From Hot Flashes to Hot Topics: Menopause Therapies, Label Changes, and Pharmacy Practice Updates

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Disclosure

I do not have a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation (within the last 12 months).

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Pharmacist Objectives

1. Evaluate current pharmacologic and nonpharmacologic therapy options for managing menopausal symptoms based on evidence-based, patient-specific considerations.
2. Discuss recent updates in FDA labeling, safety warnings, and clinical guideline recommendations for menopausal therapies to optimize patient care.
3. Apply the Pharmacists' Patient Care Process to counsel patients, assess appropriateness of therapy, and collaborate with prescribers in developing individualized treatment plans for menopause management.

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Pharmacy Technician Objectives

1. Identify prescription and nonprescription treatment options for menopausal symptoms and their general uses.
2. Recognize key labeling changes and safety considerations for menopausal therapies that require pharmacist intervention.
3. Describe the pharmacy technician's role in menopause management, including supporting medication access, reinforcing pharmacist-provided education, identifying situations requiring pharmacist referral, and promoting adherence and patient safety.

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Abbreviations – What Does This All Mean?

Abbreviation	Key
WHI	Women's Health Initiative
FDA	Food and Drug Administration
US	United States
ADE	Adverse Drug Event
CBT	Cognitive-behavioral therapy
VMS	Vasomotor Symptoms
VVA	Vulvovaginal Atrophy
CNS	Central Nervous System
MHT	Menopausal Hormone Therapy
HRT	Hormone Replacement Therapy
LFT	Liver Function Test(s)
ALP	Alkaline Phosphatase

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Abbreviations – What Does This All Mean?

Abbreviation	Key
ULN	Upper Limit of Normal
CVD	Cardiovascular Disease
GSM	Genitourinary Syndrome of Menopause
BBW	Black Box Warning
VTE	Venous Thromboembolism
CEE	Conjugated Equine Estrogen
MPA	Medroxyprogesterone Acetate
SSRI	Selective Serotonin Reuptake Inhibitor
SNRI	Serotonin-Norepinephrine Reuptake Inhibitor
SERMs	Selective Estrogen Receptor Modulators
MTM	Medication Therapy Management

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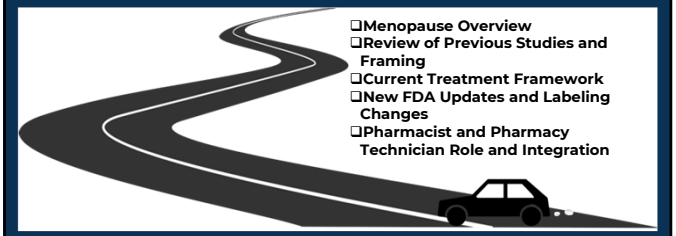
Sparkling Presentation Roadmap



- ❑Menopause Overview
- ❑Review of Previous Studies and Framing
- ❑Current Treatment Framework
- ❑New FDA Updates and Labeling Changes
- ❑Pharmacist and Pharmacy Technician Role and Integration

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MENOPAUSE OVERVIEW

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Definitions

Perimenopause
- Begins with onset of menstrual irregularities and ends 12 months after last menstrual period

Menopause
- Occurs with permanent cessation of menses and starts 12 months after the last menstrual cycle

Postmenopause
- Begins approximately 12 months after menopause begins until death

1. NAMS 2023

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Symptoms

- Vasomotor (Hot Flashes and Night Sweats)
- Dyspareunia and Sexual Dysfunction
- Urogenital Atrophy
- Urinary Incontinence
- Dysfunctional Uterine Bleeding (During Perimenopause)

1. NAMS 2023
2. Kornstein et al, 2015
3. NAMS GSM Position Statement, 2020
4. NAMS HT Position Statement, 2022

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Symptoms

- Mood Changes (Anxiety and Depression)
- Decreased Concentration and Memory
- Sleep Disturbances
- Metabolic Changes
- Bone Loss, Increase Fracture Risk, and Arthralgia

1. NAMS 2023
4. NAMS HT Position Statement, 2022
5. Maki et al, 2018

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WOMEN'S HEALTH INITIATIVE (WHI) STUDY

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Let's Revisit WHI

Study Design	Randomized, double-blind, placebo-controlled trial started in 1993 in women aged 50-79 with overall goal to evaluate effects of menopausal hormonal therapy (MHT) on heart disease, osteoporosis, and cancer
Patient Population	Postmenopausal women aged 50–79
Treatment Arms	Systemic estrogen + progestogen with intact uterus and those on systemic estrogen monotherapy following a hysterectomy • CEE + MPA arm (intact uterus) • CEE-alone arm (prior hysterectomy)
Study Duration	• CEE + MPA arm - Median follow-up was 5.6 years, and it was stopped early because risk>benefit on the major clinical outcomes • CEE-alone arm – Median follow-up was 7.2 years, and it was stopped early due to excess stroke risk with no benefit to coronary heart disease

4. NAMS HT Position Statement, 2022
6. WHI Investigators. JAMA. 2002;288(3):321-333.

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Significant Outcomes of WHI

Participants using oral estrogen had twofold increased risk of venous thromboembolism (VTE) compared to placebo, with highest risk during first 1-2 years of MHT therapy

CEE + MPA arm vs placebo:
VTE risk (HR 2.06; 95% CI, 1.57–2.70)

CEE-alone arm vs placebo:
VTE risk (HR 1.48; 95% CI, 1.06–2.07)

4. NAMS HT Position Statement, 2022
6. WHI Investigators. JAMA. 2002;288(3):321-333.

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Significant Outcomes of WHI

Increased risk of invasive breast cancer with combined progestogen and estrogen therapy, but not with estrogen monotherapy

CEE + MPA arm vs placebo:
Invasive breast cancer risk (HR 1.24; 95% CI, 1.01–1.53), which persisted through 19.4 years of cumulative follow-up (HR 1.28; 95% CI, 1.13–1.45)

CEE-alone arm vs placebo:
Invasive breast cancer risk (HR 0.79; 95% CI, 0.61-1.02)

4. NAMS HT Position Statement, 2022
6. WHI Investigators. JAMA. 2002;288(3):321-333.

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Key WHI Takeaways

- Extended follow up showed those who initiated MHT 10+ years after menopause were at increased coronary heart disease (CHD) risk compared to those who initiated therapy within 10 years of menopause
- Vaginal estrogens not associated with increased cardiovascular disease (CVD) risk
- Endocrine Society recommends evaluating breast cancer risk prior to MHT initiation and avoiding systemic MHT in high risk or patient with history of breast cancer

4. NAMS HT Position Statement, 2022
6. WHI Investigators. JAMA. 2002;288(3):321-333.
7. Stuenkel CA, et al. J Clin Endocrinol Metab. 2015

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Key WHI Takeaways

- Endocrine Society recommends evaluating 10-year CVD risk using ACC/AHA calculator prior to initiation of MHT therapy
  - High risk (>10%) – avoid systemic MHT therapy
  - Moderate risk (5-10%) – transdermal/topical estrogen preferred over oral formulations
- Patients with intact uterus should always be treated with estrogen + progestogen for endometrial protection although tissue-selective estrogen complex (estrogen/bazedoxifene) can be given as alternative
- Unclear evidence about safety of MHT and ovarian cancer risk

4. NAMS HT Position Statement, 2022
6. WHI Investigators. JAMA. 2002;288(3):321-333.
7. Stuenkel CA, et al. J Clin Endocrinol Metab. 2015

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Key WHI Takeaways

- MHT associated with increased risk of cholecystitis, cholelithiasis, and cholecystectomy
- MHT demonstrated reduced risk in fractures at the hip, spine, and wrist
- MHT improved depression
- MHT shows conflicting evidence related to cognitive decline
- Post-hoc WHI trial revealed increased lung cancer deaths in patients in estrogen + progestogen arm who were at elevated risk (smokers)
- Study did not explore various formulations of MHT and limited enrollment of women with bothersome VMS or in perimenopause

4. NAMS HT Position Statement, 2022
6. WHI Investigators. JAMA. 2002;288(3):321-333.
8. Chlebowski et al. JAMA. 2020

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WHI Aftermath

- Led the FDA to require class-wide boxed warnings on estrogen and estrogen–progestin menopausal hormone therapies starting in 2003, even for products not directly studied, based on extrapolated cardiovascular and cancer risks.

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS, PROBABLE DEMENTIA, and BREAST CANCER

- Study did not explore various formulations of MHT and limited enrollment of women with bothersome VMS or in perimenopause.
- Following WHI study, younger women and those with more VMS were less likely to receive hormone therapy (HT).

4. NAMS HT Position Statement, 2022
9. Pfizer. PREMARIN® (conjugated estrogens) tablets, USP: prescribing information.

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Black Box Warning

WARNING: ENDOMETRIAL CANCER, CARDIOVASCULAR DISORDERS, BREAST CANCER and PROBABLE DEMENTIA
See full prescribing information for complete boxed warning.

Estrogen-Alone Therapy

- There is an increased risk of endometrial cancer in a woman with a uterus who uses unopposed estrogens (5.2)
- Estrogen-alone therapy should not be used for the prevention of cardiovascular disease or dementia (5.1, 5.3)
- Women's Health Initiative (WHI) estrogen-alone substudy reported increased risks of stroke and deep vein thrombosis (DVT) (5.1)
- The WHI Memory Study (WHIMS) estrogen-alone ancillary study of WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age and older (5.3)

Estrogen Plus Progestin Therapy

- Estrogen plus progestin therapy should not be used for the prevention of cardiovascular disease or dementia (5.1, 5.3)
- The WHI estrogen plus progestin substudy reported increased risks of stroke, DVT, pulmonary embolism (PE), and myocardial infarction (MI) (5.1)
- The WHI estrogen plus progestin substudy reported increased risks of invasive breast cancer (5.2)
- The WHIMS estrogen plus progestin ancillary study of WHI reported an increased risk of probable dementia in postmenopausal women 65 years of age and older (5.3)

9. Pfizer. PREMARIN® (conjugated estrogens) tablets, USP: prescribing information.

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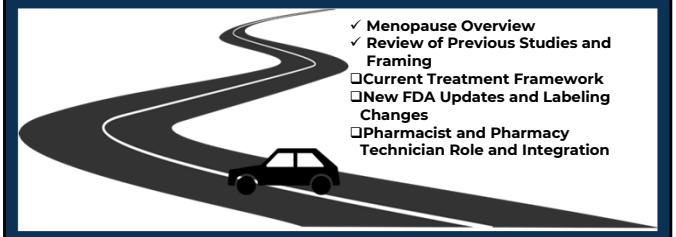
Sparkling Presentation Roadmap



- ✓ Menopause Overview
- ✓ Review of Previous Studies and Framing
- ❑Current Treatment Framework
- ❑New FDA Updates and Labeling Changes
- ❑Pharmacist and Pharmacy Technician Role and Integration

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TREATMENT FRAMEWORK

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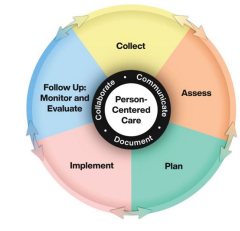
Pharmacists' Patient Care Process



Pharmacists, as medication experts and integral members of the health care team, are essential health care providers who use a person-centered approach to optimize each patient's medication and health outcomes.

Guided by evidence, clinical reasoning, and complexity of patient needs, pharmacists apply the five steps of the Pharmacists' Patient Care Process to help patients meet their health goals.

Collect
The pharmacist ensures the collection of necessary subjective and objective information about the patient to understand the relevant medication and medical history, overall health status, and other pertinent factors. Information may be gathered and verified from multiple sources (e.g., the patient, caregiver, observations, existing patient records, and other health care professionals).

Assess
The pharmacist assesses the collected information to identify and prioritize patient needs to inform the establishment of a care plan.

Plan
The pharmacist develops a person-centered, evidence-based, cost-conscious care plan in partnership with the patient and/or caregiver, and in coordination with other care team members.

Implement
In providing person-centered care, the pharmacist implements a prioritized care plan in partnership with the patient and/or caregiver and in coordination with other care team members.

Follow Up: Monitor and Evaluate
The pharmacist follows up to monitor and evaluate the implementation of the care plan and the patient's overall health in collaboration with the patient, caregiver, and other care team members, as needed.

10. Joint Commission of Pharmacy Practitioners. Pharmacists' Patient Care Process. Updated May 21, 2025. Accessed April 12, 2026. https://jcpp.net/patient-care-process/

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Treatment Algorithm

Non-pharmacologic options for mild symptoms

If non-pharmacologic options are ineffective or moderate/severe symptoms, consider non-hormonal treatment options in women with contraindications to hormonal therapies

Hormonal options should only be given after careful risk vs benefit analysis and in those with moderate to severe vasomotor symptoms

Use lowest effective dose for shortest time	Topical options preferred over systemic

1. NAMS 2023
4. NAMS HT Position Statement, 2022

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Non-pharmacologic Options

Evidence Lacking
- Cooling techniques
- Avoiding triggers
- Exercise and yoga
- Dietary modifications
- Mindfulness-based interventions
- Paced respiration
- Relaxation
- Acupuncture
- Chiropractic intervention

Evidence-Based
- Weight management and loss
- Cognitive-behavioral therapy (CBT)
- Clinical hypnosis
- Stellate ganglion block
- Vaginal lubricants and moisturizers

1. NAMS 2023

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Prescription Non-hormonal Options

Evidence Lacking
- Pregabalin
- Clonidine
- Suvorexant

Evidence-Based
- Selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs)
- Gabapentinoids
- Oxybutynin
- **Neurokinin receptor antagonists**

1. NAMS 2023

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Prescription Non-hormonal Dosing

Drug	Dosing	Clinical Caveats
Paroxetine	10 - 25 mg/day	Serotonin syndrome; anticholinergic properties[2]; sedating; increased bleeding risk
Citalopram	10 - 20 mg/day	Serotonin syndrome; increased bleeding risk
Escitalopram	10 - 20 mg/day	
Venlafaxine	37.5 – 150 mg/day	
Desvenlafaxine	100 – 150 mg/day	

1. NAMS 2023

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Prescription Non-hormonal Dosing

Drug	Dosing	Clinical Caveats
Gabapentin	900 mg (300 mg three times/day) – 2,400 mg/day	Somnolence, dizziness
Oxybutynin	2.5 mg or 5 mg twice daily up to 15 mg extended-release daily	Anticholinergic properties; long-term is associated with cognitive decline
Fezolinetant	**45 mg/day**	**Risk of hepatotoxicity; contraindicated with CYP1A2 inhibitors and if GFR ≤ 30 mL/min/1.73 m²**
Elinzanetant	**120 mg/day at bedtime**	**Increased LFT, causes somnolence, seizure risk precaution**

1. NAMS 2023
11. AGS Beers Criteria®, 2023 update (J Am Geriatr Soc.)
12. Bayer HealthCare Pharmaceuticals Inc. Lynkuet® (elinzanetant) capsules, for oral use: prescribing information. March 2026.

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OTC Non-hormonal Options

- Soy foods and soy extracts
- Soy metabolite equol
- Pollen extract
- Ammonium succinate
- *Lactobacillus acidophilus*
- Rhubarb
- Black cohosh
- Wild yam
- Dong quai
- Evening primrose
- Maca
- Ginseng
- *Labisia pumila/Eurycoma longifolia*
- Chasteberry
- Milk thistle
- Omega-3 fatty acid
- Vitamin E

1. NAMS 2023

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Hormonal Options

- FDA approved for moderate to severe VMS; prevention of osteoporosis in postmenopausal women; treatment of hypoestrogenism caused by hypogonadism, bilateral oophorectomy, or primary ovarian insufficiency; and treatment of moderate to severe vulvovaginal symptoms.
- For genitourinary syndrome of menopause (GSM), estrogen is most effective treatment option with local estrogen recommended for sole vaginal symptoms.
- Use systemic hormone to treat moderate to severe vasomotor symptoms.
- Adverse Drug Event (ADE) of estrogen therapy include nausea, headache, breast tenderness, heavy bleeding.
- ADE of progestogen therapy include irritability, weight gain, bloating, headache, and premenstrual syndrome (PMS) like symptoms.
- Compounded bioidentical hormone pellets are available in US.

4. NAMS HT Position Statement, 2022

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Hormonal Options

Intact Uterus	Without Intact Uterus (hysterectomy)
• Estrogen + progestogen • Tissue-selective estrogen complex (estrogen/bazedoxifene)	• Estrogen monotherapy

4. NAMS HT Position Statement, 2022

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Prescription Hormonal Options

Drug	Dosing Range	Clinical Caveats
Conjugated equine estrogens	0.3 - 1.25 mg/day	Oral systemic formulations; available as localized vaginal cream with low systemic exposure
Esterified estrogens	0.3 – 1.25 mg/day	Oral, systemic formulations; given 3 weeks on and 1 week off
17B-estradiol vaginal insert	1 – 2 mg/day	Oral, systemic formulations; given 3 weeks on and 1 week off
17B-estradiol transdermal	0.025 – 0.1 mg/day	Transdermal patch applied once or twice weekly

4. NAMS HT Position Statement, 2022

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Prescription Hormonal Options

Drug	Dosing Range	Clinical Caveats
17B-estradiol topical	Gel: 0.25–1.25 g/day Spray: 1.53 mg/spray given 1–3 sprays/day	Topical formulations (gels or spray) applied to various areas of body
Estradiol acetate vaginal ring	12.4 – 24.8 mg ring/3 months	Systemic absorption; approved for GSM and VMS symptoms
17B-estradiol vaginal ring	2 mg ring/3 months	Minimally systemic absorption; approved for VMS symptoms only

4. NAMS HT Position Statement, 2022

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Prescription Hormonal Options

Drug	Dosing Range	Clinical Caveats
17B-estradiol vaginal cream	Given daily or once or twice weekly; available as 0.01% cream	Available as tube with calibrated applicator
17B-estradiol vaginal insert	4 – 10 mcg twice weekly	
Estradiol hemihydrate vaginal tablet	10 mcg twice weekly	
Medroxyprogesterone acetate	5 – 10 mg/day for 12 – 14 days/month	
Micronized progesterone	200 mg/day for 12 – 14 days/month	
Norethindrone acetate	5 mg/day for 12 – 14 days/month	

4. NAMS HT Position Statement, 2022

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Other Treatment Options

- Selective estrogen receptor modulators (SERMs) are nonsteroidal compounds, chemically distinct from estradiol, but act on estrogen receptors with specific, high affinity binding.
  - Second generation: raloxifene
  - Third generation: bazedoxifene, ospemifene
- Intravaginal DHEA is FDA approved for vulvovaginal atrophy (VVA) and GSM.

4. NAMS HT Position Statement, 2022

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Sparkling Presentation Roadmap

- ✓ **Menopause Overview**
- ✓ **Review of Previous Studies and Framing**
- ✓ **Current Treatment Framework**
- ❑ **New FDA Updates and Labeling Changes**
- ❑ **Pharmacist and Pharmacy Technician Role and Integration**

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NEW FDA UPDATES AND LABELING CHANGES

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The SKYLIGHTs of Fezolinetant

Study Design	Randomized, double-blind, placebo-controlled trials evaluating the efficacy and safety of fezolinetant for the treatment of moderate to severe VMS associated with menopause
Patient Population	Menopausal individuals aged 40–65 years experiencing ≥ 7 moderate-to-severe hot flashes per day
Dosing	30 mg and 45 mg
Study Duration	12 weeks (placebo-controlled) + 40 weeks (active treatment extension phase)
Primary Outcomes	Change in frequency of moderate-to-severe VMS and change in severity of VMS at weeks 4 and 12

13. Lederman et al, 2023 (SKYLIGHT 1)
14. Johnson et al, 2023 (SKYLIGHT 2)

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The SKYLIGHTs of Fezolinetant

- Significant reduction in VMS frequency and severity at weeks 4 and 12, maintained through 52 weeks (22.5% mean improvement) with greater efficacy with 45 mg dosing
- Trial demonstrated improvements in VMS as early as week 1
- Elevations in LFT occurred in a small percentage of participants; these were typically asymptomatic, transient, and reversible with monitoring or discontinuation

13. Lederman et al, 2023 (SKYLIGHT 1)
14. Johnson et al, 2023 (SKYLIGHT 2)

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OPTION-VMS Phase IV Observational Study

- OPTION-VMS is an ongoing Phase IV, longitudinal, real-world observational study designed to evaluate the effectiveness, safety, and patient-reported outcomes of fezolinetant and other nonhormonal therapies for moderate to severe VMS associated with menopause in routine clinical practice.
- Includes more than 900 women aged 40-75 with confirmed or menopausal VMS who were prescribed nonhormonal therapies at approximately 50 US clinical sites

15. Astellas Pharma Inc. Press release. October 22, 2025.

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Deeper Drive into the Neurokinin Receptor Antagonist

	Fezolinetant
Mechanism of Action	Works as Neurokinin 3 receptor antagonist and restores normal activity to thermoregulatory center in hypothalamus
FDA Approval	Dosed at 45 mg orally daily for the treatment of moderate to severe VMS symptoms due to menopause
BBW	• **Updated due to postmarketing surveillance demonstrating hepatoxicity** • Baseline liver function tests (LFTs) required. • Monthly LFT, alkaline phosphatase (ALP), and direct bilirubin monitoring for first 3 months, then at 6 months and 9 months after initiation. • Discontinue therapy if experience signs or symptoms of liver injury, transaminase elevations are > 5x's upper normal limit (ULN), or if transaminase elevations are > 3x's ULN and the total bilirubin level is > 2x's ULN. • If transaminase elevations > 3x's ULN occur, perform more frequent follow-up hepatic laboratory tests until resolution.

16. Astellas Pharma Inc. VEOZAH® (fezolinetant) tablets, for oral use: prescribing information. February 26, 2026.

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Deeper Drive into the Neurokinin Receptor Antagonist

	Fezolinetant
Contraindications	• Known cirrhosis or patients with ALT, AST, or total bilirubin ≥ 2x's UNL at medication initiation • Concurrent CYP1A2 inhibitor use • Severe renal impairment or end-stage renal disease (GFR < 30 mL/min/1.73 m²)
Common Adverse Effects	Abdominal pain, diarrhea, insomnia, back pain, hot flush, and ALT or AST elevations
Clinical Pearls and Caveats	• Must swallow tablet whole and cannot be cut, crushed, or chewed • Can be administered with or without food, but should be taken with liquids

16. Astellas Pharma Inc. VEOZAH® (fezolinetant) tablets, for oral use: prescribing information. February 26, 2026.

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The OASIS of Elinzanetant

Study Design	Two, randomized, double-blind, placebo-controlled trials evaluating the efficacy and safety of elinzanetant for the treatment of moderate to severe VMS associated with menopause
Patient Population	Postmenopausal individuals aged 40–65 years experiencing ≥ 50 moderate-to-severe VMS events per 7 days during screening
Dosing	120 mg (2, 60-mg capsules)
Study Duration	12 weeks (placebo-controlled) + 14 weeks (active treatment extension) + 4 weeks post-treatment follow-up
Primary Outcomes	Change in frequency and severity of moderate-to-severe VMS from baseline to weeks 4 and 12, measured by an electronic hot flash daily diary

17. Pinkerton et al, 2023 (OASIS 1 and 2)

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The OASIS of Elinzanetant

- Significant reductions in VMS frequency and severity from baseline to weeks 4 and 12 compared to placebo, with reduction seen as early as 1 week after treatment initiation
- Significant improvement in sleep disturbances and menopause-related quality of life at week 12
- Most treatment-emergent adverse effects were of mild or moderate intensity, with headache and fatigue occurring more frequently during the 12-week, placebo-controlled period.

17. Pinkerton et al, 2023 (OASIS 1 and 2)

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The Third OASIS of Elinzanetant

Study Design	Randomized, double-blind, placebo-controlled, 52-week trial evaluating the efficacy and safety of elinzanetant for the treatment of moderate to severe VMS associated with menopause
Patient Population	Postmenopausal individuals aged 40–65 years experiencing VMS with no minimum frequency
Dosing	120 mg (2, 60-mg capsules)
Study Duration	52 weeks (placebo-controlled) + 4 weeks post-treatment follow-up
Primary Outcome	Change in frequency of daily moderate-to-severe VMS from baseline to week 12

18. Panay et al, 2025 (OASIS 3)

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The Third OASIS of Elinzanetant

- Significant reduction in daily VMS frequency at week 12, corresponding to a 73.8% reduction from baseline compared to placebo
- Not powered appropriately for secondary endpoints focused on impact on sleep disturbances and menopause-related quality of life
- Most treatment-emergent adverse effects were of mild or moderate intensity, with somnolence, fatigue, and headache most reported
- During OASIS-3 trial, there were no hepatotoxicity, no endometrial hyperplasia, and no meaningful changes in bone density.

18. Panay et al, 2025 (OASIS 3)

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The Fourth OASIS of Elinzanetant

Study Design	Randomized, double-blind, placebo-controlled, 52-week trial
Patient Population	Women aged 18–70 years with moderate-to-severe VMS associated with endocrine therapy (tamoxifen or aromatase inhibitors) for hormone receptor (HR) positive breast cancer or its prevention
Dosing	120 mg (2, 60-mg capsules)
Study Duration	12 weeks (placebo-controlled) + 40 weeks (active treatment extension) + 4 weeks post-treatment follow-up
Primary Outcome	Change in frequency of daily moderate-to-severe VMS from baseline to weeks 4 and 12

19. Cardoso et al, 2025 (OASIS 4)

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The Fourth OASIS of Elinzanetant

- Significant reduction in frequency of VMS in treatment group at week 4 (57% reduction) and 12 (68% reduction) compared to placebo
- During the OASIS-4 trial, elinzanetant demonstrated a favorable safety profile with no hepatotoxicity in women with breast cancer receiving endocrine therapy who had contraindications to MHT for VMS.
- 91.6% of participants completing initial 52-week trial continued with optional 2-year extension

19. Cardoso et al, 2025 (OASIS 4)
20. Pogoda et al, 2026

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Deeper Drive into the Neurokinin Receptor Antagonist

Elinzanetant	
Mechanism of Action	Works as Neurokinin 1 and 3 receptor antagonist and restores normal activity to thermoregulatory center in hypothalamus
FDA Approval	Dosed at 120 mg (two 60 mg capsules) orally at bedtime for the treatment of moderate to severe VMS symptoms due to menopause
Warnings and Precautions	• CNS depressant effects and daytime impairment • LFT elevations • Risk of pregnancy loss • Risk of seizures in patients with history of seizures
Contraindications	Pregnancy

12. Bayer HealthCare Pharmaceuticals Inc. Lynkuet® (elinzanetant) capsules, for oral use: prescribing information. March 2026.

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Deeper Drive into the Neurokinin Receptor Antagonist

Elinzanetant	
Common Adverse Effects	Headache, fatigue, dizziness, somnolence
Clinical Pearls and Caveats	• Do not start therapy in patients if ALT, AST, or total bilirubin ≥ 2x's UNL • Discontinue therapy if experience signs or symptoms of liver injury, transaminase elevations are > 5x's ULN, or if transaminase elevations are > 3x's ULN and the total bilirubin level is > 2x's ULN • Re-evaluate LFT three months after medication initiation • Acts as major substrate of CYP3A4 • Not recommended for patients with end stage renal disease or moderate to severe hepatic impairment • Must swallow capsule whole and cannot be cut, crushed, or chewed • Can be administered with or without food, but should be taken with water

12. Bayer HealthCare Pharmaceuticals Inc. Lynkuet® (elinzanetant) capsules, for oral use: prescribing information. March 2026.

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FDA NEWS RELEASE

FDA Approves Labeling Changes to Menopausal Hormone Therapy Products

For Immediate Release: February 12, 2026

The U.S. Food and Drug Administration has approved drug labeling changes to six menopausal hormone therapy products, also known as hormone replacement therapy (HRT), to clarify risk considerations for these drugs. Specifically, risk statements related to cardiovascular disease, breast cancer and probable dementia were removed from the "boxed warning," the agency's most prominent safety-related warning.

Hot Off the Presses

21. FDA MHT Labeling Change, February 12, 2026

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FDA Update

- FDA approved changes to the labeling of six MHT products to reflect current scientific evidence, including systemic combination therapy, systemic estrogen-alone therapy, systemic progestogen-alone therapy for women with a uterus using systemic estrogen, and topical vaginal estrogen therapies.
- Removal of black boxed warning statements linking MHT therapies to CVD, breast cancer, and probable dementia
- BBW remains for estrogen-alone products in patients with an intact uterus
- Removal of mandate for lowest effective dose for the shortest duration of time

22. HHS HRT Warning Update, November 10, 2025
21. FDA MHT Labeling Change, February 12, 2026
23. Manson et al., 2024

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FDA Update

- Recommend initiating MHT if < 60 years of age OR within 10 years of the onset of menopause
  - Reduction in all-cause mortality ~ 30%
  - Reduction in CVD by as much as 50%
  - Reduction in bone fractures by 50-60%
  - Increased VTE risk
- Recommend removal of arbitrary age-based stopping rule with treatment duration based on indication and shared decision-making
- Important caveat that MHT therapy should not be used to prevent CVD as a primary indication

22. HHS HRT Warning Update, November 10, 2025
21. FDA MHT Labeling Change, February 12, 2026
23. Manson et al., 2024

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Why the Update?

- New data from 2025 WHI Secondary Analysis demonstrated strong evidence supporting MHT use in younger women with avoidance in older age
- Population reviewed: 27, 347 postmenopausal women
- Women aged 50-59 with moderate to severe V MS
  - Conjugated equine estrogen (CEE) alone and CEE plus medroxyprogesterone acetate (MPA) reduced VMS symptoms
  - No significant increase in ASCVD risk (CEE alone: HR0.85, 95% CI 0.53-1.35; CEE plus MPA: HR 0.84, 95% CI 0.44-1.57)
- Women aged ≥ 70 years with moderate to severe VMS
  - Showed significant ASCVD risk (CEE alone: HR 1.95, 95% CI 1.06-3.59; CEE plus MPA:HR 3.22, 95% CI 1.36-7.63)

24. Rossouw et al. *JAMA Intern Med.* 2025
8. Chlebowski et al. *JAMA.* 2020

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Why the Update?

- Long-term WHI follow-up data (up to 20 years) demonstrated that estrogen-only therapy in women with prior hysterectomy was associated with lower breast cancer risk and breast cancer-associated mortality, particularly in younger women
- CEE plus MPA saw an increase in breast cancer incidence with no mortality benefit

24. Rossouw et al. *JAMA Intern Med.* 2025
8. Chlebowski et al. *JAMA.* 2020

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Other Significant Approvals

- The FDA is also approving two new drugs to expand treatment options for menopausal symptoms.
  - Approval of a generic version of Premarin (conjugated estrogens)
  - Approval of non-hormonal treatment for moderate to severe VMS, such as hot flashes, associated with menopause.

22. HHS HRT Warning Update, November 10, 2025

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Treatment Algorithm Changed

Non-pharmacologic options for mild symptoms

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If non-pharmacologic options are ineffective or moderate/severe symptoms, consider non-hormonal treatment options in women with ***contraindications*** to hormonal therapies

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Hormonal options should only be given after ***careful risk vs benefit analysis*** and in those with moderate to severe vasomotor symptoms

~~Use lowest effective dose for shortest time~~	Topical options preferred over systemic if solely GSM symptoms

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Sparkling Presentation Roadmap

- ✓ **Menopause Overview**
- ✓ **Review of Previous Studies and Framing**
- ✓ **Current Treatment Framework**
- ✓ **New FDA Updates and Labeling Changes**
- ❑ **Pharmacist and Pharmacy Technician Role and Integration**

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PHARMACIST AND PHARMACY TECHNICIAN ROLE AND INTEGRATION

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Impact and Relevance of Menopause Labeling Update

Historical FDA Warning Effects

- Early FDA black boxed warnings shaped menopause treatment and patients and providers perspective for decades

Updated Labeling and Guidance

- Recent FDA elimination of black boxed warnings clarifies safety monitoring for both hormonal and nonhormonal therapies, broadening available treatment options

Role of Pharmacists and Pharmacy Technicians

- Provide consistent, evidence-based counseling and shared decision making

22. HHS HRT Warning Update, November 10, 2025
21. FDA MHT Labeling Change, February 12, 2026

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Pharmacist Role

Key Considerations for Patients Using Fezolinetant

1. Educate them to recognize hepatotoxicity symptoms and discontinue therapy immediately if symptoms appear
2. Ensure ALT, AST, and bilirubin are regularly monitored and patient attends monthly initial follow-up visits
3. Review the patient's medications for any CYP1A2 inhibitors
4. Counsel on common adverse effects

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Pharmacist Role

- Pharmacist should address misconceptions, improve adherence, evaluate appropriateness of medication use, and promote preventive care
- Incorporate FDA and CDC resources into training and protocols ensures consistent, evidence-based menopause care
- Stay abreast to evidence-based literature, updated guidelines, and current clinical trials

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Pharmacy Technician Role

Complete Medication Reconciliations and Histories	Escalate Hepatoxicity Symptoms to Pharmacists	Flag Missing Labs
Assist with Formulary and Inventory Management	Identify Medication Therapy Management (MTM) Opportunities	Assist with Insurance and Affordability

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Summary

- FDA removed boxed warnings on cardiovascular disease, breast cancer, and dementia for many menopausal hormone therapies after review.
- New labeling emphasizes individualized risk, initiation timing, formulation, and administration route over broad class warnings.
- Systemic estrogen-alone products still carry boxed warnings for endometrial cancer in patients with intact uterus.
- Fezolinetant carries an FDA boxed warning for hepatotoxicity, requiring careful liver safety monitoring during therapy. It is contraindicated in cirrhosis, severe renal impairment, or CYP1A2 inhibitor use, emphasizing pharmacist vigilance.
- Elinzanetant does not carry an FDA boxed warning for hepatotoxicity, but baseline LFT labs are required before medication initiation. It is contraindicated in pregnancy and has been studied as a viable option to relieve VMS symptoms in women with breast cancer on endocrine therapy.

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Questions?

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From Hot Flashes to Hot Topics: Menopause Therapies, Label Changes, and Pharmacy Practice Updates

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Thank you!

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