Menopause — Non-Hormonal Pharmacotherapy

SSRIs/SNRIs & other established agents for VMS

CLINICAL PATHWAY

When MHT is contraindicated, declined, or insufficient, several non-hormonal agents have evidence for vasomotor symptoms (VMS) — first-line agents reduce VMS frequency by roughly 50–65%. Choice depends on comorbidities, drug interactions (especially tamoxifen) and renal function. See companion sheet WH-06B for the newer NK receptor antagonist class.

WHEN TO CHOOSE NON-HORMONAL

- Current or past hormone-sensitive breast, ER+ ovarian or endometrial cancer — systemic MHT contraindicated.
- Prior unprovoked VTE, known thrombophilia or active anticoagulation — transdermal MHT may still be an option case-by-case.
- Patient preference — many decline MHT despite eligibility; validate the choice and offer effective alternatives.
- Refractory VMS despite optimised MHT — consider adding a non-hormonal agent rather than escalating estrogen indefinitely.

SSRIs/SNRIs — FIRST-LINE FOR VMS

- Venlafaxine: best evidence base for VMS; start low and titrate. Useful if low mood. Watch BP; taper slowly when stopping.
- Escitalopram: well tolerated; safe with tamoxifen (unlike paroxetine/fluoxetine). Useful if anxious or low-mood phenotype.
- Avoid paroxetine and fluoxetine with tamoxifen — strong CYP2D6 inhibition reduces tamoxifen activation.
- Desvenlafaxine: similar efficacy and BP-watch profile to venlafaxine; useful if venlafaxine is not tolerated.

GABAPENTINOIDS

- Gabapentin: useful for night-time VMS and sleep; titrate gradually. Caution if eGFR under 60 (renally cleared).
- Pregabalin: similar profile, more predictable absorption. Watch sedation and weight gain; renal dose-adjust.
- Either is a reasonable alternative or add-on if an SSRI/SNRI is contraindicated or not tolerated.

OTHER AGENTS

- Oxybutynin: anticholinergic; a reasonable option for breast cancer survivors, but avoid in frail or elderly patients (cognitive risk).
- Clonidine: modest VMS benefit with significant side effects (sedation, hypotension, dry mouth) — generally superseded by newer options.
- Tibolone: synthetic, not strictly non-hormonal; avoid in breast cancer survivors (LIBERATE trial showed increased recurrence). May help low libido.

PRACTICAL CHOICE

A reasonable start is an SSRI/SNRI matched to comorbidity — escitalopram if anxious/low mood and on tamoxifen, venlafaxine otherwise — adding a gabapentinoid at night if VMS disrupts sleep. Reserve oxybutynin, clonidine and tibolone for specific scenarios above.

■ SAFETY

- Never combine paroxetine or fluoxetine with tamoxifen — CYP2D6 inhibition can meaningfully cut tamoxifen efficacy.
- Gabapentinoids carry sedation and dependence potential and need renal dose adjustment — taper rather than stop abruptly.

■ RED FLAGS / REFER

- Refractory VMS despite an adequate trial of non-hormonal therapy — consider an NK receptor antagonist (companion sheet WH-06B).
- Diagnostic uncertainty about the cause of VMS-like symptoms.
- Complex psychiatric comorbidity needing specialist dose titration.

Companion sheets: WH-06B (NK receptor antagonists), WH-06C (GSM, lifestyle & complementary). See also WH-05A/B for MHT.
Verify against AMS guidance and the IMS 2024 White Paper; confirm drug interactions at the AMH before prescribing.