Pharmacotherapy for Menopause[5,7,10,14,16, 22, 25,26, 28-73]

Menopause is a continuum that encompasses several stages, beginning with perimenopause, the years leading up to menopause, often marked by irregular menstrual cycles and VMS/GSM. The menopausal transition can start up to 10 years before the last menstrual period (LMP) and includes both perimenopause and the first 12 months following the LMP.

Menopause pharmacotherapy, including hormone therapy and non-hormonal therapy, should be considered for individuals with moderate to severe menopause-associated symptoms that significantly affect quality of life, such as VMS, GSM, and mood or sleep disturbances. It is particularly appropriate for those < 60 or < 10 years since LMP, provided there are no contraindications. In primary ovarian insufficiency (POI), HRT is recommended, likely at a high dose, to replace estrogen and reduce long-term risks such as osteoporosis and cardiovascular disease. Treatment should continue until the average age of natural menopause (~50 years of age) and aim to mimic physiologic premenopausal hormone levels. Sexual dysfunction in menopausal individuals should be categorized as being related to desire, arousal, pain, and orgasm with Hypoactive Sexual Desire Disorder (HSDD) considered if there is a persistent lack of sexual desire for greater than 6 months that causes distress and cannot be explained by another condition.

Click on the heading to go to the section: GSM Pharmacotherapy, VMS Pharmacotherapy, or HSDD Pharmacotherapy; vaginal estrogen, systemic estrogen, progestogen, or combo MHT

Cautions and Contraindications for MHT

		Possible Solutions
Use MHT with caution	• <60yr or <10yr since LMP with moderate CV risk factors (e.g., smoking, hypertension, diabetes, dyslipidemia, obesity)	• Consider transdermal MHT
	• Migraine with aura	• Consider transdermal MHT
	• History of gallstones	• Use with caution
	• Moderate breast cancer risk	• Individualized risk assessment for MHT
	• Women ≥60yr or >10yr LMP (even with moderate risk)	• Non-hormonal therapy preferred; Individualized risk assessment for MHT
Absolute Contraindication to MHT	**Contraindications to estrogen:** • Unexplained vaginal bleeding • Acute liver disease • Clotting disorders • Uncontrolled hypertension • History/high risk of CHD, stroke, TIA, VTE, PAD • Estrogen-dependent cancers (breast, endometrial, ovarian) or high breast cancer risk • Women with moderate CV or breast cancer risk who are ≥60yr and >10yr LMP • Known or suspected pregnancy **Contraindications to progestogen:** • Undiagnosed abnormal vaginal bleeding • Active breast cancer or personal history of breast cancer	For those with contraindications or higher risk: Consider non-hormonal options: • NK3 receptor antagonists (e.g., fezolinetant) • Gabapentin • Antidepressants • Oxybutynin

Troubleshooting MHT[10,65-69]

Troubleshooting	Adjustment
Vaginal bleeding (May occur if < 6 months on MHT)	• Assess adherence • ↓ ET dose • ↑ PT dose • Switch ET to oral (including combo MHT) from transdermal • Switch PT regimen (continuous to cyclical or vice versa) • Switch PT to LNG-IUS (Mirena®) If > 6 month with bleeding or new onset after 6 months on MHT, consider investigation for abnormal uterine bleeding.
Breast symptoms	• ↓ ET • Switch progestin product • Switch to conjugated estrogen + bazedoxifene (Duavive®) • Switch to vaginal PT • Switch to tibolone (Tibella®) • Trial LNG-IUS (Mirena®) (may still cause breast pain)
Progesterone Intolerance	• Switch to bioidentical PT (i.e., micronized progesterone) • Consider non-hormonal management of VMS with NK antagonist • Consider ET alone in people with hysterectomy • Consider trial of Duavive® or Tibella®
Mood changes, bloating, acne or drowsiness	• Switch progestin product • Switch PT regimen (continuous to cyclical or vice versa)
Headaches	• Consider transdermal ET • Switch progestin product • Switch PT regimen (continuous to cyclical or vice versa)
Sleeping Issues	• Consider micronized progesterone (↑ sedation) • Optimize dosing • Rule out sleep disorders • Consider CBT for insomnia and sleep hygiene
Symptoms persist	• Assess adherence • Switch routes of administration • Optimize dosing • Consider a different treatment option (e.g., NK antagonist) • Look for other diagnosis that may be causing symptoms

Medication	Considerations	Dosing	Cost and coverage (3-month supply) [70-72]
Pharmacological Options for GSM			
Estrogen-based Vaginal estrogen may be added to systemic estrogen therapy and continued at lowest effective dose indefinitely if beneficial.			
conjugated estrogen (CE) (Premarin® Vaginal Cream) 0.625 mg/g	**Hormone Type:** Mixture of conjugated estrogens derived from natural sources including estrone, equilin and 17α-dihydroequilin. **Indication:** Local treatment for GSM **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 8 weeks. **Formulation and Packaging:** • Vaginal cream provides localized effect with minimal systemic absorption • Supplied in 30 g tubes with calibrated applicators • Premarin® is floral scented (may cause sensitivity) • Weakens latex condoms, diaphragms or cervical caps • 0.5 g of cream = 0.3125 mg of CE	**Standard:** 0.5 g of cream (0.3125mg CE) intravaginally/topically: • Loading phase: 0.5 g daily HS x 14 days, then Maintenance phase: 0.5 mg HS 2-3x HS weekly **Troubleshoot:** If symptom control insufficient after 12 weeks: • Consider a loading phase for 28 days or • Consider alternative route/option[11] **Administration:** Apply intravaginally using supplied calibrated applicator. Clean applicator with mild soap and warm water (do not boil) after each use.	**Brand:** $76-203 **Generic**: N/A **ODB:** ✓ **NIHB:** ✓
estrone (Estragyn® Vaginal Cream) 1 mg/g	**Hormone Type:** Estrone, a naturally occurring estrogen bioidentical to endogenous human estrogen **Indication:** Local treatment for GSM **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 8 weeks. **Formulation and Packaging:** • Vaginal cream provides localized effect with minimal systemic absorption • Supplied in 45 g tubes with calibrated applicators • Weakens latex condoms, diaphragms or cervical caps • 0.5 g of cream = 0.5 mg of estrone	**Standard:** 0.5-2 g of cream intravaginally/topically: • Loading phase: 0.5 g daily HS x 14 days, then Maintenance phase: 0.5-2 g 2-3x HS weekly (*can also be dosed in a 21-days on, 7-days off regimen, however not commonly used*) **Troubleshoot:** If symptom control insufficient after 12 weeks: • Consider a loading phase for 28 days or • Consider alternative route/option[11] **Administration:** Apply intravaginally using supplied calibrated applicator. Clean applicator with mild soap and warm water (do not boil) after each use.	**Brand:** $57-354 **Generic**: N/A **ODB:** X **NIHB:** ✓

Medication	Considerations	Dosing	Cost and coverage (3-month supply)
estradiol (Vagifem®) 10mcg vaginal insert	**Hormone Type:** 17β-estradiol, bioidentical to endogenous human estrogen **Indication:** Local treatment for GSM **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 8 weeks. **Formulation and Packaging:** • Provides localized effect with minimal systemic absorption • Vaginal insert (film-coated and 6mm in diameter) • Supplied in preloaded single-use applicators • Less messy than creams • Not intended for oral use • Each box contains 18 inserts	**Standard:** Loading phase: 1 vaginal insert daily HS x 14 days, then Maintenance phase: 1 vaginal insert 2-3x HS weekly **Troubleshoot:** If symptom control insufficient after 12 weeks: • Consider a loading phase for 28 days or • Consider alternative route/option[11] **Administration:** • Inserted intravaginally using supplied preloaded single-use applicator. • Should be inserted as far as comfortably possible into the lower third of the vagina (~2 inches into vaginal canal). • Alternatively, manual insertion without applicator of small end up into the lower third of the vagina (~2 inches into vaginal canal).[11] • If an insert is expelled shortly after insertion, replace with a new one.	**Brand:** $140-193 **Generic:** N/A **ODB:** ✓ **NIHB:** ✓
estradiol (Imvexxy®) 4, 10 mcg vaginal softgel ovule	**Hormone Type:** 17β-estradiol, bioidentical to endogenous human estrogen **Indication:** Local treatment for GSM **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 8 weeks. **Formulation and Packaging:** • Provides localized effect with minimal systemic absorption • Manual insertion (no applicator) • Vaginal ovule that is a tear-shaped, pink softgels packaged in individual blisters. • Less messy than creams. • Not intended for oral use • Each box contains 18 softgel ovules	**Standard:** Loading phase: 1 vaginal insert daily HS x 14 days, then Maintenance phase: 2-3x HS weekly **Troubleshoot:** If symptom control insufficient after 12 weeks: • Consider a loading phase for 28 days or • Consider alternative route/option[11] **Administration:** Wash hands before and after insertion. Manual insertion without applicator of small end up into the lower third of the vagina (~2 inches into vaginal canal).	**Brand:** $114-156 **Generic:** N/A **ODB:** ✓ **NIHB:** ✓

Medication	Considerations	Dosing	Cost and coverage (3-month supply)
estradiol (Estring®) 7.5 mcg/day vaginal ring	**Hormone Type:** 17β-estradiol, bioidentical to endogenous human estrogen **Indication:** Local treatment for GSM **Onset:** Clinical response to improve vaginal and urinary symptoms begins within 2–3 weeks, restoring vaginal and urinary tract tissue to a healthier state with meaningful relief in most patients by 8 weeks. **Formulation and Packaging:** • Silicone elastomer vaginal ring that contains 2 mg of estradiol, releasing 7.5 mcg/day over 90 days • Ring dimensions: outer diameter 55 mm, cross-sectional diameter 9 mm • Each box contains 1 ring	**Standard:** Insert one vaginal ring every 90 days **Titration:** N/A **Max:** Only one ring in place at a time for 90 days with a max duration of **continuous treatment for ~2 years.** **Administration:** • Wash hands before and after insertion. • Insert manually into the upper third of the vagina, compressing the ring b/w thumb and index finger. • Can be worn during most activities (e.g., bathing, exercise, intercourse). • If expelled, rinse with lukewarm water and reinsert. • Ring remains in place continuously for 90 days, then is removed and replaced if therapy continues. • *Removal*: Hook finger into ring and pull down and out.	**Brand:** $134 **Generic:** N/A **ODB:** ✓ **NIHB:** ✓
Selective Estrogen Receptor Modulator (SERM)			
ospemifene (Osphena®) 60 mg **oral** tablet	**Hormone Type:** Bind to estrogen receptors. In the vaginal tissue and mimics estrogen's effects, improving epithelial thickness, mucosal integrity, and pH to relieve GSM symptoms. Unlike systemic estrogen, SERMs selectively avoid stimulation of breast and uterine tissues. **Indication:** GSM **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 8 weeks. **Formulation and Packaging:** • Oral systemic therapy • Blister card of 30 tablets	**Initial:** 60 mg daily **Titration:** N/A **Max:** 60 mg daily **Administration:** Once daily with food (↑ bioavailability) *Benefit if a patient is not comfortable with inserting a vaginal product for GSM. May worsen VMS symptoms initially.*	**Brand:** $175 **Generic:** N/A **ODB:** X **NIHB:** X
Prohormone			
prasterone (Intrarosa®) 6.5 mg vaginal ovules *Controlled substance*	**Hormone Type:** Prasterone is a bioidentical precursor to estrogen and androgen (also known as dehydroepiandrosterone or DHEA). It is not active on its own but is converted locally in vaginal cells into estrogens and androgens. **Indication:** Local treatment of GSM **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 8 weeks. **Formulation and Packaging:** • Local intravaginal therapy • Bullet-shaped ovule; 28 mm long and 8.6 mm in diameter • Packaged in cartons of 28 ovules + 6 reusable applicators	**Initial:** 6.5 mg intravaginally **daily** at bedtime **Titration:** N/A **Max:** 6.5 mg daily **Administration:** • Wash hands before and after. • Can be inserted intravaginally using the provided reusable applicator (1 week per applicator) or fingers. • Insert as deeply as comfortable.	**Brand:** $182 **Generic:** N/A **ODB:** X **NIHB:** X

Pharmacological Options for VMS

Estrogen products relieve menopausal symptoms by replacing declining endogenous estrogen, which helps restore normal function and structure of estrogen-responsive tissues. For genitourinary symptoms, this includes thickening the vaginal and urethral epithelium, increasing vaginal lubrication, reducing pH, and improving blood flow, which collectively reduce symptoms like vaginal dryness, dyspareunia and urinary discomfort. For vasomotor symptoms, estrogen stabilizes the hypothalamic thermoregulatory set point and widens the thermoneutral zone leading to a reduction in frequency and severity of symptoms.

Estrogen-*based*

Oral

In women with an intact uterus, a progestin should also be taken to ↓ the risk of endometrial hyperplasia.

Medication	Considerations	Dosing (Adults)	Cost and coverage (3-month supply)
estradiol (Estrace®) 0.5, 1, 2 mg tablet	**Hormone Type:** Micronized 17β-estradiol, bioidentical to endogenous human estrogen **Indication:** VMS *May be helpful for osteoporosis prevention.* **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks. **Formulation and Packaging:** • Oral systemic therapy • 100 tablet bottles	**Initial:** 0.5 mg daily **Standard:** 1 mg daily **Max:** 2 mg daily *(max dose typically reserved for POI/SM)* **Titration:** If symptom control insufficient after 12 weeks, may ↑ to 1 mg daily **Administration:** Same time each day with or without food.	**Brand:** D/C **Generic:** $25-53 **ODB:** ✓ **NIHB:** ✓
conjugated estrogen (Premarin®) 0.3, 0.625, 1.25 mg tablet	**Hormone Type:** Mixture of conjugated estrogens derived from natural sources including estrone, equilin and 17α-dihydroequilin. *Conjugated estrogen may have ↑ VTE risk compared to estradiol. (Vinogradova, 2019)* **Indication:** VMS *May be helpful for osteoporosis prevention.* **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks. **Formulation and Packaging:** • Oral systemic therapy • 28-card blisters	**Initial:** 0.3 mg daily **Standard:** 0.625 mg daily **Max:** 1.25 mg daily *(max dose typically reserved for POI/SM)* **Titration:** If symptom control insufficient after 12 weeks, may ↑ to 0.625 mg daily **Administration:** Same time each day with or without food.	**Brand:** $54-58 **Generic:** N/A **ODB:** ✓ (LU 398; only 0.625mg covered) **NIHB:** ✓

Medication	Considerations	Dosing (Adults)	Cost and coverage (3-month supply)
Estrogen-based *Transdermal patch (*May be preferred in those at ↑ risk for VTE, migraines or metabolic concerns as it avoids first-pass hepatic metabolism)* [5,10] *In women with an intact uterus, a progestin should also be taken to ↓ the risk of endometrial hyperplasia.*			
estradiol (Estradot®) 25, 37.5, 50, 75, 100 mcg/day patch	**Hormone Type:** 17β-estradiol, bioidentical to endogenous human estrogen **Indication:** VMS *May be helpful for osteoporosis prevention.* **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks. **Formulation and Packaging:** • Transdermal systemic delivery via skin absorption • Matrix-type patches • Can be cut • 8 patches per box • Estradot® 50 and 100 patch size is 5 cm^2 Estradot® 100 patch size is 10 cm^2	**Initial:** 25-37.5 mcg/day patch applied **twice** weekly **Standard:** 50 mcg **Max:** 100 mcg/day patch *(max dose typically reserved for POI/SM)* **Titration:** If symptom control insufficient after 12 weeks, may ↑ dose **Administration:** • Apply patch to clean, dry, intact area of the lower abdomen, lower back, hip or upper buttock (avoid waistline) **twice** weekly (i.e., Monday/Thursday). • Press firmly for 10 sec and apply to same area of body, but different site with each new patch; avoid applying to/near breasts. • If patch falls off, reapply if good adhesion or use a new patch and keep original patch-change schedule.	**Brand:** $143-171 **Generic:** N/A **ODB:** X **NIHB:** ✓
estradiol (Climara®) 25, 50, 75 mcg/day patch	**Hormone Type:** 17β-estradiol, bioidentical to endogenous human estrogen **Indication:** VMS *May be helpful for osteoporosis prevention (≥ 50mcg/day).* **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks. **Formulation and Packaging:** • Transdermal systemic delivery via skin absorption • Matrix-type patches • Can be cut • 4 patches per box • Climara® 25 patch size is 6.5 cm^2 Climara® 50 patch size is 12.5 cm^2 Climara® 75 patch size is 18.75 cm^2	**Initial:** 25 mcg/day applied **once** weekly **Standard:** 50 mcg **Titration:** If symptom control insufficient after 12 weeks, may ↑ dose **Max:** 100 mcg/day patch *(max dose typically reserved for POI/SM)* **Administration:** • Apply patch to clean, dry, intact area of the lower abdomen, lower back, hip or upper buttock (avoid waistline) **once** weekly. • Press firmly for 10 sec and apply to same area of body, but different site with each new patch; avoid applying to/near breasts. • If patch falls off, reapply if good adhesion or use a new patch and keep original patch-change schedule.	**Brand:** $92-104 **Generic**: N/A **ODB:** X **NIHB:** ✓

Medication	Considerations	Dosing (Adults)	Cost and coverage (3-month supply)
Estrogen-based *Transdermal gel (*May be preferred in those at ↑risk for VTE, migraines or metabolic concerns as it avoids first-pass hepatic metabolism)* [5,10] *In women with an intact uterus, a progestin should also be taken to ↓ the risk of endometrial hyperplasia.*			
estradiol (EstroGel® 0.06%) 0.75 mg/pump	**Hormone Type:** 17β-estradiol, bioidentical to endogenous human estrogen **Indication:** VMS *May be helpful for osteoporosis prevention (≥ 2 pumps daily)* **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks. **Formulation and Packaging:** • Transdermal systemic delivery via topical gel absorbed through the skin • 1 pump = 1.25 g of gel = 0.75 mg estradiol • Metered-dose with 64 pumps of full dose per container	**Initial:** 1 pump daily (0.75m g of estradiol) **Standard:** 1-2 pumps daily (0.75-1.5 mg of estradiol) **Titration:** If symptom control insufficient after 12 weeks, may ↑ dose **Max:** 2-3 pumps daily (1.5-2.25 mg estradiol) *(up to 4 pumps daily for POI/SM)* **Administration:** • Once daily spread thinly over a large area of the clean, dry, intact skin of the upper arms and shoulders (both arms if >1 pump). Could also apply to abdomen or inner thighs. • **Apply to same area daily to allow for reservoir to build over time.** [11] • Do not apply on breasts, face, or irritated skin. • Allow to dry completely before dressing and avoid washing the application site for ~1hr after application.	**Brand:** $122-340 **Generic**: N/A **ODB:** X **NIHB:** ✓
estradiol (Divigel® 0.1%) 0.25, 0.5, 1mg sachets	**Hormone Type:** 17β-estradiol, bioidentical to endogenous human estrogen **Indication:** VMS *Also used for GSM and osteoporosis prevention (≥ 1mg daily)* **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks. **Formulation and Packaging:** • Transdermal systemic delivery via topical gel absorbed through the skin • *Can be useful if travelling due to small form factor* • Supplied in unit-dose packets of 0.25, 0.5 and 1 mg estradiol per packet • 30 sachets per box	**Initial:** 0.25 mg daily **Standard:** 0.5-1 mg daily **Max:** 2 mg daily *(max dose typically reserved for POI/SM)* **Titration:** If symptom control insufficient after 12 weeks, dose may be ↑ to 0.5 mg/day or 1 mg/day **Administration:** • Once daily to clean, dry, intact skin of upper thigh. • Spread over an area of about the size of two palms. • **Apply to same area daily to allow for reservoir to build over time.** [11] • Do not apply to breasts, face, or irritated skin. • Allow to dry completely before dressing and avoid washing the application site for ~1hr after application. • Wash hands after use and avoid skin-to-skin contact with others until gel is dry.	**Brand:** $115 **Generic**: N/A **ODB:** X **NIHB:** ✓

Medication	Considerations	Dosing (Adults)	Cost and coverage (3-month supply)
Progesterone products help manage menopausal symptoms primarily by opposing estrogen's proliferative effects on the endometrium (reducing the risk of endometrial hyperplasia) and carcinoma in women with an intact uterus receiving systemic estrogen therapy. While progesterone does not directly treat vasomotor symptoms, it plays a crucial protective role in combined hormone therapy regimens.			
Progestogen-*based* *Oral* **Progestin required for all patients with a uterus and on systemic estrogen therapy to ↓ the risk of endometrial cancer.* *The decision between cyclical vs. continuous progestin regimens depends on the time since the LMP. **Cyclical** regimens may be more appropriate in those where their LMP < 1 year prior to reduce breakthrough bleeding, while **continuous** regimens may be suitable for those preferring amenorrhea or LMP > 1 year prior.* [7]			
micronized progesterone (Prometrium®) 100 mg capsules	**Hormone Type:** micronized progesterone, bioidentical to endogenous human progestin *May have ↑lethargy and ↓VTE, ↓CV and ↓breast cancer risk vs. medroxyprogesterone.* **Indication:** Used as an adjunct to estrogen therapy in women with an intact uterus to ↓ the risk of endometrial hyperplasia and carcinoma associated with estrogen replacement therapy. **Initiation Window:** At the same time as starting systemic ET. **Formulation and Packaging:** • Oral systemic therapy • If peanut allergy, avoid generics: Teva, Reddy and Auro • Sunflower oil used in: Prometrium®, PMS, Sanis and Mantra • In 30- or 100-count bottles **Cyclical regimen**: Causes monthly withdrawal bleeding; can help reduce breakthrough bleeding. **Continuous regimen**: may be more suitable in those preferring amenorrhea and often preferred if LMP > 1yr prior.	The dose of progestin should be proportional to the dose of estrogen. Refer to the Canadian Menopause Society MHT Equivalency Table for additional detail. As a general guide: For Low ET dose: **Cyclical PT:** 200 mg x 12-14 days per month **Continuous PT:** 100 mg qHS For Standard ET dose: **Cyclical PT:** 200 mg x 12-14 days per month **Continuous PT:** 100-200 mg qHS For High ET dose: **Cyclical PT:** 200-300 mg x 12-14 days per month (≥ 200 may be required if ET doses are very high for POI/SM) **Continuous PT:** 200 mg qHS (≥ 200 may be required if ET doses are very high for POI/SM) **Administration:** • With or without food (food can ↑ bioavailability) • 200 mg dose taken as one dose in the evening • 300 mg dose can be divided as 100 mg in the morning (≥ 2hr before breakfast) and 200 mg in the evening If side effects from oral administration, can be administered intravaginally at bedtime. [11]	**Brand:** $104-285 **Generic:** $79-212 **ODB:** ✓ **NIHB:** ✓

Medication	Considerations	Dosing (Adults)	Cost and coverage (3-month supply)
medroxy-progesterone (Provera®) 2.5, 5, 10 mg tablets	**Hormone Type:** medroxyprogesterone acetate, sourced from soybeans **Indication:** Used as an adjunct to estrogen therapy in women with an intact uterus to ↓ the risk of endometrial hyperplasia and carcinoma. **Initiation Window:** At the same time as starting systemic ET. **Formulation and Packaging:** • Oral systemic therapy • In 100-count bottles **Cyclical regimen**: Causes monthly withdrawal bleeding; can help reduce breakthrough bleeding **Continuous regimen**: may be more suitable in those preferring amenorrhea and often preferred if LMP > 1yr prior	The dose of progestin should be proportional to the dose of estrogen. Refer to the Canadian Menopause Society MHT Equivalency Table for additional detail. As a general guide: For Low ET dose: **Cyclical PT:** 5 mg x 10-12 days per month **Continuous PT:** 2.5 mg daily For Standard ET dose: **Cyclical PT:** 10 mg x 10-12 days per month **Continuous PT:** 2.5-5 mg daily For High ET dose: **Cyclical PT:** 10 mg x 10-12 days per month **Continuous PT:** 5 mg daily **Administration:** With or without food (food can ↑ bioavailability)	**Brand:** $26-63 **Generic:** $18-24 **ODB:** ✓ **NIHB:** ✓
Progestogen-based *Intrauterine system (IUS)* **Progestin required for all patients with a uterus and on systemic estrogen therapy to ↓ the risk of endometrial cancer.*			
levonorgestrel † (Mirena®) 52 mg IUS Delivers ~21 mcg/day	**Hormone Type:** levonorgestrel, a synthetic progestin **Indication:** Used as an adjunct to estrogen therapy in women with an intact uterus to ↓ the risk of endometrial hyperplasia and carcinoma. *Option if oral progestin not tolerated, contraception desired or to ↓ bleeding during perimenopause.* **Onset:** Local effects on the endometrium begin shortly after insertion. Amenorrhea and ↓ bleeding typically develop over several months. **Duration of Action:** Typically replaced after 5 years for endometrial protection. **Initiation Window:** Timing of insertion should align with estrogen start (either before or at initiation of estrogen therapy). **Formulation and Packaging:** • T-shaped plastic device with rate-controlling membrane	**Standard:** One IUS inserted once into the uterine cavity by a trained healthcare professional **Titration:** N/A; the device is preloaded and provides consistent release of levonorgestrel over time (no adjustment required if ET dose changes). **Max:** One device at a time. A new device can be inserted after removal of the old device at ~5-year intervals for endometrial protection.	$445 (once per ~5 years) **ODB:** ✓ **NIHB:** ✓

Medication	Considerations	Dosing (Adults)	Cost and coverage (3-month supply)
Selective Tissue Estrogenic Activity Regulator (STEAR) *Oral*			
tibolone (Tibella®) 2.5 mg tablets *No progestin required* *Controlled substance*	**Hormone Type:** Synthetic steroid with tissue-selective estrogenic, progestogenic, and androgenic activity. Tibolone itself is inactive but is converted into three active metabolites with estrogenic, progestogenic and androgenic effects. **Indication:** VMS *May have ↓ vaginal bleeding vs. ET.* *↑ risk of stroke, endometrial cancer and breast cancer.* **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks. **Formulation and Packaging:** • Oral systemic therapy • Blister packs of 28 tablets	**Initial:** 2.5 mg daily **Titration:** N/A **Max:** 2.5 mg daily **Administration:** • Oral tablet, taken whole with water or a drink. • May be taken with or without food. • Do not chew or crush tablets. **Hepatic**: Caution in patients with active or past liver dysfunction or disease. Discontinue if cholestatic jaundice or liver function deterioration occurs during use.	**Brand:** $364 **Generic:** N/A **ODB:** X **NIHB:** X
Fixed-dose Combination *(For patients with an intact uterus)* *Oral* *If renal/hepatic impairment, refer to monograph.*			
estradiol + progesterone (Bijuva®) 1 mg / 100 mg capsules	**Hormone Type:** 17β-estradiol, bioidentical to endogenous human estrogen and micronized progesterone **Indication:** VMS **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks. **Formulation and Packaging:** • Oral systemic therapy • ↓ dosing flexibility, as cannot be divided (split/cut) • Blister packs of 30 capsules	**Initial:** 1 mg / 100 mg daily **Titration:** N/A **Max:** 1 tablet daily **Administration:** In the evening with food.	**Brand:** $107 **Generic:** N/A **ODB:** ✓ **NIHB:** ✓

Medication	Considerations	Dosing (Adults)	Cost and coverage (3-month supply)
estradiol + norethindrone (Activelle®, Activelle® LD) 1 mg / 0.5 mg, 0.5 mg / 0.1 mg tablets	**Hormone Type:** 17β-estradiol (bioidentical to endogenous human estrogen) and norethindrone acetate (NETA; a synthetic progestin) **Indication:** VMS **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks; little difference between the two doses for VMS. **Formulation and Packaging:** • Oral systemic therapy • ↓ dosing flexibility, as cannot be divided (split/cut) • Blister packs of 28 tablets	**Initial:** 0.5 mg / 0.1 mg daily **Titration:** If symptom control insufficient after 12 weeks, may ↑ dose to 1 mg / 0.5 mg **Max:** 1 tablet daily **Administration:** Once daily with or without food.	**Brand:** $296 **Generic:** N/A **ODB:** X **NIHB:** X
estradiol + drospirenone (Angeliq®) 1 mg / 1 mg tablets	**Hormone Type:** 17β-estradiol (bioidentical to endogenous human estrogen) and drospirenone (synthetic progestin with antiandrogenic and anti-mineralocorticoid properties) **Indication:** VMS **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks. **Formulation and Packaging:** • Oral systemic therapy • ↓ dosing flexibility, as cannot be divided (split/cut) • Blister packs of 28 tablets	**Initial:** 1 mg / 1 mg daily **Titration:** N/A **Max:** 1 tablet daily **Administration:** Once daily with or without food.	**Brand:** $89 **Generic:** N/A **ODB:** X **NIHB:** X
conjugated estrogen + bazedoxifene (Duavive®) 0.45 mg / 20 mg tablets *Bazedoxifene is a SERM, selective estrogen receptor modulator* *No progestin required as TSEC mitigates endometrial hyperplasia risk*	**Hormone Type:** conjugated estrogen and bazedoxifene (SERM) which together form a Tissue-Selective Estrogen Complex (TSEC) *Conjugated estrogen may have ↑ VTE risk compared to estradiol.* **Indication:** VMS *May be a preferred option in women with ↑ breast density, breast tenderness or if progestin is not tolerated.* **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks. **Formulation and Packaging:** • Oral systemic therapy • ↓ dosing flexibility, as cannot be divided (split/cut) • Blister packs of 28 tablets	*Do not take with progestogens, additional estrogens, or other SERMs.* **Initial:** 0.45mg / 20mg daily **Titration:** N/A **Max:** 1 tablet daily **Administration:** Once daily with or without food (food may ↑ bazedoxifene absorption, but no dose adjustment necessary).	**Brand:** $314 **Generic:** N/A **ODB:** X **NIHB:** X

Medication	Considerations	Dosing (Adults)	Cost and coverage (3-month supply)
Fixed-dose Combination *(For patients with an intact uterus)* *Transdermal Patch*			
estradiol + norethindrone (Estalis®) 50/140 mcg/day, 50/250 mcg/day transdermal patch	**Hormone Type:** estradiol-17β (bioidentical, endogenous to human estrogen) and norethindrone acetate (NETA; synthetic progestin) **Indication:** VMS **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks **Formulation and Packaging:** • Systemic therapy through matrix-style transdermal patch • Avoid cutting due to insufficient evidence of progestin protection • 50 mcg/140 mcg 9 cm^2 round patch • 50 mcg/250 mcg is a 16 cm^2 round patch • Box contains 8 patches	**Initial:** Apply 1 50/140 mcg/day patch **twice** weekly **Titration:** If symptom control insufficient after several weeks, may ↑ dose from 50/140 mcg/day to 50/250 mcg/day **Max:** 50/250 mcg/day delivered in a twice weekly patch **Administration:** • Apply to clean, dry, intact skin of the lower abdomen or upper buttocks (avoid waistline) **twice** weekly. • Press firmly for 10 sec and apply to same area of body, but different site with each new patch; avoid applying to/near breasts. • If patch falls off, reapply if good adhesion or use a new patch and keep original patch-change schedule.	**Brand:** $178 **Generic:** N/A **ODB:** X **NIHB:** X
Neurokinin-3 receptor antagonists (NK-3 RAs) block the binding of neurokinin B (NKB) to NK-3 receptors on kisspeptin/NKB/dynorphin (KNDy) neurons in the hypothalamus, which are involved in thermoregulation. During menopause, ↓ estrogen leads to ↑ NKB activity, disrupting the body's temperature control and triggering hot flashes. NK-3 RAs, help restore balance in this pathway, reducing the frequency and severity of vasomotor symptoms.			
Neurokinin-3 receptor antagonist *Oral*			
fezolinetant (Veozah®) 45 mg tablet	**Hormone Type:** Non-hormonal **Indication:** VMS **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks *Baseline liver tests (e.g., ALT, AST, ALP, total and direct bilirubin) required before initiation and then again at Month 1, 2, 3, 6 and 9).* Do not start if: - ALT or AST ≥ 2x ULN - Total bilirubin ≥ 2x ULN - Proceed with caution if ALT/AST > 1.5x ULN and < 2x ULN **Formulation and Packaging:** • Oral systemic therapy • Do not crush, chew or split • Blister card of 30 tablets	**Initial:** 45 mg daily **Titration:** N/A **Max:** 45 mg daily **Administration:** Once daily with or without food (food slightly ↓ bioavailability, but not clinically significant). **Renal**: Mild/moderate impairment (CrCl 30-89 mL/min): No dose adjustment Severe impairment (CrCl < 30 mL/min): Contraindicated **Hepatic**: Mild (Child-Pugh A): No dose adjustment Moderate (Child-Pugh B): Not recommended Severe (Child-Pugh C): Not studied Cirrhosis: Contraindicated	**Brand:** $587 **Generic:** N/A **ODB:** X **NIHB:** X

Medication	Considerations	Dosing (Adults)	Cost and coverage (3-month supply)
Neurokinin-1, 3 receptor antagonists *Oral*			
elinzanetant (Lynkuet®) 60 mg capsule *Health Canada approved, but not commercially available yet	**Hormone Type:** Non-hormonal **Indication:** VMS **Onset:** Symptom relief begins ≤ few weeks; meaningful relief in most patients by 6-9 weeks **Formulation and Packaging:** • Oral systemic therapy • Do not crush, chew or split	**Initial:** 120 mg daily HS **Titration:** N/A **Max:** 120 mg daily HS **Administration:** Once daily with or without food.	**Brand:** pending **Generic:** N/A **ODB:** X **NIHB:** X

Pharmacological Options for HSDD

Currently, only testosterone therapy in postmenopausal women is indicated to address hypoactive sexual desire disorder. It works by enhancing sexual function through actions on the androgen receptors in the brain and genital tissues, increasing sexual desire, arousal, orgasm, and satisfaction. It is not effective in treating vasomotor or genitourinary symptoms. [62]

Testosterone[34,61,62,73] *Transdermal gel*			
Testosterone gel 1% † (Androgel® Pump) 12.5 mg/pump (Androgel® Sachet) 25, 50 mg	**Hormone Type:** Androgen, specifically bioidentical testosterone **Indication:** Supports sexual function, particularly in postmenopausal women with Hypoactive Sexual Desire Disorder (HSDD). It improves sexual desire, arousal, orgasm, pleasure, and ↓ distress associated with low libido. **Onset:** Improvements in sexual function occur within 12-24 weeks. **Duration of Action:** Androgel® is a daily transdermal gel designed for once-daily application, providing stable testosterone levels over 24 hours in men. In women, effects are dose-dependent and must be carefully titrated to not exceed premenopausal physiological levels. **Initiation Window:** There is no fixed initiation window for testosterone therapy in postmenopausal women, but it should only be considered in those diagnosed with HSDD after ruling out other causes. It may be used with or without concurrent estrogen therapy. **Formulation and Packaging:** • Transdermal systemic delivery via topical gel absorbed through the skin • Androgel® Pump contains 60 metered dose pumps • Androgel® Pump delivers 12.5 mg of testosterone/pump • Androgel® Sachet 25 mg and 50 mg delivers the equivalent of 2 and 4 pumps, respectively	**Initial:** • 1/2 pump on posterior calf once daily or • 1/4 of 2 5mg sachet on posterior calf once daily or • **1 pump 3x weekly on posterior calf** *(~1/10 male dose = 6.25 mg of T)* **Titration:** Based on symptom response and total T levels with re-assessment of baseline T levels at 3-6 weeks. **Max:** • Target T levels should remain within the premenopausal range (Total T < 2.8 nmol/L). • Doses resulting in T levels above the female physiological range are not recommended, as they ↑ risk of androgenic side effects (e.g., acne, hirsutism, voice deepening). • Discontinue if no benefit by 24 weeks. **Administration:** • Spread thinly over a small area of the clean, dry, intact skin of the back of the calf. • Do not apply on breasts, face, or irritated skin. • Wash hands and allow gel to dry before dressing.	**Brand:** Pump - $89-540 Sachet - $274-474 **Generic:** Pump - N/A Sachet - $54-306 **ODB:** ✓ (LU 397 male patients for sachets only) **NIHB:** ✓

Medication	Considerations	Dosing (Adults)	Cost and coverage (3-month supply)
Other (5-HT Receptor Modulator) *Oral*			
flibanserin (Addyi®) 100 mg tablet	**Mechanism:** Non-hormonal; Exact mechanism in treating HSDD is unknown; acts on multiple serotonin receptors as an agonist and antagonist, with additional antagonism at dopamine D4 receptors. **Indication:** HSDD **Onset:** Discontinue after 8 weeks if no improvement in sexual desire and/or a reduction in associated distress. **Formulation and Packaging:** • Oral systemic therapy • Contraindicated with use of moderate or strong inhibitors of CYP3A4 (e.g., ketoconazole, itraconazole, fluconazole, ritonavir, or clarithromycin) • Start Addyi® ≥ 2 weeks after stopping a moderate or strong CYP3A4 inhibitor OR start such inhibitors ≥ 2 days after stopping ADDYI, unless earlier initiation is clinically necessary, in which case, monitor closely for hypotension and syncope.	**Initial:** 100 mg daily HS **Titration:** N/A **Max:** 100 mg daily HS **Administration:** Once daily with or without food (fatty meals may ↑ absorption by 1-1.5-fold). *Dosed at bedtime because administration during waking hours increases the risks of hypotension, syncope, and CNS depression (such as somnolence and sedation).* **Renal**: Mild/moderate impairment (CrCl 30-89 mL/min): 1.1-fold increase in concentration, but no dose adjustment suggested. Severe impairment (CrCl < 30 mL/min): 1.2-fold increase in concentration, but no dose adjustment suggested. **Hepatic**: Contraindicated with any degree of hepatic impairment as it significantly increases flibanserin concentrations (4.5-fold and $t_{1/2}$ to 26h from 10h).	**Brand:** $849 **Generic:** N/A **ODB:** X **NIHB:** X

† off-label use

Legend
CE = conjugated estrogen; **CHD** = coronary heart disease; **CrCl** = creatinine clearance; **CV** = cardiovascular; **D/C** = discontinued; **DVT** = deep vein thrombosis; **ET** = estrogen therapy; **GSM** = genitourinary syndrome of menopause; **HRT** = hormonal replacement therapy; **HS** = at bedtime; **HSDD** = hypoactive sexual desire disorder; **MHT** = Menopause Hormone Therapy; **N/A** = not applicable; **NIHB** = Non-Insured Health Benefit; **ODB** = Ontario Drug Benefit; **PAD** = peripheral artery disease; **PT** = progestogen/progestin therapy; **qHS** = every night at bedtime; **SM** = surgical menopause; **T** = testosterone; **TIA** = transient ischemic attack; **VMS** = vasomotor symptoms; **VTE** = venous thromboembolism; **ULN** = upper limit of normal

Cost: An approximate range for a 3-month supply using the initial and max dose (includes a markup of 10% and a dispensing fee of $12.99)
Titration: Initiate hormone therapy at the lowest effective dose based on symptom severity, timing since menopause, and individual risk factors. Adjust dose based on symptom control, tolerability, and patient preference [5,7,10,14]
Dosing: Choose estrogen-only HRT for individuals without a uterus, and combined estrogen-progestogen therapy for those with an intact uterus. Using shared –decision-making, select cyclical regimens for perimenopausal individuals (< 1yr LMP) and continuous regimens for those postmenopausal (> 1yr LMP). [5,7,10]
Duration of Therapy: For many patients, a duration of 3-5 years may be necessary, but some may require shorter or longer durations.
Follow-up: Reassess within 3–6 months of initiation, and then at least annually thereafter. Evaluate symptom relief, adverse effects, and continued need for therapy. Engage in shared decision-making and discuss possible adjustments or discontinuation. [5,10]
Monitoring: Monitor for breast changes, abnormal bleeding, blood pressure, and any cardiovascular, thromboembolic, or cognitive symptoms. Offer mammograms and other age-appropriate screenings. For local MHT therapy, explain minimal systemic absorption and reassure regarding long-term use when appropriate. Consider periodic assessment of ongoing need and lowest effective dose (e.g., every 3–6 months) [10,11]
Discontinuation: There is no mandatory duration for HRT. Consider gradual tapering or abrupt cessation, individualized to the patient (similar rates of symptom recurrence with either method). Reinitiation can be considered if symptoms recur and benefits outweigh risks. Vaginal estrogen may be continued at lowest effective dose indefinitely if beneficial. [5,7,10]