 2nd line after individualized risk assessment.* Expert opinion. NAMS '22

See RxFiles Menopause FAQs for more information about using MHT in patients who experience migraines.

WHI 2013: Subgroup Analysis
Risk Estimate of using MHT for 5 years; Age 50-59. (per 1000 women)

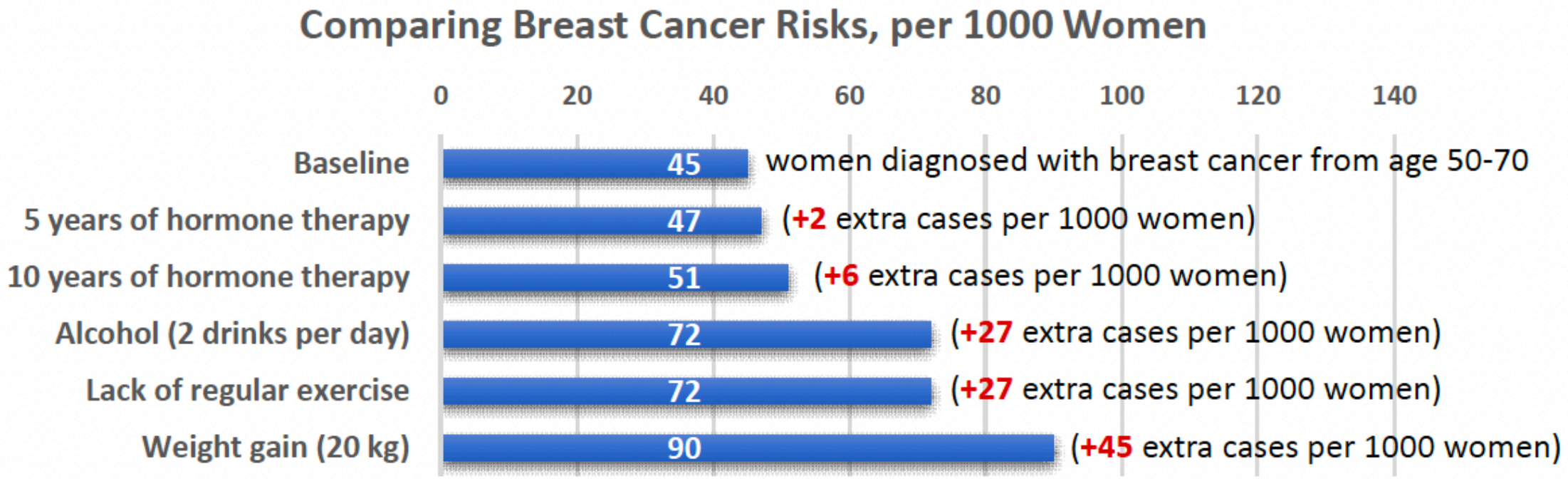
Figure 2. Benefits & Harms of MHT for ♀ aged 50-59 (subgroup analysis)[7]
Data is from the WHI intervention phase (2013 analysis). Note: these subgroup analyses are not statistically significant; however, they are the best available estimates at present.

Inconsistent results across multiple studies

Consistent results across multiple studies

Manson JE, Chlebowski RT, Stefanick ML, et al. Menopause hormone therapy and health outcomes during the intervention and extended post stopping phases of the WHI randomized trials. (WHI 2013). JAMA. 2013;310(13): 1353-1368.

Breast Cancer Risk in Perspective



Note: for women without a uterus and taking only estrogen, the WHI trial showed no increase in breast cancer.[7]

PRACTICE POINT

For women without a uterus and taking only estrogen, the WHI trial showed no increase in breast cancer. WHI 2013

SIGMA Canadian Menopause Society. **MENOPAUSE Times Have Changed. Let's Talk.** Pages 1-9.

Manson JE, Chlebowski RT, Stefanick ML, et al. WHI 2013. JAMA. 2013;310(13): 1353-1368

Checking in with our patient...

- She is agreeable to start menopause hormone therapy and would like to hear about the options.
  - She emphasized desire for lowest possible dose, given her concerns about stroke and clot in family history.
- Optimized on SNRI dose.

Systemic Estrogen

		Generic / TRADE	Initial & Max Dosing	Cost/30d
ORAL		**Conjugated equine estrogen PREMARIN** 0.3, 0.625, 1.25mg tab	**Initial**: 0.3-0.625mg po daily **Max**: 1.25mg po daily	$17-18 $18
ORAL		**Micronized Estradiol-17β ESTRACE, g** 0.5[g], 1[g], 2[g] mg tab	**Initial**: 0.5-1mg po daily **Max**: 2mg po daily	$15-18 $24
TRANSDERMAL	PATCH	**Estradiol-17β** [matrix patch – can cut to ↓cost] ☎ ▼ **ESTRADOT** (generic [g] = Sandoz-Estradiol Derm) 25, 37.5, 50[g], 75[g], 100[g] mcg/day patch	**Initial**: 25-50mcg 2x/wk (e.g. M&F) **Max**: 75-100mcg patch 2x/wk *ESTRADOT = smallest patch size*	$36-37 $39-40
TRANSDERMAL	PATCH	**Estradiol 17β CLIMARA** [matrix patch – can cut] 25, 50, 75mcg/day patch ☎ ▼ See: BC Children's cutting patches	**Initial**: 25-50mcg patch weekly **Max**: 75mcg patch weekly	$33-34 $36
TRANSDERMAL	GEL	**Estradiol-17β DIVIGEL** ☎ ▼: 0.25, 0.5, 1mg gel sachets (0.1%)	**Initial**: 0.25mg [1 sachet] daily to right or left upper thigh (alternating) **Max**: 1.25mg [1 sachet] daily	$40 $40
TRANSDERMAL	GEL	**Estradiol-17β ESTROGEL** 0.06% gel pump ☎ ▼	**Initial**: 1 pump [0.75mg estradiol] to one or both arms daily (wait 2 min before putting on clothes)	$57

DO NOT apply to breast. **AVOID** skin-to-skin transfer.

PRACTICE POINT

Guidelines and experts recommend transdermal products as the preferred treatment in those with CV risk factors, based on observational data.

RxFiles Menopause Newsletter pg 3: Menopause Hormone Therapy & Efficacy

Additional Resource- Canadian Menopause Society: Systemic MHT Equivalency Table

Systemic Progestogen

- A **progestogen is required** for all women with a uterus & on systemic estrogen to decrease the risk of endometrial cancer.

	Generic / TRADE	Usual Dosing	Cost/30d
ORAL	**Medroxyprogesterone** PROVERA, g 2.5$, 5$, 10$ mg tab	**If under the max estrogen dose**: 2.5mg po daily or cyclic: 5mg daily 12-14 days each month **If on max estrogen dose**: 5mg po daily or cyclic: 10mg daily 12-14 days each month	$15
ORAL	**Micronized progesterone** PROMETRIUM, g 100mg cap peanut oil in g Teva, Reddy, Auro. sunflower oil BRAND & g PMS, Sanis.	**If under the max estrogen dose**: 100mg po HS or cyclic: 200mg HS 12-14 days each month **If on max estrogen dose**: 200mg po HS or cyclic: 100mg po AM + 200mg po HS 12-14 days each month	$23-35
ORAL	**Norethindrone** NORLUTATE ✗ ⊗	**Initial / Usual:** 5mg once daily SOGC	$83
IUD	**Levonorgestrel** MIRENA 52mg intrauterine device	**Off-label**: insert q5yr.[50,51,87] Extended intervals unstudied. (Approved in Europe for women on any estrogen dose.)	$7 ($400 up front)

PRACTICE POINT

PROMETRIUM can be sedating, some find this beneficial to help with sleep.

RxFiles Menopause Newsletter pg 3: Menopause Hormone Therapy

Did you know?

- The **levonorgestrel IUD MIRENA** has data for 5 years of endometrial protection (off-label).[6,7] Candidates include those who require contraception, do not tolerate an oral progestogen, prefer the convenience, or have perimenopausal heavy menstrual bleeding. It can be used for patients on any estrogen dose.

PRACTICE POINT

Although data supports the extended use of **MIRENA** up to 8 years for contraception, data only supports the use of **MIRENA** up to 5 years for endometrial protection in women on estrogen therapy.

RxFiles Menopause Newsletter pg 1 & 8: Cover page and Menopause FAQs

Does progesterone alone work for VMS reduction?

- Progesterone monotherapy is off-label for management of VMS.
- No long-term studies have assessed the safety of progestogen-only therapy.
- 1 RCT: n=133, suggests that high-dose, oral micronized progesterone (300mg daily) may decrease frequency/severity of hot flashes compared to placebo in menopausal women (12 weeks)
  - 55% reduction in VMS vs 29% placebo
- Lack of RCT evidence in peri-menopausal population.

RxFiles Menopause Newsletter pg 5: Efficacy and Safety of MHT: Trial Evidence Summary

Hitchcock CL, Prior JC. Oral micronized progesterone for vasomotor symptoms--a placebo-controlled randomized trial in healthy postmenopausal women. Menopause 2012;19:886-93.

Estrogen + Progestogen

- Combination products increase convenience, but can limit dose flexibility with titrating / tapering.

	Generic / TRADE	Strength	Usual Dose	Cost/30d
ORAL	Estradiol-17β + micronized progesterone BIJUVA	1/100mg cap	1/100mg po HS	$40
	Estradiol-17β + drospirenone ANGELIQ	1/1mg tab ✗ ⊗	1 tab po daily	$31
	Estradiol-17β + norethindrone ACTIVELLE	1/0.5mg tab, 0.5/0.1mg LD tab ✗ ⊗	1/0.5mg po daily	$97
	Bazedoxifene + conjugated estrogen DUAVIVE	20/0.45mg tab ✗ ⊗	1 tab po daily	$115
PATCH	Estradiol-17β + norethindrone ESTALIS	50/140mcg, 50/250mcg patch ☎ ▼	1 patch twice/week	$43

PRACTICE POINT

<u>Do not cut</u> the estrogen + progestogen (i.e. ESTALIS) patch.
Note: All **estrogen-only** patches can be cut.

RxFiles Menopause Newsletter pg 3: Menopause Hormone Therapy (MHT)

Checking in on how these options sound to our patient...

- Her values:
  - does not want an IUD; her friend had a previous bad experience with insertion and strong preference for wanting to have monthly withdrawal bleeding
  - did not want a CHC (not even low-dose was desirable to her), due to her sister's DVT experience

Using shared decision making, our patient chose:

Transdermal Patch:

- Estradiol-17B 25ug

Directions:

- Apply one patch twice weekly

Oral progestogen:

- Micronized progesterone 100mg

Directions (cyclic dosing):

- Take 2 capsules (200mg) at bedtime for first 12-14 days of each month

4 Week Follow-Up

- Elated with response; feels fantastic and drenching night sweats have almost dissipated.
- She mentions that day 1 of the patch works best, and then a slow tapering effect that wears off the day before the patch switch.
- Requested a dose increase.

July 2025: Update

- Patient attended clinic appt for PAP
- Cycles are regular, no breakthrough bleeding
- Mood stable on venlafaxine 112.5mg/day
- Not smoking
- Plan: continue MHT, reassess in 1 year

Today we focused mainly on vasomotor symptoms.

Other areas the newsletter can support your discussions: www.rxfiles.ca/menopause

- mood
- decreased libido
- sleep
- memory concerns / brain fog
- bone health
- cardiovascular health
- body weight

Will systemic MHT help with other issues?

? Mood changes	Limited evidence (small RCT data) suggests estrogen therapy may be effective in the management of depressive disorders during **perimenopause.** **See Menopause FAQ pg 9 for details**.
? Sleep disturbances	↑ sleep quality and satisfaction in women with bothersome VMS. Limited evidence suggests that MHT may improve sleep independent of VMS.
✗ Sexual desire	Largely neutral effect on sexual desire. **See Menopause FAQ pg 9 for details.**
✗ Weight gain	Neutral effect on weight; may ↓ visceral fat and ↑ lean body mass.
✗ Cognitive concerns	Neutral in perimenopause and early post-menopause. May ↑ risk of dementia when initiated in older **post-menopausal women ≥65yrs**; **NNT=114**/4 years.[WHIMS] **See Menopause FAQ pg 8 for details.**

PRACTICE POINT

Counselling points:

- Mood and sleep *may* improve.
- Effect on sexual desire is *unpredictable*; some women will note benefit, others won't.
- Effect on weight is neutral.
- Effect on cognition appears neutral when started in women < 65 years.

RxFiles Menopause Newsletter pg 2 & 5: Menopause Overview & Efficacy and Safety of MHT

Key Take-Aways

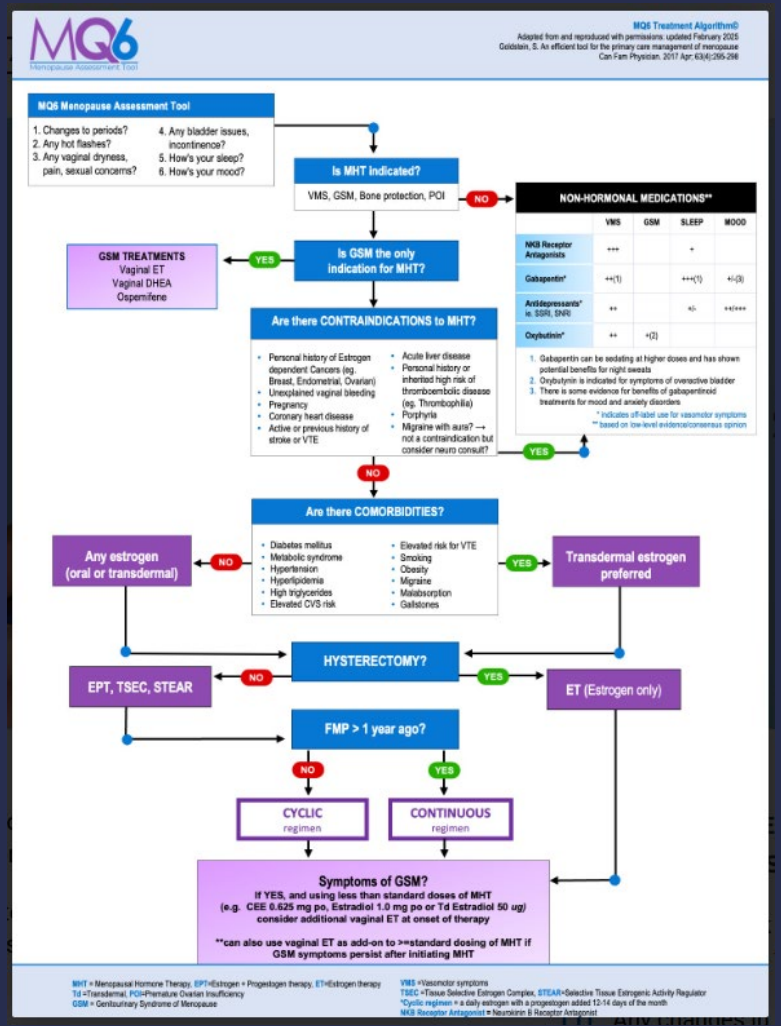
- Newer agents (NK3 antagonists) are available in Canada but are limited by cost and coverage.
- Non-hormonal options can help manage VMS for those unable / unwilling to use systemic MHT.
- Utilize available tools to educate patients and help them put the benefits and harms of MHT into perspective.
- Individualize therapy: choosing between options for systemic MHT or management of GSM is largely based on patient preference, values and comorbidities.
- Most evidence for systemic MHT is for the management of VMS. However, patients may have benefit for other symptoms.

Menopause Quick 6 (MQ6) Assessment Tool

ASSESSING THE MENOPAUSAL PATIENT: THE MENOPAUSE QUICK 6 SCREEN (MQ6)

Key questions to ask perimenopausal and menopausal women in assessing their need for treatment.

1. Any changes in your periods?
2. Are you having any hot flashes?
3. Any vaginal dryness or pain or sexual concerns?
4. Any bladder issues or incontinence?
5. How is your sleep?
6. How is your mood?



www.mq6.ca

RxFiles Menopause Newsletter pg 10: MQ6 algorithm

Other Menopause Resources

- For Providers:
  - SIGMA Pocket Guide
  - MHT Counselling List
    - www.mq6.ca
  - Menopause Rating Scale
- For Patients:
  - NAMS MenoNotes
  - Gynaecology QI Collaboration
  - SOGC Menopause & U

THANK YOU!

PLEASE FILL OUT YOUR SESSION EVALUATION NOW!

FMF
Family Medicine Forum
Forum en médecine familiale

THE COLLEGE OF FAMILY PHYSICIANS OF CANADA
LE COLLÈGE DES MÉDECINS DE FAMILLE DU CANADA

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Extra Slides

Did you know?

Low-dose Vaginal Estrogen:

- Can be used at any age, during the menopause transition or post-menopause.
- Therapy can be continued for as long as benefit is perceived by the patient (may be continued indefinitely).
- Vaginal estrogen does not appear to increase the risk of breast cancer, endometrial cancer, VTE or CV disease.

PRACTICE POINT

When counselling patients, advise that the black box warnings on the product label do not apply to low-dose, vaginal estrogen products. Low-dose vaginal estrogen does not require a progestogen.

Canadian Family Physician Article (RxFiles 2024): How to help patients navigate GSM

RxFiles Menopause Newsletter pg 1 & 7: Cover page and Menopause FAQs

Bioidentical Hormone Therapy (BHT)

RxFiles Menopause Newsletter pg 8: Menopause FAQs

Bioidentical refers to a hormone with the same molecular structure as a hormone that is endogenously produced or "body identical" (See Table 1).

Non-regulated, BHT compounds are not recommended:

- lack of quality control (e.g. chance of overdosing/underdosing, impurities, untested combinations)
- lack of evidence to support their safety and efficacy
- Administered via unstandardized routes (e.g. topical creams, pellets)

Table 1: Regulated hormone products

Synthetic Hormones	Bioidentical Hormones
Estrogens:	
➢ Conjugated equine estrogen (CEE) **PREMARIN**	➢ Estradiol-17β (E2) e.g. **ESTRACE, g; ESTRADOT, g** ➢ Estrone **ESTRAGYN**
Progestogens:	
➢ Medroxyprogesterone acetate (MPA) **PROVERA, g**	➢ Micronized progesterone (MP) **PROMETRIUM, g**

***Highly recommend these articles by Dr. Jen Gunter (August 2025)**

Gunter J. Addressing the Challenges of Online Misinformation. Obstet Gynecol. 2025 Jun 26;146(2):189-194.

https://vajenda.substack.com/p/natural-bioidentical-plant-basedoh https://vajenda.substack.com/p/the-birth-of-bioidentical-tracing

Mood

- Proven therapeutic options for depression (e.g. psychotherapy, antidepressants) remain first-line treatment for peri- and post-menopausal depression.
- Limited evidence suggests that **estrogen (oral and transdermal) may be effective** in the management of depressive disorders during **peri-menopause and early post-menopause**.
- Several small RCTs suggest estrogen in ineffective in treating depressive disorders in late post-menopausal women.
- Data on estrogen + progestogen MHT are sparse and inconclusive.

Sexual Drive

- Available evidence suggests systemic MHT has a neutral effect on sexual desire (may reduce sexual pain).
- If a women has libido concerns, consider transdermal formulations (gel or patch), as oral estrogens may reduce the bioavailability of testosterone.
- Hypoactive sexual desire disorder (HSDD):
  - transdermal testosterone (off-label) in post-menopausal women with HSDD not primarily related to modifiable factors or co-morbidities
  - 1% testosterone gel - starting dose: ½ pump
  - apply to calf, upper outer thigh or buttock
  - total testosterone levels should be assessed in 3 to 6 weeks

RxFiles Menopause Newsletter pg 9: The Menopause Transition & Post-Menopause FAQs