The specialist authority for menopause & post reproductive health

Management of unscheduled bleeding on hormone replacement therapy (HRT)

The British Menopause Society (BMS) is the specialist authority for menopause and post reproductive health in the UK. The BMS educates, informs and guides healthcare professionals, working in both primary and secondary care, on menopause and all aspects of post reproductive health.

BMS guidelines, prepared by the BMS medical advisory council in partnership with other specialist organisations and Royal Colleges, address key disorders and controversial topics relating to menopause and post reproductive health. They reflect new studies together with recent medical and scientific information from articles in professional journals, plus informal consensus.

The guidelines are evidence-based, comprehensively referenced and peer reviewed and they are regularly updated.

This joint guideline has been prepared on behalf of the British Menopause Society, in partnership with the British Society of Gynaecological Endoscopy, British Gynaecological Cancer Society, Faculty of Sexual & Reproductive Healthcare, Getting It Right First Time (GIRFT), Royal College of General Practitioners and the Royal College of Obstetricians & Gynaecologists.

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Key Messages

Assessment of women presenting with unscheduled bleeding on HRT

- **When women present with unscheduled bleeding on HRT, clinical assessment should start with a comprehensive review detailing bleeding patterns, HRT preparations and individual risk factors for cancer. Offer an examination (abdominal, pelvic) and, where relevant, initial investigations such as cervical screening, lower genital tract swabs and body-mass index (BMI).**

Endometrial cancer risk factors in women taking HRT

- **Risk factors for endometrial hyperplasia and cancer, independent of HRT, should be identified. Major risk factors are BMI ≥ 40 and hereditary conditions such as Lynch or Cowden syndrome. Minor risk factors include BMI 30-39, diabetes and polycystic ovarian syndrome (PCOS). Optimisation of modifiable factors can, in themselves, reduce episodes of unscheduled bleeding on HRT and endometrial cancer risk.**
- **A monthly progestogen dose, in proportion to the estrogen dose, is recommended in women with a uterus.**
- **In women using sequential HRT (sHRT), offer a minimum of 10 days norethisterone (NET) or medroxyprogesterone acetate (MPA), or 12 days of micronised progesterone, per month.**
- **Women taking a sequential preparation (sHRT) over the age of 45 should be offered, after five years of use or by age 54 (whichever comes first), a change to continuous combined (ccHRT).**

When to investigate unscheduled bleeding on HRT

- **In the absence of risk factors for endometrial cancer, offer adjustments in the progestogen or HRT preparation, for 6 months in total, if unscheduled bleeding a) occurs within six months of starting HRT or b) is persisting three months after a change in HRT dose or preparation.**
- **If unscheduled bleeding continues in low-risk women, after six months of adjustments, discuss the options of an urgent ultrasound (within six weeks) versus weaning off HRT and consideration of non-hormonal alternatives (to avoid invasive investigations).**
- **For those women who elect to stop HRT, if the bleeding has settled at a 4-week follow-up, and continued cessation of HRT is acceptable, no further investigations are required. If the bleeding has settled at a 4-week follow-up and there is a preference to restart HRT, offer adjustments in HRT for six months and then an urgent ultrasound if bleeding is heavy / persistent during the 6 months or, is continuing after this interval.**
- **Offer an urgent TVS (within 6 weeks) if the first presentation with bleeding occurs more than six months after initiating, or three months after changing, the HRT preparation.**
- **Offer an urgent TVS (within 6 weeks), irrespective of interval since starting, or changing, HRT preparations if a) bleeding is prolonged / heavy or, b) there are 2 minor risk factors for endometrial cancer.**
- **Offer an urgent suspicion of cancer pathway (USCP) referral to women with one major or three minor risk factors for endometrial cancer – irrespective of bleeding type or interval since starting or changing HRT preparations. Adjustments to the progestogen, or stopping HRT, should be offered whilst awaiting assessment.**

How should unscheduled bleeding on HRT be investigated

- **Women with unscheduled bleeding, in the presence of a uniform endometrium which is fully visualised, and measures ≤ 4 mm with ccHRT or ≤ 7 mm with sHRT, can be reassured that the risk of endometrial cancer is low. Offer HRT adjustments for 6 months and then offer endometrial assessment, on an urgent pathway, if bleeding increases during the 6 months or, is continuing after this interval.**
- **Women with a thickened endometrium on TVS (> 4 mm for ccHRT or > 7 mm for sHRT) should be offered referral to the urgent suspicion of cancer pathway (USCP) for endometrial assessment (biopsy and / or hysteroscopy).**
- **In the presence of a normal endometrial biopsy, discuss adjustments in the progestogen and provide reassurance for three months. If hysteroscopy *and* biopsy are normal, reassurance can be provided for six months.**

Adjusting HRT to reduce unscheduled bleeding episodes

- **Assess adherence and understanding of how to use the prescribed preparation including dose and duration of progestogen – for example, would a combined patch or pill reduce administration errors when compared to a separate estrogen and progestogen component.**
- **Offer all women a 52 mg LNG-IUD; this preparation reduces episodes of unscheduled bleeding when compared to all other preparations.**
- **Oral preparations provide higher rates of amenorrhoea when compared to transdermal preparations and could be offered, if there are no risk factors for thrombosis, as a) a first-line therapy or b) to women who have recurrent unscheduled bleeding with transdermal preparations.**
- **Offer vaginal estrogens if there are atrophic findings on examination.**