IMS 2025 Guidelines

Clinical Case Scenarios in Menopause Management

7 Evidence-Based Cases | Perimenopausal & Postmenopausal Women

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Panay N et al. IMS Recommendations and Key Messages on Women's Midlife Health and Menopause. Climacteric. 2025;28(6):634–656

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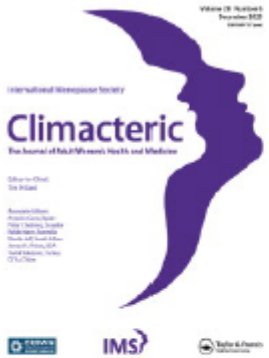

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International Menopause Society (IMS) recommendations and key messages on women's midlife health and menopause

Nick Panay, Anna Fenton, Haitham Hamoda, Timothy Hillard, Rakibul Islam, Hugo Pedder, Lorena Romero, Amanda J. Vincent & The IMS Recommendations Writing Group

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IMS 2025 Guidelines — At a Glance

342	285	57	40
Total Recommendations	Research-Supported	Good Practice Points	Key Messages

Key Topics Covered (30 Sections)

- Midlife body changes & metabolic principles
- Vasomotor symptoms & MHT — gold standard first-line therapy
- Neurokinin-targeted therapies (fezolinetant, elinzanetant) — new Grade A non-hormonal options
- Genitourinary syndrome of menopause (GSM) — chronic, progressive, treatable
- Osteoporosis, sarcopenia, cardiometabolic & CNS health
- Breast, ovarian, endometrial & other malignancy-specific guidance
- Premature ovarian insufficiency — treat promptly, regardless of symptoms
- Perimenopausal contraception — 52mg LNG IUD as optimal option
- Compounded bioidentical hormones — not recommended
- Androgen therapy — HSDD is evidence-based indication for testosterone

Certainty of Evidence — The ⊕ Symbols

⊕⊕⊕⊕	**HIGH**	Further research is very unlikely to change our confidence in the estimate of effect.
⊕⊕⊕◯	**MODERATE**	Further research is likely to have an important impact and may change the estimate.
⊕⊕◯◯	**LOW**	Further research is very likely to have an important impact and likely to change the estimate.
⊕◯◯◯	**VERY LOW**	Any estimate of effect is very uncertain.

◯ = filled circle (evidence present) ◯ = open circle (evidence uncertain/absent)

Strength of Recommendation — A to D

A

Strong Recommendation FOR

Benefits clearly and substantially outweigh risks. Applies to most patients in most circumstances. Clinicians should follow unless there is a compelling contraindication.

B

Moderate Recommendation FOR

Benefits outweigh risks, but the balance is less certain. Consider individual patient factors, values, and preferences.

C

Weak / Conditional

Benefits and risks closely balanced or uncertain. Patient preferences and clinical context play a major role.

D

Recommendation AGAINST

Risks outweigh benefits. Clinicians should generally not use the intervention, or use only in exceptional, well-justified circumstances.

STRAW+10 · Stages of Reproductive Aging Workshop

Harlow et al., Climacteric 2012 | IMS 2025

REPRODUCTIVE				MENOPAUSAL TRANSITION			POSTMENOPAUSE			
−5 Early Reproductive	**−4** Peak Reproductive	**−3b** Late Repro (no Δ cycle)	**−3a** Late Repro (subtle Δ)	**−2** Early Transition	**−1** Late Transition	**FMP**	**+1a** Early Post (yr 0–2)	**+1b** Early Post (yr 2–6)	**+1c** Early Post (yr 6+)	**+2** Late Postmenopause

Reproductive (−5 to −3a)

- −5 Early: Variable cycles; early follicular recruitment; highest oocyte reserve
- −4 Peak: Regular cycles; optimal fertility window; AFC and AMH at their best
- −3b Late: Regular cycles but FSH beginning to rise; AFC and AMH declining
- −3a Late: Subtle cycle irregularity (>7 days); FSH >25 IU/L; AMH low

Menopausal Transition (−2 and −1) + FMP

- −2 Early: Cycle length variation ≥7 days from usual; FSH >25 IU/L
- −1 Late: ≥2 skipped cycles; amenorrhoea ≥60 days; AMH undetectable
- FMP: Final Menstrual Period — confirmed retrospectively after 12 months
- VMS, sleep disruption and mood changes peak during Stage −1 / peri-FMP

Postmenopause (+1a to +2)

- +1a (0–12 m): Peak VMS; FSH surges; rapid bone mineral density loss starts
- +1b (12–24 m): Ongoing VMS; urogenital atrophy (GSM) begins to emerge
- +1c (2–6 y): FSH stabilises at plateau; accelerated bone loss phase concludes
- +2 (>6 y): Late postmenopause — cardiometabolic, urogenital & cognitive sequelae

Harlow SD et al. Executive summary of the Stages of Reproductive Aging Workshop +10. Climacteric 2012;15(2):105–114. | IMS 2025 Global Consensus Statement on Menopause.

Case 1

Case 1: Perimenopausal Woman — High Cardiometabolic Risk

47-year-old P1G1 | Irregular bleeding & climacteric symptoms | BMI 39.5
Hypertension | Hyperlipidaemia | Sexually active | No contraception

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Panay N et al. IMS Recommendations. Climacteric. 2025;28(6):634–656 | DOI: 10.1080/13697137.2025.2585487

Case 1 · Perimenopausal Woman — High Cardiometabolic Risk

47-year-old P1G1 | BMI 39.5 | Hypertension | Hyperlipidaemia | No contraception | Climacteric symptoms

Q **Regarding the management of this perimenopausal woman, which of the following statements are TRUE?**

A Oral combined oestrogen-progestogen MHT is the preferred first-line route for her vasomotor symptoms given her age and symptom severity.

TRUE / FALSE

B A 52mg levonorgestrel intrauterine device (LNG IUD) can simultaneously provide contraception, endometrial protection and serve as the progestogen component of MHT.

TRUE / FALSE

C Transdermal oestradiol does not increase VTE risk, even in the presence of obesity or other additional risk factors.

TRUE / FALSE

D Menopausal hormone therapy (MHT) is an effective treatment for both vasomotor symptoms and weight management in obese perimenopausal women.

TRUE / FALSE

Case 1 — Clinical Issues & Priorities

Case 1

🔴 Immediate Concerns

- Perimenopausal — STRAW+10 Stage -1 (cycles >60 days apart)
- No contraception: pregnancy risk is REAL in perimenopause
- BMI 39.5: elevated VTE risk — oral oestrogen contraindicated
- Hypertension + hyperlipidaemia: significant cardiometabolic burden
- VMS & climacteric symptoms impairing quality of life
- Irregular, potentially heavy bleeding — endometrial assessment may be needed

📋 IMS Principles Applied

- MHT is most effective for VMS — offer if no significant contraindications (⊕⊕⊕⊕ A)
- Oral oestrogen NOT recommended with elevated VTE/cardiovascular risk (⊕⊕⊕⊕ A)
- Transdermal oestrogen does NOT increase VTE risk even with obesity (⊕⊕⊕◯ B)
- 52mg LNG IUD is optimal perimenopausal option — contraception + endometrial protection + progestogen arm of MHT (⊕⊕⊕◯ B)
- Anti-obesity medications appropriate at BMI 39.5 (⊕⊕⊕⊕ A)
- Behavioural modification, calorie restriction & exercise: most important lifestyle interventions (⊕⊕⊕⊕ A)

Case 1 — Management Plan

Case 1

Priority	Action / Management	Grade
1	Insert 52mg LNG IUD— contraception + endometrial protection + progestogen arm	⊕⊕⊕◯ B
2	Add transdermal oestradiol gel/patch (50mcg) — VMS relief. NO oral oestrogen.	⊕⊕⊕⊕ A
3	Assess baseline breast cancer risk: Gail / CanRisk / IBIS before IUD insertion	⊕⊕⊕◯ B
4	GLP-1 agonist referral — qualifies at BMI 39.5 as adjunct to lifestyle	⊕⊕⊕⊕ A
5	Mediterranean diet + ≥150 min/week exercise + 2× resistance sessions	⊕⊕⊕⊕ B
6	Optimise antihypertensive and lipid-lowering therapy	⊕⊕⊕◯ A
7	Review at 3 months; annual mammogram + BP + lipids thereafter	GPP

Case 1 · Perimenopausal Woman — High Cardiometabolic Risk

47-year-old P1G1 | BMI 39.5 | Hypertension | Hyperlipidaemia | No contraception | Climacteric symptoms

2 TRUE

Q **Regarding the management of this perimenopausal woman, which of the following statements are TRUE?**

A Oral combined oestrogen-progestogen MHT is the preferred first-line route for her vasomotor symptoms given her age and symptom severity.

FALSE

FALSE — Oral oestrogen is NOT recommended in women at increased VTE risk. BMI 39.5 + hypertension contraindicate oral oestrogen. Transdermal route is mandated. (IMS ⊕⊕⊕⊕ A)

B A 52mg levonorgestrel intrauterine device (LNG IUD) can simultaneously provide contraception, endometrial protection and serve as the progestogen component of MHT.

TRUE

TRUE — The 52mg LNG IUD is the optimal perimenopausal option, addressing all three needs in a single device. (IMS ⊕⊕⊕◯ B)

C Transdermal oestradiol does not increase VTE risk, even in the presence of obesity or other additional risk factors.

TRUE

TRUE — Unlike oral oestrogen, transdermal oestradiol bypasses hepatic first-pass and does not increase VTE risk even with obesity. (IMS ⊕⊕⊕◯ B)

D Menopausal hormone therapy (MHT) is an effective treatment for both vasomotor symptoms and weight management in obese perimenopausal women.

FALSE

FALSE — MHT effectively manages menopause symptoms but does NOT have a direct impact on body weight and is NOT indicated for weight management. (IMS ⊕⊕⊕⊕ A)

Case 2

Case 2: Postmenopausal Bleeding — Diabetic Patient

55-year-old P0G0 | Type 2 Diabetes Mellitus | 4 years amenorrhoea
Postmenopausal bleeding — investigation & management

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Case 2 · Postmenopausal Bleeding — Type 2 Diabetic Patient

55-year-old P0G0 | Type 2 Diabetes Mellitus | 4 years amenorrhoea | Postmenopausal bleeding

Q **Regarding the assessment and management of this patient presenting with postmenopausal bleeding, which statements are TRUE?**

A The initial investigation of choice in a patient presenting with postmenopausal bleeding is a transvaginal ultrasound (TVS).

TRUE / FALSE

B An endometrial thickness of 3mm on TVS in a postmenopausal woman not on MHT is considered abnormal and requires immediate endometrial biopsy.

TRUE / FALSE

C Type 2 diabetes mellitus is an independent risk factor for endometrial cancer and combined with nulliparity represents a significant risk constellation.

TRUE / FALSE

D Optimising glycaemic control and BMI in this patient may directly reduce her risk of endometrial cancer.

TRUE / FALSE

Case 2 — Clinical Issues & Priorities

🛑 Red Flags — Urgent Investigation

- PMB after 4 years amenorrhoea = endometrial malignancy until proven otherwise
- Type 2 DM = major independent risk factor for endometrial cancer
- Nulliparity adds further risk loading
- Risk constellation mandates IMMEDIATE investigation
- Do not delay to 'watch and wait'
- Endometrial thickness >4mm on TVS = abnormal in postmenopausal non-MHT user

📋 IMS Principles Applied

- If ≥1 major risk factor for endometrial cancer → investigate IMMEDIATELY (⊕⊕⊕⊕ A)
- Initial investigation: transvaginal ultrasound (⊕⊕⊕◯ A)
- ET >4mm on continuous combined MHT = abnormal; same threshold applies to non-MHT users (⊕⊕⊕⊕ A)
- Endometrial biopsy (Pipelle) or hysteroscopy + sampling if ET abnormal (⊕⊕◯◯ B)
- Optimising BMI and diabetes reduces endometrial cancer risk (⊕⊕⊕◯ A)
- Refer urgently to gynaecological oncology if atypia or cancer confirmed (⊕⊕⊕◯ A)

Case 2 — Management Plan

Case 2

Priority	Action / Management	Grade
1	URGENT: Transvaginal ultrasound — endometrial thickness + morphology	⊕⊕⊕◯ A
2	If ET >4mm or inadequate visualisation → outpatient Pipelle biopsy	⊕⊕◯◯ B
3	If Pipelle inadequate or high suspicion → hysteroscopy + directed biopsy	⊕⊕◯◯ B
4	Concurrent: HbA1c, fasting lipids, BMI assessment — optimise metabolic control	⊕⊕⊕◯ A
5	Lower genital tract infection screen to exclude concurrent pathology	GPP
6	Oncology referral (Prof Snyman / Dr Howard) if atypia or malignancy confirmed	⊕⊕⊕◯ A
7	If benign: counsel re MHT with endometrial protection for long-term health	⊕⊕⊕◯ A

Case 2 · Postmenopausal Bleeding — Type 2 Diabetic Patient

55-year-old P0G0 | Type 2 Diabetes Mellitus | 4 years amenorrhoea | Postmenopausal bleeding

3 TRUE

Q **Regarding the assessment and management of this patient presenting with postmenopausal bleeding, which statements are TRUE?**

A The initial investigation of choice in a patient presenting with postmenopausal bleeding is a transvaginal ultrasound (TVS).

TRUE

TRUE — TVS is mandated as the initial investigation. Endometrial thickness >4mm on continuous combined MHT (or in non-MHT users) is considered abnormal. (IMS ⊕⊕⊕◯ A)

B An endometrial thickness of 3mm on TVS in a postmenopausal woman not on MHT is considered abnormal and requires immediate endometrial biopsy.

FALSE

FALSE — The threshold for abnormal endometrial thickness on continuous combined MHT is >4mm. In a non-MHT user, 3mm does not meet the threshold requiring biopsy in isolation. (IMS ⊕⊕⊕⊕ A)

C Type 2 diabetes mellitus is an independent risk factor for endometrial cancer and combined with nulliparity represents a significant risk constellation.

TRUE

TRUE — DM, nulliparity, and obesity are well-established independent risk factors for endometrial carcinoma. One major risk factor mandates immediate investigation. (IMS ⊕⊕⊕◯ A)

D Optimising glycaemic control and BMI in this patient may directly reduce her risk of endometrial cancer recurrence or development.

TRUE

TRUE — Optimisation of modifiable factors such as BMI and diabetes can reduce endometrial cancer risk. (IMS ⊕⊕⊕◯ A)

Case 3

Case 3: Climacteric Symptoms — Requests Combined EPT

50-year-old P3G4A1 | Climacteric symptoms | Intact uterus | 7 months amenorrhoea

Requests combined oestrogen-progestogen therapy (EPT)

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Case 3 · Climacteric Symptoms — Intact Uterus, Requests EPT

50-year-old P3G4A1 | Climacteric symptoms | Intact uterus | 7 months amenorrhoea | Requests combined EPT

Q **Regarding initiation of menopausal hormone therapy in this patient, which of the following statements is TRUE?**

A At 50 years of age with 7 months of amenorrhoea, sequential combined MHT is the appropriate starting regimen, with transition to continuous combined MHT planned by age 54 or after 5 years.

TRUE / FALSE

B Oestrogen-only therapy (ET) is appropriate for this patient as she has completed her family and is essentially postmenopausal.

TRUE / FALSE

C Medroxyprogesterone acetate (MPA) is the progestogen of first choice in combined MHT due to its superior evidence base for endometrial protection.

TRUE / FALSE

D A serum FSH level must confirm postmenopausal status before MHT can be safely initiated in this patient.

TRUE / FALSE

Case 3 — Clinical Issues & Priorities

📍 Clinical Context

- STRAW+10 Stage -1 to +1a: late menopausal transition / very early postmenopause
- VMS + 7 months amenorrhoea — clinical diagnosis, bloods not required to initiate MHT
- Intact uterus → combined EPT mandatory (no oestrogen-only)
- At 50 with 7 months amenorrhoea → sequential combined MHT (not yet continuous)
- Transition to continuous combined MHT by age 54 or after 5 years of sequential
- Contraception still relevant — HRT is NOT contraceptive

📋 IMS Principles Applied

- MHT is most effective for VMS — offer within 10 years of menopause / <60 years (⊕⊕⊕⊕ A)
- Sequential MHT at this stage — minimum 12 days micronized progesterone or dydrogesterone per cycle (⊕⊕⊕⊕ A)
- Micronized progesterone and dydrogesterone carry most favourable breast cancer risk profile (⊕⊕⊕◯ B)
- Switch to continuous combined MHT after 5 years or by age 54 (⊕⊕⊕◯ B)
- Micronized progesterone at bedtime improves sleep — important if sleep disturbance prominent (⊕⊕◯◯ C)
- 52mg LNG IUD + transdermal oestradiol: optimal — covers contraception + EPT (⊕⊕⊕◯ B)

Case 3 — Management Plan

Case 3

Priority	Action / Management	Grade
1	Transdermal oestradiol 50–75mcg/day (gel or patch) — VMS first-line	⊕⊕⊕⊕ A
2	Micronized progesterone (Utrogestan) 200mg for 12 days/cycle OR dydrogesterone 10mg 12–14 days	⊕⊕⊕⊕ A
3	Alternative: 52mg LNG IUD as progestogen + transdermal oestradiol — covers contraception	⊕⊕⊕◯ B
4	Micronized progesterone at BEDTIME if sleep disturbance is prominent (GABAergic benefit)	⊕⊕◯◯ C
5	Counsel: HRT is NOT contraceptive — discuss ongoing contraceptive need	⊕⊕⊕◯ A
6	Baseline: BP, weight/BMI, mammogram (if not recent). TVS not routinely indicated.	GPP
7	Plan transition to continuous combined MHT at age 54 or after 5 years of sequential	⊕⊕⊕◯ B

Case 3 · Climacteric Symptoms — Intact Uterus, Requests EPT

50-year-old P3G4A1 | Climacteric symptoms | Intact uterus | 7 months amenorrhoea | Requests combined EPT

1 TRUE

Q **Regarding initiation of menopausal hormone therapy in this patient, which of the following statements is TRUE?**

A At 50 years of age with 7 months of amenorrhoea, sequential combined MHT is the appropriate starting regimen, with transition to continuous combined MHT planned by age 54 or after 5 years.

TRUE

TRUE — Sequential MHT is appropriate for women not yet clearly postmenopausal. Transition to continuous combined MHT is recommended after 5 years or by age 54. (IMS ⊕⊕⊕◯ B)

B Oestrogen-only therapy (ET) is appropriate for this patient as she has completed her family and is essentially postmenopausal.

FALSE

FALSE — ET is recommended ONLY for women WITHOUT an intact uterus. She has an intact uterus; unopposed oestrogen would increase her endometrial cancer risk. (IMS ⊕⊕⊕⊕ A)

C Medroxyprogesterone acetate (MPA) is the progestogen of first choice in combined MHT due to its superior evidence base for endometrial protection.

FALSE

FALSE — Micronized progesterone and dydrogesterone are preferred as they carry a more favourable breast cancer risk profile than synthetic progestogens including MPA. (IMS ⊕⊕⊕◯ B)

D A serum FSH level must confirm postmenopausal status before MHT can be safely initiated in this patient.

FALSE

FALSE — The diagnosis of menopause is a CLINICAL diagnosis not dependent on special investigations. FSH is used only as supportive criteria or when staging cannot be based on menstrual history. (IMS GPP)

Case 4

Case 4: Premature Ovarian Insufficiency — Asymptomatic

38-year-old | POI/POF | Amenorrhoea | Asymptomatic | Caucasian | Low BMI
Routine check-up — discuss risks and management

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Case 4 · Premature Ovarian Insufficiency — Asymptomatic

38-year-old | POI / POF | Amenorrhoea | Asymptomatic | Caucasian | Low BMI | Routine check-up

Q **Regarding premature ovarian insufficiency (POI) in this asymptomatic patient, which of the following statements are TRUE?**

A Hormone therapy should be withheld until the patient develops symptomatic oestrogen deficiency, as treating an asymptomatic woman carries unnecessary risk.

TRUE / FALSE

B Women with POI may require higher doses of HT than those used for standard postmenopausal women to achieve adequate symptom control and bone protection.

TRUE / FALSE

C DXA bone densitometry is indicated at baseline in this patient given her low BMI and amenorrhoea.

TRUE / FALSE

D There is no evidence that the risk of breast cancer with HT in women with POI is higher than in age-matched women with normal ovarian function.

TRUE / FALSE

Case 4 — Clinical Issues & Priorities

⚠️ Why Asymptomatic POI Still Requires Treatment

- POI affects up to 3.5–3.7% of the global female population (⊕⊕⊕⊕ A)
- Untreated POI associated with DECREASED LIFE EXPECTANCY
- Increased risk: CVD, osteoporosis, cognitive decline, dementia, Parkinsonism
- Low BMI = additional bone health risk — DXA baseline mandatory
- Caucasian + low BMI = highest osteoporosis risk category
- Absence of symptoms does NOT negate systemic oestrogen-deprivation consequences
- HT must be offered whether symptomatic or not — primary prevention mandate (⊕⊕◯◯ A)

🔬 Investigations for POI Aetiology

- Confirm diagnosis: FSH >25 IU/L on two occasions ≥4–6 weeks apart (ESHRE 2024)
- Repeat FSH/LH/E2/AMH — staging and baseline
- Thyroid function, adrenal antibodies (21-hydroxylase), anti-ovarian antibodies
- Coeliac screen — especially relevant in Caucasian women with low BMI
- Karyotype — exclude Turner mosaic (45X0 or mosaic)
- FMR1 premutation — Fragile X carrier screening
- DXA bone densitometry — baseline mandatory
- Pelvic ultrasound — ovarian morphology

Case 4 — Management Plan

Case 4

Priority	Action / Management	Grade
1	Initiate HT promptly: transdermal oestradiol 75–100mcg/day (higher than standard postmenopausal dose)	⊕⊕◯◯ B
2	Cyclic micronized progesterone 200mg (12 days/cycle) for endometrial protection	⊕⊕◯◯ A
3	DXA bone densitometry at baseline; repeat every 2–3 years	GPP
4	Calcium 1200mg + Vitamin D 800 IU daily; weight-bearing and resistance exercise	⊕⊕⊕◯ A
5	Fertility counselling: counsel re spontaneous conception (~5%) and donor oocyte/ART	⊕⊕⊕◯ A
6	Reassure: no evidence that HT risk of breast cancer is higher than age-matched peers with normal ovarian function	⊕⊕◯◯ C
7	Continue HT until at least natural menopausal age (51); annual CV risk + bone monitoring	⊕⊕◯◯ A

Case 4 · Premature Ovarian Insufficiency — Asymptomatic

38-year-old | POI / POF | Amenorrhoea | Asymptomatic | Caucasian | Low BMI | Routine check-up

3 TRUE

Q **Regarding premature ovarian insufficiency (POI) in this asymptomatic patient, which of the following statements are TRUE?**

A Hormone therapy should be withheld until the patient develops symptomatic oestrogen deficiency, as treating an asymptomatic woman carries unnecessary risk.

FALSE

FALSE — HT should be offered whether there are symptoms or not, for primary prevention to reduce risks of morbidity and mortality. Untreated POI is associated with decreased life expectancy. (IMS ⊕⊕◯◯ A)

B Women with POI may require higher doses of HT than those used for standard postmenopausal women to achieve adequate symptom control and bone protection.

TRUE

TRUE — Standard postmenopausal MHT doses are often insufficient in a 38-year-old with POI. Higher doses of oestrogen are frequently required. (IMS ⊕⊕◯◯ B)

C DXA bone densitometry is indicated at baseline in this patient given her low BMI and amenorrhoea.

TRUE

TRUE — Low BMI, Caucasian ethnicity, and oestrogen deficiency from POI are major osteoporosis risk factors. Baseline DXA is mandatory. (IMS GPP)

D There is no evidence that the risk of breast cancer with HT in women with POI is higher than in age-matched women with normal ovarian function.

TRUE

TRUE — HT in POI essentially restores oestrogen levels to what age-matched peers experience physiologically. Breast cancer risk is not elevated above that of peers. (IMS ⊕⊕◯◯ C)

Case 5

Case 5: Perimenopausal — New Relationship, Multiple Issues

47-year-old | No contraception | New relationship | Sexually active
Irregular menses (amenorrhoea up to 90 days) | Hot flushes | Dyspareunia | Post-coital cystitis

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Case 5 · Perimenopausal — New Relationship, Multiple Concurrent Issues

47-year-old | No contraception | New relationship | Irregular menses | Hot flushes | Dyspareunia | Post-coital cystitis

Q **Regarding the priority management of this perimenopausal patient, which of the following statements are TRUE?**

A A urinary hCG test must be performed before initiating any hormonal therapy in this patient.

TRUE / FALSE

B Standard HRT (oestrogen + progestogen) provides reliable contraception in perimenopausal women and no additional contraceptive method is required.

TRUE / FALSE

C Vaginal oestrogen therapy is recommended for the prevention of recurrent urinary tract infections in perimenopausal and postmenopausal women.

TRUE / FALSE

D Genitourinary syndrome of menopause (GSM) is a self-limiting condition that typically resolves spontaneously once full menopause is established.

TRUE / FALSE

Case 5 — Priority Clinical Issues

🔴 Priority 1: Exclude Pregnancy — Mandatory Before Any Hormonal Therapy

- Urinary hCG FIRST — irregular cycles + sexually active + no contraception = ectopic or intrauterine pregnancy until excluded
- Do not initiate MHT or any hormonal therapy before pregnancy is ruled out

🔬 Priority 2: Sexual Health Screening — New Relationship

- NAAT for Chlamydia/Gonorrhoea, Trichomonas, Bacterial vaginosis screen — pelvic & lower genital tract infection screen mandated (GPP)
- Cervical cytology — confirm up to date; consider HIV risk assessment

💊 Priority 3: Contraception — Urgent, Often Overlooked

- HRT is NOT contraceptive unless combined with intrauterine progestogen-releasing device (⊕⊕⊕◯ A)
- 52mg LNG IUD: optimal solution — contraception + irregular bleeding + endometrial protection + progestogen arm of MHT (⊕⊕⊕◯ B)

🌡 Priority 4: GSM + Dyspareunia + Post-Coital Cystitis

- Vaginal oestrogen therapy recommended for prevention of RUTIs (⊕⊕⊕⊕ A) and to improve genitourinary symptoms (⊕⊕⊕⊕ A)
- GSM is chronic — does not resolve without treatment (⊕⊕⊕◯ B); local vaginal oestrogen + lubricants/moisturisers as first line

Case 5 — Management Plan

Case 5

Priority	Action / Management	Grade
1	Urinary hCG — exclude pregnancy before any hormonal therapy	GPP
2	Lower genital tract infection screen + cervical cytology review (new partner)	GPP
3	Insert 52mg LNG IUD — contraception + bleeding control + progestogen arm of MHT	⊕⊕⊕◯ B
4	Add transdermal oestradiol 25–50mcg (gel/patch) for VMS after IUD confirmed in situ	⊕⊕⊕⊕ A
5	Local vaginal oestrogen (Vagifem 10mcg or Ovestin) for dyspareunia + GSM — independent of systemic MHT	⊕⊕⊕⊕ A
6	Vaginal lubricant/moisturiser (hyaluronic acid gel) for immediate dyspareunia relief	⊕⊕⊕⊕ A
7	MSU if active UTI; post-coital voiding advice; short-term prophylactic antibiotic as bridge	GPP
8	Biopsychosocial sexual function assessment — new relationship context + anticipatory pain anxiety	GPP

Case 5 · Perimenopausal — New Relationship, Multiple Concurrent Issues

47-year-old | No contraception | New relationship | Irregular menses | Hot flushes | Dyspareunia | Post-coital cystitis

2 TRUE

Q **Regarding the priority management of this perimenopausal patient, which of the following statements are TRUE?**

A A urinary hCG test must be performed before initiating any hormonal therapy in this patient.

TRUE

TRUE — She is sexually active with no contraception and has irregular cycles. Pregnancy — including ectopic — must be excluded before any hormonal therapy is commenced. (IMS GPP)

B Standard HRT (oestrogen + progestogen) provides reliable contraception in perimenopausal women and no additional contraceptive method is required.

FALSE

FALSE — HRT should NOT be regarded as contraceptive unless combined with an intrauterine progestogen-releasing device. Spontaneous ovulation continues intermittently in perimenopause. (IMS ⊕⊕⊕◯ A)

C Vaginal oestrogen therapy is recommended for the prevention of recurrent urinary tract infections in perimenopausal and postmenopausal women.

TRUE

TRUE — Vaginal oestrogen restores urethral/bladder epithelium and Lactobacillus-dominant flora, directly preventing RUTIs. Grade A recommendation. (IMS ⊕⊕⊕⊕ A)

D Genitourinary syndrome of menopause (GSM) is a self-limiting condition that typically resolves spontaneously once full menopause is established.

FALSE

FALSE — GSM is a CHRONIC condition that does NOT resolve without treatment and may return upon discontinuation of therapy. Progressive without intervention. (IMS ⊕⊕⊕◯ B)

Case 6

Case 6: Severe VMS — Stroke & Breast Cancer Family History

52-year-old | Severe VMS (daily function impaired) | Sleep disturbance | Low libido | Irritability
Family history: stroke (maternal) | Maternal breast cancer age 55

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Panay N et al. IMS Recommendations. Climacteric. 2025;28(6):634–656 | DOI: 10.1080/13697137.2025.2585487

Case 6 · Severe VMS — Family History of Stroke & Breast Cancer

52-year-old | Severe VMS | Sleep disturbance | Low libido | Maternal stroke | Maternal breast cancer age 55

Q **Regarding risk assessment and treatment options for this patient, which of the following statements are TRUE?**

A A first-degree family history of postmenopausal breast cancer (maternal, age 55) is an absolute contraindication to all forms of menopausal hormone therapy.

TRUE / FALSE

B Women who initiate MHT before age 60 or within 10 years of menopause onset have a similar risk of stroke compared to women who do not take MHT.

TRUE / FALSE

C Fezolinetant and elinzanetant are neurokinin receptor antagonists supported by Grade A randomised controlled trial evidence for the treatment of vasomotor symptoms.

TRUE / FALSE

D Oral oestrogen at a low dose is an acceptable alternative to transdermal oestradiol in this patient, provided a body-identical progestogen is used.

TRUE / FALSE

Case 6 — Risk Assessment & MHT Route Decisions

Case 6

⚠️ Breast Cancer Risk — Quantify, Don't Assume

- Formal risk assessment MANDATORY: use CanRisk / IBIS / Gail tool (⊕⊕⊕◯ B)
- Maternal breast cancer at 55 = postmenopausal — lower hereditary loading than pre-menopausal onset
- MHT attributable breast cancer risk is small — similar to lifestyle factors (obesity, alcohol) (⊕⊕⊕⊕ A)
- Progestogen choice is the key safety lever: micronized progesterone or dydrogesterone preferred (⊕⊕⊕◯ B)
- Increased breast density → additional mammographic surveillance (⊕⊕⊕◯ B)
- MHT not recommended for women WITH breast cancer or at HIGH risk (⊕⊕⊕⊕ A)

🩺 Stroke Risk — Route is Everything

- Women initiating MHT <10 years of menopause / <60 years: SAME stroke risk as non-users (⊕⊕⊕⊕ A)
- At 52 she IS within the safe initiation window
- Oral oestrogen at >10 years post-menopause / >60 years: increased stroke risk (⊕⊕⊕⊕ A)
- Transdermal route reduces stroke risk vs oral — preferred in ALL women with stroke family history (⊕⊕◯◯ C)
- Oral oestrogen EXCLUDED in this patient — transdermal only
- Screen for migraine with aura — if present, non-hormonal options preferred

Case 6 — Management Plan

Case 6

Priority	Action / Management	Grade
1	Formal breast cancer risk: CanRisk/IBIS; mammogram with density report; current bloods	⊕⊕⊕◯ B
2	Transdermal oestradiol 50mcg + micronized progesterone 100mg nocte (continuous combined)	⊕⊕⊕⊕ A
3	If high breast cancer risk: fezolinetant or elinzanetant as Grade A non-hormonal alternative	⊕⊕⊕⊕ A
4	CBT-I referral — first-line for sleep disturbance regardless of MHT decision	⊕⊕⊕⊕ A
5	Proactively screen for GSM — add local vaginal oestrogen if atrophy identified	⊕⊕⊕⊕ A
6	Reassess libido at 3 months after VMS/GSM treated; if HSDD confirmed → transdermal testosterone	⊕⊕⊕⊕ A
7	Annual mammogram with density monitoring; CBT for mood/irritability alongside pharmacotherapy	GPP

Case 6 · Severe VMS — Family History of Stroke & Breast Cancer

52-year-old | Severe VMS | Sleep disturbance | Low libido | Maternal stroke | Maternal breast cancer age 55

2 TRUE

Q **Regarding risk assessment and treatment options for this patient, which of the following statements are TRUE?**

A A first-degree family history of postmenopausal breast cancer (maternal, age 55) is an absolute contraindication to all forms of menopausal hormone therapy.

FALSE

FALSE — Family history alone is NOT an absolute contraindication. Baseline risk must be formally quantified using validated tools (Gail/IBIS/CanRisk). MHT risk is small and similar to common lifestyle risk factors. (IMS ⊕⊕⊕◯ B)

B Women who initiate MHT before age 60 or within 10 years of menopause onset have a similar risk of stroke compared to women who do not take MHT.

TRUE

TRUE — The timing window is key. At 52 years, she falls within the safe initiation window. Risk increases only when MHT is initiated >10 years after menopause or >60 years of age. (IMS ⊕⊕⊕⊕ A)

C Fezolinetant and elinzanetant are neurokinin receptor antagonists supported by Grade A randomised controlled trial evidence for the treatment of vasomotor symptoms.

TRUE

TRUE — Both are NK-receptor antagonists with Phase 3 RCT data and government approvals. Elinzanetant additionally has evidence in endocrine therapy-associated VMS in breast cancer. (IMS ⊕⊕⊕⊕ A)

D Oral oestrogen at a low dose is an acceptable alternative to transdermal oestradiol in this patient, provided a body-identical progestogen is used.

FALSE

FALSE — Oral oestrogen is contraindicated in this patient given her family history of stroke. Transdermal oestradiol is the ONLY acceptable route — route of delivery is not interchangeable with dose adjustment. (IMS ⊕⊕◯◯ C)

Case 7

Case 7: ER+ Breast Cancer on Tamoxifen — GSM & Recurrent UTIs

45-year-old | Tamoxifen for ER+ breast cancer | Dyspareunia
Recurrent urinary tract infections | Significantly impaired quality of life

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Panay N et al. IMS Recommendations. Climacteric. 2025;28(6):634–656 | DOI: 10.1080/13697137.2025.2585487

Case 7 · ER+ Breast Cancer on Tamoxifen — GSM & Recurrent UTIs

45-year-old | Tamoxifen for ER+ breast cancer | Dyspareunia | Recurrent UTIs | Significantly impaired QoL

Q **Regarding the management of GSM and recurrent UTIs in this patient on tamoxifen, which of the following statements are TRUE?**

A Paroxetine is an appropriate SSRI to prescribe for mood support or hot flush management in a patient taking tamoxifen for ER+ breast cancer. TRUE / FALSE

B Low-dose local vaginal oestrogen (e.g., oestradiol 10mcg pessary) appears safe in women on tamoxifen and is supported by IMS evidence for GSM management. TRUE / FALSE

C Systemic MHT (transdermal oestradiol + progestogen) is recommended as the preferred first-line treatment for GSM in breast cancer survivors when non-hormonal measures have failed. TRUE / FALSE

D Elinzanetant has been specifically demonstrated to be effective for endocrine therapy-associated vasomotor symptoms in women with breast cancer. TRUE / FALSE

Case 7 — Clinical Framework & Key Principles

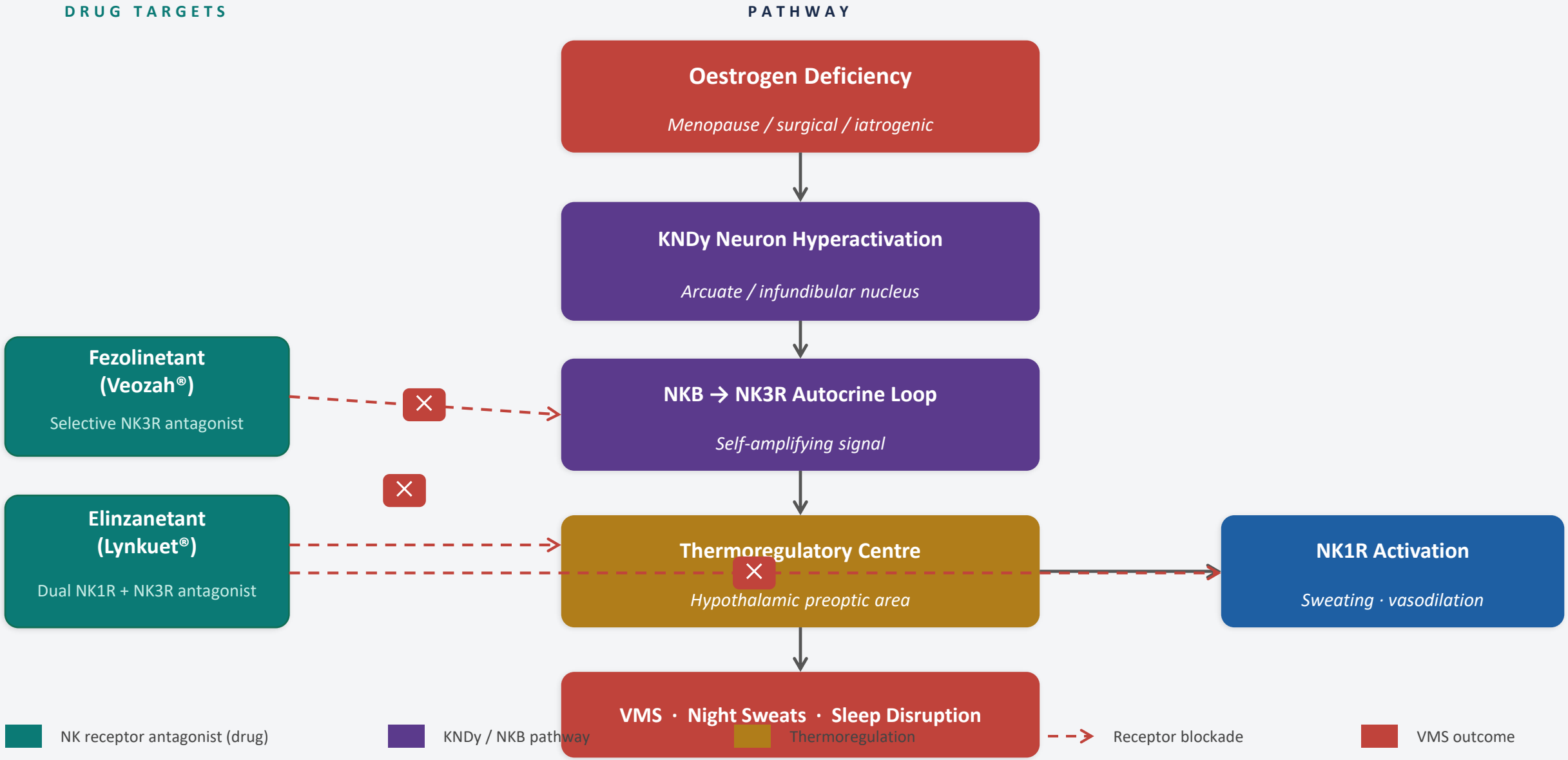
⚕️ Why GSM Cannot Be Ignored Here

- Tamoxifen acts as oestrogen ANTAGONIST at vaginal/urethral epithelium — severe functional oestrogen deprivation at local level
- GSM is frequent and can be severe in breast cancer survivors (⊕⊕⊕◯ B)
- Proactive management improves QoL AND tamoxifen adherence (⊕⊕⊕◯ A)
- Tamoxifen non-adherence due to intolerable side effects = documented cause of breast cancer recurrence
- Treating GSM is therefore also an oncological intervention
- PAROXETINE IS ABSOLUTELY CONTRAINDICATED with tamoxifen — inhibits CYP2D6 (⊕⊕⊕◯ B)

📋 IMS Principles Applied — Breast Cancer Survivors

- MDT communication with oncologist before any hormonal/near-hormonal therapy — mandatory
- Non-hormonal topical therapies FIRST: vaginal lubricants + moisturisers — Grade A, no cancer risk (⊕⊕⊕⊕ A)
- Vaginal oestrogen therapy for RUTIs — Grade A evidence (⊕⊕⊕⊕ A)
- Vaginal oestrogen appears safe in women on tamoxifen (⊕⊕⊕◯ B)
- Intravaginal DHEA (prasterone) — effective alternative; minimal systemic absorption (⊕⊕⊕⊕ A)
- Elinzanetant — specifically trialled in endocrine therapy-treated breast cancer VMS (⊕⊕⊕⊕ A)

KNDy Pathway & NK Receptor Antagonism in Menopausal VMS



NK = neurokinin · NKB = neurokinin B · KNDy = kisspeptin / neurokinin B / dynorphin · VMS = vasomotor symptoms

Case 7 — Treatment Ladder

Step 1: Non-Hormonal Measures (Mandatory First-Line — Safe in All Breast Cancer Survivors)

- Vaginal moisturiser: hyaluronic acid gel (Hyalofemme) or Replens — 3× weekly for ongoing hydration and pH restoration
- Vaginal lubricant (water-based YES WB) for intercourse — immediate symptom relief
- Pelvic floor physiotherapy — secondary hypertonicity from chronic dyspareunia → referral
- Post-coital voiding, D-mannose, culture-directed antibiotics for active UTI

Step 2: Low-Dose Local Vaginal Oestrogen (After Oncological Discussion)

- Vagifem 10mcg pessary: serum E2 remains within postmenopausal range — negligible systemic absorption
- Vaginal oestrogen appears safe in women on tamoxifen (⊕⊕⊕◯ B) and is recommended for RUTIs (⊕⊕⊕⊕ A)
- Tamoxifen antagonises oestrogen systemically but NOT at the vaginal epithelium — local oestrogen acts independently

Step 3: Intravaginal DHEA/Prasterone — if Oncologist Prefers Oestrogen-Free Option

- Prasterone (Intrarosa 6.5mg) — intracrine mechanism; serum oestradiol and testosterone remain postmenopausal (⊕⊕⊕⊕ A)
- Effective for dyspareunia secondary to VVA; does not appear to have systemic oestrogenic effect

Step 4: Co-existing VMS on Tamoxifen — Elinzanetant is the Preferred Agent

- Elinzanetant (NK1/NK3 antagonist): specifically trialled for endocrine therapy-associated VMS in breast cancer patients (⊕⊕⊕⊕ A)
- Non-hormonal, centrally-acting, no oestrogenic activity — completely safe in ER+ context
- Venlafaxine is preferred SNRI if antidepressant needed — NOT paroxetine (CYP2D6 inhibition reduces tamoxifen efficacy)

Case 7 · ER+ Breast Cancer on Tamoxifen — GSM & Recurrent UTIs

45-year-old | Tamoxifen for ER+ breast cancer | Dyspareunia | Recurrent UTIs | Significantly impaired QoL

2 TRUE

Q **Regarding the management of GSM and recurrent UTIs in this patient on tamoxifen, which of the following statements are TRUE?**

A Paroxetine is an appropriate SSRI to prescribe for mood support or hot flush management in a patient taking tamoxifen for ER+ breast cancer.

FALSE

FALSE — Paroxetine is ABSOLUTELY CONTRAINDICATED with tamoxifen. It inhibits CYP2D6, converting tamoxifen to its inactive metabolite (endoxifen), thereby reducing its anti-cancer efficacy. Use venlafaxine instead. (IMS ⊕⊕⊕◯ B)

B Low-dose local vaginal oestrogen (e.g., oestradiol 10mcg pessary) appears safe in women on tamoxifen and is supported by IMS evidence for GSM management.

TRUE

TRUE — Ultra-low-dose vaginal oestrogen produces negligible systemic absorption, maintaining serum E2 within postmenopausal range. Vaginal oestrogen appears safe in women on tamoxifen. (IMS ⊕⊕⊕◯ B)

C Systemic MHT (transdermal oestradiol + progestogen) is recommended as the preferred first-line treatment for GSM in breast cancer survivors when non-hormonal measures have failed.

FALSE

FALSE — Systemic MHT is NOT recommended in breast cancer survivors. There is a lack of safety data. Vaginal lubricants and moisturisers are mandated first-line, followed by local therapies after oncological discussion. (IMS ⊕⊕⊕◯ B)

D Elinzanetant has been specifically demonstrated to be effective for endocrine therapy-associated vasomotor symptoms in women with breast cancer.

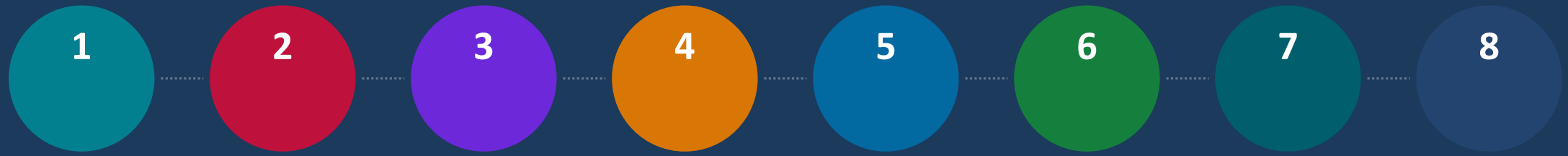
TRUE

TRUE — Elinzanetant (dual NK1/NK3 antagonist) has Phase 3 trial evidence specifically in women receiving endocrine therapy for breast cancer — the only agent with this specific evidence base. (IMS ⊕⊕⊕⊕ A)

Clinical Decision Making in MHT

An 8-Step Thought Process Framework

A structured approach to safe, individualised, evidence-based prescribing



Panay N et al. IMS Recommendations and Key Messages on Women's Midlife Health and Menopause. Climacteric. 2025;28(6):634–656

Clinical Decision Making — Steps 1 to 4

1 AGE

< 40 yrs	POI — Initiate HT promptly, continue until natural menopausal age (~51). Higher doses often needed. Fertility counselling.
40–45 yrs	Early menopause — same risks as POI. HT indicated. Discuss long-term health consequences.
45–60 yrs	Optimal window for MHT — benefit-risk most favourable. Initiate within 10 years of menopause. (⊕⊕⊕⊕ A)
> 60 yrs	Initiation after 10 years of menopause carries increased CVD and stroke risk. Reassess indication carefully; use lower doses.

2 UNDERLYING RISK FACTORS

VTE / Obesity	Oral oestrogen contraindicated. Transdermal oestradiol mandatory — does not increase VTE risk even with obesity. (⊕⊕⊕◯ B)
Cardiovascular	MHT in women <60 yrs / <10 yrs post-menopause reduces CHD and all-cause mortality. Transdermal preferred if uncontrolled risk factors.
Breast cancer Hx/risk	Formal risk assessment (CanRisk/IBIS/Gail) mandatory. Micronized progesterone or dydrogesterone preferred progestogens. Tibolone and MPA carry higher risk.
Migraine with aura	Oral oestrogen contraindicated (↑ stroke risk). Transdermal preferred. Non-hormonal options if risk high. (⊕⊕⊕◯ B)

3 MENOPAUSAL CLASSIFICATION

Premenopausal	Regular cycles, no symptoms — MHT not indicated. Refer for investigation if irregular cycles/symptoms in a young woman (exclude POI).
Perimenopausal	Irregular cycles ± VMS. Contraception still required. Sequential MHT + 52mg LNG IUD is optimal. Confirm staging clinically (STRAW+10).
Early postmenopause	< 5 years amenorrhoea. Ideal window for MHT initiation. Sequential → transition to continuous combined by year 5 or age 54. (⊕⊕⊕◯ B)
Late postmenopause	> 5–10 years amenorrhoea. Risk-benefit shifts. Lower doses, transdermal route. Screen for new risk factors before initiating or continuing.

4 DOSAGE

Low dose	Starting dose in perimenopausal/older women. Oestradiol 25–37.5mcg (patch) or 0.5mg/day (gel). Reduces risk; adequate for bone protection in most.
Standard dose	Oestradiol 50mcg (patch) or 1–1.5mg/day (gel). Effective for VMS in >80% of women. Most commonly used initiation dose. (⊕⊕⊕⊕ A)
Higher dose (POI)	POI women often require oestradiol 75–100mcg (patch) or 1.5–3mg/day (gel). Standard postmenopausal doses frequently insufficient at age <40. (⊕⊕◯◯ B)
Dose titration	If symptom control inadequate: stepwise dose escalation, change in preparation or route. Monitor serum E2 in POI, inadequate response, or persistent side effects. (GPP)

Clinical Decision Making — Steps 5 to 8

5 ROUTE OF ADMINISTRATION

Oral	Acceptable in low-risk women. Avoid if: VTE risk, obesity (BMI>30), hypertension, migraine with aura, active liver disease, or family history of stroke.
Transdermal	Preferred route in most women. Does NOT increase VTE or stroke risk. Gel (daily), patch (twice weekly or weekly). Mandated in VTE risk, CVD risk, obesity, migraine.
Vaginal / local	For GSM only — not a systemic treatment for VMS. Safe in breast cancer survivors (vaginal E2 10mcg). Minimal systemic absorption. Indicated for RUTIs. (⊕⊕⊕⊕ A)
Intranasal / spray	Alternative transdermal delivery (Lenzetto). Useful for poor skin absorption or skin reactions to gel/patch. Similar VTE profile to standard transdermal.

6 TYPE OF MHT REGIMEN

Oestrogen-only (ET)	ONLY in women WITHOUT an intact uterus (post-hysterectomy). Associated with lower breast cancer risk than combined MHT. (⊕⊕⊕◯ B)
Sequential combined	Intact uterus + perimenopausal / early postmenopausal (<5 years). Progestogen for 12–14 days/cycle. Transition to continuous combined by age 54 or after 5 years. (⊕⊕⊕⊕ A)
Continuous combined	Intact uterus + clearly postmenopausal (>1 year amenorrhoea). No withdrawal bleed. Amenorrhoeic users have lower endometrial cancer risk than non-MHT users. (⊕⊕⊕◯ A)
Progestogen choice	Micronized progesterone or dydrogesterone preferred — most favourable breast cancer risk profile. Avoid MPA/NET in breast cancer risk. LNG IUD valid as progestogen arm. (⊕⊕⊕◯ B)

7 DURATION OF THERAPY

VMS-driven use	Continue for duration of symptoms. No arbitrary time limit in healthy women <60 yrs. Reassess annually; if stopping, VMS recur in up to 87% of cases. (⊕⊕◯◯ C)
Bone protection	MHT significantly reduces fracture risk but cessation leads to rapid bone loss. If bone protection is the indication, consider transition to bone-specific agents (bisphosphonates) on cessation. (⊕⊕⊕◯ A)
POI	HT should be continued at minimum until the natural age of menopause (~51 years). Do not stop early — untreated POI reduces life expectancy. (⊕⊕◯◯ A)
Stopping MHT	No evidence-based protocol for discontinuation. Gradual dose reduction over 3–6 months often preferred. VMS frequently recur; reinitiation is acceptable if clinically needed. (⊕⊕◯◯ C)

8 FOLLOW-UP & MONITORING

6–8 weeks	Initial review: VMS response, tolerability, bleeding pattern, mood and sleep. Adjust dose or preparation if needed. Confirm IUD position if in situ.
3 months	Reassess sexual function, GSM symptoms, HSDD (consider testosterone if applicable). Confirm blood pressure normalisation on new MHT.
Annual review	Clinical breast examination. Mammogram every 1–2 years with density monitoring. BP, weight, fasting lipids, HbA1c if DM. TVS if unscheduled bleeding occurs. Cervical cytology as per guidelines.
Endometrial alert	Unscheduled bleeding on MHT → TVS. ET >4mm (continuous combined) or >7mm (sequential, post-bleed) → Pipelle biopsy or hysteroscopy. If hyperplasia or cancer → refer urgently. (⊕⊕⊕⊕ A)

Quick Reference — MHT Prescribing Decision Checklist

GP LEVEL

1 — AGE

Is she <40 (POI), 40–45 (early), 45–60 (optimal window), or >60 (late)?

→ POI/early → higher doses, HT to age 51. >60 → lower doses, transdermal, careful risk-benefit.

2 — RISK FACTORS

VTE? Cardiovascular disease? Breast cancer risk (baseline score)? Migraine with aura?

→ VTE/CVD/migraine → transdermal only. Breast ca risk → CanRisk/IBIS score; prefer micronized P4 or dydrogesterone.

3 — CLASSIFICATION

Premenopausal / Perimenopausal / Early postmenopausal / Late postmenopausal?

→ Peri → contraception needed; sequential MHT + LNG IUD optimal. Postmenopause >1yr → continuous combined.

4 — DOSAGE

Low (25mcg), Standard (50mcg), or Higher dose (75–100mcg for POI)?

→ Start low-standard; titrate to response. POI often needs higher doses. Serum E2 if inadequate response.

5 — ROUTE

Oral (low risk only) or Transdermal (VTE, obesity, migraine, CVD risk, preference)?

→ Transdermal is the default safe option. Oral only in low-risk, no VTE/CVD/stroke risk factors. Vaginal for GSM only.

6 — TYPE

Oestrogen-only (no uterus) / Sequential combined (peri) / Continuous combined (post)?

→ Intact uterus → always combined. Sequential → continuous by age 54 or 5 years. Prefer micronized P4 or dydrogesterone.

7 — DURATION

Is MHT for VMS relief, bone protection, or POI? What is the stopping plan?

→ No arbitrary time limit in healthy <60yr women. POI → continue to age 51. Annual reassessment mandatory. Stopping = VMS recur in 87%.

8 — FOLLOW-UP

Initial review (6–8 wks), 3-month review (sexual function/HSDD), annual (breast/endo/CVD)?

→ Annual: mammogram, BP, weight, lipids. Unscheduled bleeding → TVS immediately. Cervical cytology per guidelines.

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