Bleeding Management Pathway

Step 1 – Continuous Oral Regimen

- Estrogel: 2 pumps daily (~1.5 mg estradiol absorbed transdermally)
- Evidence: This dose is effective for bone protection and cardiovascular benefits. The KEEPS trial and the E3N cohort confirm improvements in bone mineral density and cardiometabolic health with this transdermal dose, without increasing clotting risk.
- Prometrium: 100 mg orally at night continuously (no break)
- Note: This regimen is convenient and works well for most women. If breakthrough bleeding occurs, it may be due to continuous endometrial stimulation without a reset. Introducing a 3-day break (Days 1–25 dosing) can help reset progesterone receptor sensitivity, improving endometrial responsiveness.
- Evidence: Continuous HRT can cause receptor desensitisation. A 3-day break has been shown to re-sensitise progesterone receptors, reducing bleeding (SAGE Journals, 2021; Menopause Matters Forum). A 100 mg/day regimen for 25 days per month with a 3-day break has a high rate of amenorrhea and endometrial safety.

Step 2 – Cyclical Oral Regimen (if bleeding occurs on continuous use)

- Estrogel: 2 pumps daily
- Prometrium: 100 mg orally at night, Days 1–25, then 3-day break
- Note: This mimics a cyclical pattern to reset receptor sensitivity without triggering full withdrawal bleeds. Suitable for women who don't tolerate continuous progesterone or have irregular bleeding.

Step 3 – Oral to Vaginal Switch (if bleeding continues)

- Estrogel: 2 pumps daily
- Prometrium: 100 mg vaginally, Days 1–25, then 3-day break
- Note: Vaginal progesterone has stronger local endometrial action with fewer systemic effects. Avoids first-pass hepatic metabolism.
- Caution: Alternate-day vaginal use is not evidence-based in HRT. Consistent daily dosing is needed to ensure endometrial protection.
- Evidence: Studies show higher endometrial tissue levels and lower systemic effects with vaginal delivery (SAGE Journals 2021; Sheffield CCG). Alternate-day use is linked to inadequate endometrial opposition.

Step 4 – Increase Progesterone Dose (if bleeding persists)

- Estrogel: 2 pumps daily
- Prometrium: Increase to 200 mg vaginally at night – continuous (no break)
- Note: A higher local dose may improve endometrial stability and resolve bleeding in resistant cases.

Step 5 – Lower Estrogen (if bleeding persists despite adequate progesterone)

- Estrogel: Reduce to 1 pump daily
- Prometrium: 200 mg vaginally (continuous)
- Note: Estrogen excess can overstimulate the endometrium. Lowering the estrogen dose while maintaining high progesterone may resolve bleeding.

Step 6 – Two Weeks On, Two Weeks Off Regimen (Alternative Approach)

- Estrogel: 2 pumps daily (continuous)
- Prometrium: 200 mg orally or vaginally at night for 14 days/month, followed by 14 days off
- Note: Mimics natural luteal phase, inducing predictable withdrawal bleeding. Suitable for early postmenopausal women, those with cyclical migraines, or those preferring predictable bleeds.
- Evidence: Used in select clinical cases, this regimen can reduce receptor desensitisation and align with a patient's hormonal rhythm. However, it's not a long-term solution due to ongoing withdrawal bleeds.

Step 7 – Persistent Bleeding

- Action: Arrange clinical review
- Referral: Consider gynaecology referral (e.g., pelvic ultrasound, hysteroscopy, biopsy if indicated)