# Management of Menopause

## Diagnosis

Coventry & Warwickshire Area Prescribing Committee

Clinical Guideline

The following can be diagnosed without laboratory tests in otherwise healthy women, trans men and non-binary people registered female at birth and aged ≥45 years with appropriate menopausal symptoms:

- Perimenopause - in woman with vasomotor and non-vasomotor symptoms (cognitive symptoms, mood disorders, sleep disturbance, fatigue, loss of libido, joint and muscle pain, headache, genitourinary symptoms) and changes in the menstrual cycle.
- Menopause - in women who have had no period for at least 12 months and are not using hormonal contraception or with menopausal symptoms without a uterus. The average age for the menopause is 51 yrs in the UK (Note: this is Caucasian age).
- Be aware of differences in menopause experience in ethnic minority women – see BMS information.

**There are circumstances when follicle stimulating hormone (FSH) levels are required:**

- Age <40 years where premature ovarian insufficiency is suspected with elevated serum FSH levels (more than 25 units/L). Repeat after 4–6 weeks only if there is diagnostic uncertainty. (See ESHRE guidance)

**These are the circumstances when FSH levels may be required:**

- Age 40-45 years with menopausal symptoms and oligomenorrhoea or amenorrhoea
- Age >45 years exhibiting atypical symptoms (including anything other than classic menopausal symptoms)

Levels greater than 30 units/L indicate a degree of ovarian insufficiency but not necessarily sterility. Isolated levels taken in the perimenopause can be misleading.

Restrict the measurement of serum FSH to support advice about stopping hormonal contraception in women **over 50** who have no periods. FSH can be measured in those using all progestogen only methods. Normal practice is to continue contraception until age 55 years. See also page 10.

**Patient Information and advice**

Ensure patients (family or carers) are given information to include:

- Symptoms include irregular/cessation of periods, hot flushes, sweats, difficulty sleeping, aches and pains, vaginal dryness, mood changes/swings, anxiety, brain fog.
- Consider use of a symptom questionnaire e.g. Menopause Matters
- Explanation of the stages of the menopause.
- Common symptoms and diagnosis.
- Lifestyle changes and interventions to help general health and well-being.
- Benefits and risks of treatments for menopausal symptoms. See page 3
- Long term health implications of the menopause.
- Contraception where required in those <55 years.
- See Patient Resources section on page 11.
- Information on medicine shortages is available from Specialist Pharmacy Services (SPS) (registration is required but is free).
- Information on HRT Prepayment Certificate, where applicable is here.
- Advise only to prescribe 3 months at a time.

**Address modifiable lifestyle factors to reduce menopausal symptoms:**

- Normalise weight with healthy balanced diet.
- Consume adequate vitamin D (10-25 micrograms or 400-1000 units/day) and calcium (700 mg/day). Useful information on the Royal Osteoporosis Society website look up 'calcium.'
- Undertake regular weight bearing exercise.
- Advise/support women in smoking cessation.
- Reduce alcohol intake.
- Ensure long-term conditions are managed appropriately.
- Avoid triggers for hot flushes if experiencing them (spicy foods, caffeine, alcohol etc.).
- Good sleep hygiene See: CG046 C&W APC insomnia management pathway
- Relaxation techniques, Cognitive Behavioural Therapy (CBT).

## Hormone Replacement Therapy (HRT)

**Indications:**

- Short term relief of hot flushes, night sweats.
- Prevention of osteoporosis (long term).*
- Premature ovarian insufficiency (POI) (including surgical menopause).
- Relief of other menopausal symptoms e.g. sleep disturbance, anxiety/depression, and sexual function.

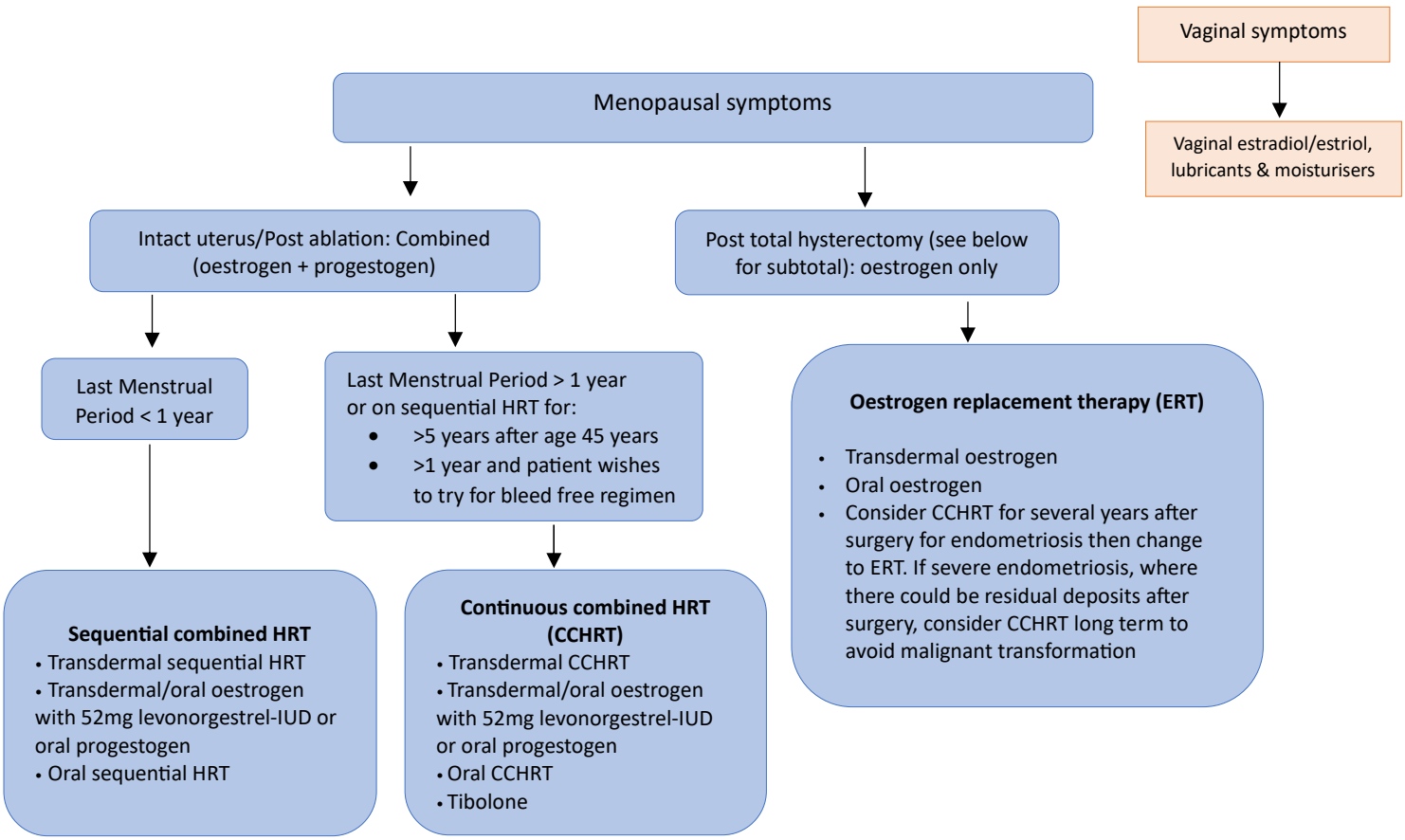
*HRT should not be prescribed solely for prevention of disease.

**Contraindications:** **see also page 2 for further information*

- Current, past or suspected breast cancer*
- Known or suspected oestrogen-dependent cancer*
- Pregnancy
- Undiagnosed abnormal vaginal bleeding*
- Untreated endometrial hyperplasia*
- Previous idiopathic or current venous thromboembolism*
- Active or recent arterial thromboembolic disorder e.g. angina or Myocardial Infarction*
- Acute or active liver disease with severely abnormal liver function tests (LFTs)
- Thrombophilic disorder*
- Caution with porphyria. See advice at: The UK porphyria Medicines Information service

# Flow chart for Hormone Replacement Therapy (HRT) prescribing

(Refer to table overleaf for formulary choices)




## Prescribing Considerations:

- **HRT is available as transdermal or oral depending on patient preference and risk factors.**
- Titrate up slowly according to symptoms and use the lowest effective dose to control symptoms.
- In women over 60 years, use lower HRT doses, either transdermal estradiol +/- progestogen or 0.5mg estradiol orally.
- **The transdermal route** avoids the first pass metabolism through the liver; leads to more stable circulating hormone levels with better symptom control, reducing cardiovascular disease (CVD) and venous thromboembolism (VTE) risks due to a better lipid and clotting profile compared to oral estradiol. Particularly indicated for:

*Body Mass Index (BMI) > 30 kg/m$^2$ *poor control or side effects on oral HRT *controlled hypertension *hypertriglyceridaemia
*history of, or risk of (VTE), consider referring to specialist for advice
*history of, or risk of CVD, consider referring to specialist for advice
*bowel disorder which may affect absorption of oral therapy
*history of migraine (benefit from steady hormonal levels)
*taking interacting drugs (hepatic enzyme inducers) e.g. anticonvulsants *lactose sensitivity *history of gallstones

- Where hysterectomy is subtotal, trial sequential HRT to see if there is any remaining endometrium in the cervical stump. If there is no bleeding after 3 months of sequential therapy, then it can be presumed that they do not require progestogen and can be prescribed oestrogen only HRT

## When to consider specialist advice / referral:

- Persistent side effects despite changing HRT
- Inadequate control of menopause symptoms despite changes in HRT (e.g. titration of HRT dose, change to route of delivery, progestogen intolerance)
- Complex medical history
- In women with hormone dependent tumours who have troublesome menopause symptoms
- Premature ovarian insufficiency (see separate box)
- Bleeding problems (see British Menopause Society (BMS) Management of unscheduled bleeding on HRT)
- Women seeking HRT 10 years after menopause or >55 years of age.

## Premature ovarian insufficiency (POI)

In POI (menopause < 40 years old) it is important to start treatment with either HRT or a combined hormonal contraceptive (CHC). Treatment should continue until the age of natural menopause (unless contraindicated) to protect against increased risks of dementia, cognitive decline, cardiovascular disease and osteoporosis.

Counsel women that:

- HRT has no effect on blood pressure and beneficial effects on metabolic parameters, when compared with CHC but is NOT a contraceptive
- Both HRT and CHC offer bone protection

Consider referring women to a specialist for help and support in the physical and psychosocial aspects of their diagnosis.

# Benefits and Points to Consider when discussing HRT with Patients

| Benefits of HRT | |
|---|---|
| ➢ Reduction in vasomotor symptoms<br>➢ Improved sleep, joint pain & Quality of Life<br>➢ Potential improvement in psychological symptoms e.g., depression & anxiety<br>➢ Relief of vaginal dryness<br>➢ Improved sexual function | ➢ Reduced risk of coronary heart disease (CHD) when oestrogen is started early (within 10 years of menopause)<br>➢ Improved bone mineral density, reduced fracture risk |

| Points to Consider when discussing HRT with Patients |
|---|
| **Coronary heart disease (CHD) and stroke**<br>• CHD risk does not increase with either oestrogen-only or combined HRT.<br>• Baseline population risk of stroke in women under 60 years is very low.<br>• Combined HRT with transdermal oestrogen is unlikely to increase stroke risk.<br>• Combined HRT with oral oestrogen may increase stroke risk- risk increases with higher oestrogen dosage and longer duration of treatment. There is a difference in risk between ethnic groups and may be greater in black people. |
| **Venous thromboembolism (VTE)**<br>• Risk is increased with oral HRT compared to baseline population risk.<br>• There is no increased risk with transdermal HRT given at standard therapeutic doses (under 50micrograms/24hr) compared to baseline population risk.<br>• Consider transdermal rather than oral HRT in women with an increased risk of VTE, e.g., BMI over 30. |
| **Dementia**<br>• For women starting HRT around the time of the menopause there is no increase in risk of dementia.<br>• Dementia risk is unlikely to increase with oestrogen-only HRT.<br>• Dementia risk may increase with combined HRT if started at age 65 years or over. |
| **Type 2 diabetes**<br>• There is no increased risk of developing type 2 diabetes with any type of HRT.<br>• HRT is not associated with an adverse effect on blood glucose control in people with diabetes. |
| **Osteoporosis**<br>• Risk of fragility fractures is decreased whilst taking HRT but increases once treatment is stopped.<br>• Give women advice on bone health and discuss any risk factors for osteoporosis. |
| **Endometrial cancer**<br>• Risk of endometrial cancer increases with oestrogen-only HRT (both oral and transdermal) in people with a uterus.<br>• Risk of endometrial cancer decreases with continuous combined HRT compared to no HRT.<br>• Risk increases slightly with sequential combined HRT; the increase may be greater with longer duration of use, increased oestrogen dose and fewer days of progesterone per cycle. |
| **Breast cancer**<br>• Baseline breast cancer risk varies depending on a person's risk factors (modifiable and non-modifiable).<br>• There is a small increased risk of breast cancer with HRT. Risk increases with duration of use, is higher in current users of HRT than in past users and persists for at least 10 years after stopping.<br>• Risk is higher with continuous combined HRT than with sequential HRT.<br>• There is a higher risk associated with combined HRT than oestrogen-only HRT.<br>• There is a very small increase in risk of death from breast cancer with combined HRT. |
| **Ovarian cancer**<br>• There is a small increased risk of ovarian cancer associated with HRT (either combined or oestrogen only HRT), both transdermal and oral. |

Further information on the risks of HRT can be found within the NICE guideline on Menopause [NG23]. See specific links:

- https://www.nice.org.uk/guidance/ng23/resources/incidence-of-medical-conditions-with-and-without-hrt-a-discussion-aid-pdf-13553199901
- https://www.nice.org.uk/guidance/ng23/resources/table-1-combined-hrt-versus-no-hrt-effect-on-specific-health-outcomes-pdf-13553206381
- https://www.nice.org.uk/guidance/ng23/resources/table-2-oestrogen-only-hrt-versus-no-hrt-effect-on-specific-health-outcomes-pdf-13553206382

# Hormone Replacement Therapy (HRT) Options

**Transdermal HRT** – see prescribing considerations box: **check individual Summary of Product Characteristics (SPCs) for specific product licensing.**
**Take into account patient preferences/factors when considering options. See table: "Features of Progestogens."**

| Type of HRT | Sequential/ cyclical combined HRT (SCHRT) | Continuous combined HRT (cycle free) | Oestrogen Replacement Therapy (ERT) only (see box on page 8 for doses) | Progestogen (See box on page 8 for features) |
|---|---|---|---|---|
| **Criteria for use** | ➢ Intact uterus/Post ablation<br>➢ Perimenopausal – had at least one natural period in last year | ➢ Intact uterus/Post ablation – had no period for 1 year (post-menopausal)<br>➢ On sequential combined HRT for:<br>• >5 years after age 45<br>• >1 year & pt wishes to try bleed free regimen | ➢ Without a uterus e.g. Post total hysterectomy (see 'prescribing considerations' for subtotal)<br>➢ Intact uterus/Post ablation – in combination with a separate progestogen preparation (see right) – unopposed oestrogens cause endometrial proliferation; women with a uterus MUST have progestogen to stop this | ➢ Required with transdermal or oral oestrogen if not had a hysterectomy |
| **Rx CHARGE** | 2 Rx charges | 1 Rx charge | 1 Rx charge | 1 Rx charge |
| Preferred | **Evorel Sequi® patch**<br>50 micrograms /24hrs release estradiol patches (days 1-14) & 50 micrograms /24hrs release estradiol & 170 micrograms /24hrs norethisterone patches (days 15-28). A treatment cycle is 28 days.<br>Change patch TWICE a week<br><br>No other transdermal sequential combined HRT available, so alternative choices would be **ERT and cyclical progestogen** (See columns on right hand side) | **Evorel Conti® patch**<br>50 micrograms /24hrs release estradiol & 170 micrograms /24hrs release norethisterone patch<br>Change patch TWICE a week<br><br>Generally lower progestogenic side effect profile:<br>**Femseven Conti® patch**<br>50 micrograms/24hrs release estradiol & 7 micrograms /24hrs release levonorgestrel patch<br>Change patch ONCE a week | **Evorel® patch** OR **Estraderm MX® Patch**<br>25, 50, 75, 100 micrograms / 24hrs release estradiol<br>NB 100 micrograms high dose)<br>Change patch TWICE a week *OR*<br><br>**FemSeven® patch**<br>50, 75, 100 micrograms /24hrs release estradiol<br>Change patch ONCE a week *OR*<br><br>**Estradot® patch**<br>25, 37.5, 50, 75, 100 micrograms /24hrs release estradiol<br>Change patch TWICE a week<br>Smaller sized patches - consider for higher doses & petite women<br><br>Alternative to patches; e.g. skin allergy to patches/ side effects:<br>**Sandrena® transdermal gel sachets**<br>500 micrograms up to 1.5 mg estradiol applied once daily *OR*<br><br>**Oestrogel® (0.06%) transdermal gel**<br>Delivered dose is 0.75 mg/pump estradiol; initial dose normally 1.5mg estradiol (2 pumps) once daily *OR*<br><br>If poor absorption with transdermal patch and gel:<br>**Lenzetto® transdermal spray:** 1.53 mg estradiol /spray; Initial dose is 1 spray once daily to the forearm. Check quantity prescribed is appropriate for dose patient is using. | Micronised progesterone has variable transdermal absorption and is unlikely to provide sufficient oestrogen opposition. A systematic review by Stute et al. (2016) concluded that transdermal micronised progesterone does not provide sufficient endometrial protection. Based on current evidence progesterone within HRT regimens should not be administered by the transdermal route, as this is unlikely to provide sufficient endometrial protection.<br><br>**See oral HRT section for details of Levonorgestrel Intrauterine Device (IUD) and oral progestogen regimens.** |

**Oral HRT** – See prescribing considerations box: **check individual SPCs for specific product licensing.**

**Take into account patient preferences/factors when considering 1st line & 2nd line options. See table: "Features of Progestogens."**

| **Type of HRT** | **Sequential/ cyclical combined HRT (SCHRT)** | **Continuous combined HRT (cycle free)** | **Oestrogen Replacement Therapy (ERT) only** (see box on page 8 for doses) | | **Progestogen** (See box on page 8 for features) |
|---|---|---|---|---|---|
| **Criteria for use** | ➢ Intact uterus/Post ablation<br>➢ Perimenopausal – had at least one natural period in last year | ➢ Intact uterus/Post ablation – had no period for 1 year (post-menopausal)<br>➢ On sequential combined HRT for:<br>• >5 years after age 45<br>• >1 year & pt wishes to try bleed free regimen | ➢ Without a uterus e.g. Post total hysterectomy (see 'prescribing considerations' for subtotal)<br>➢ Intact uterus/Post ablation – in combination with a separate progestogen preparation (see right) – unopposed oestrogens cause endometrial proliferation; women with a uterus MUST have progestogen to stop this | | ➢ Required with- transdermal or oral oestrogen if not had a hysterectomy |
| **Rx CHARGE** | 2 Rx charges | 1 Rx charge | 1 Rx charge | | 1 Rx charge |
| Preferred | **Elleste Duet® tablets:** 1 mg or 2 mg estradiol tablets for days 1-16, then 1 mg or 2mg estradiol & 1 mg norethisterone tablets for next 12 days<br>*OR*<br>**Trisequens® tablets:** Estradiol 2 mg tablets for 12 days, estradiol 2mg & norethisterone 1 mg tablets for 10 days, then estradiol 1 mg tablets for 6 days.<br>*OR*<br>**Novofem® tablets:** 1 mg estradiol tablets days 1-16, then 1 mg estradiol & norethisterone 1 mg tablets for days 17 to 28. | **Kliofem® tablets** 2 mg estradiol & 1 mg norethisterone tablets; 1 tablet daily<br>*OR*<br>**Kliovance® tablets:** 1 mg estradiol & 0.5 mg norethisterone tablet; 1 tablet daily<br>*OR*<br>**Elleste Duet® Conti tablets** 2 mg estradiol & 1 mg norethisterone tablets; 1 tablet daily | **Elleste Solo®** *OR* **Zumenon® tablets:** 1 mg or 2 mg estradiol hemihydrate tablets; 1 tablet daily | | **52mg- Levonorgestrel (LNG) intrauterine device (IUD) (Mirena® is the only licensed preparation for up to 4yrs; off-label brands but FSRH endorsed are: Levosert®, Benilexa One Handed®)** **Prescribe by brand – see** MHRA guidance maximum duration before removal &/or replacement: All 52mg LNG IUDs are FSRH endorsed for up to 5yrs, see page 10<br>*OR*<br>**Norethisterone oral 5 mg tablets**<br>Sequential regimen: 5 mg for 12-14 days (days 15-26) every month **(unlicensed use)**<br>Continuous regimen: **Norethisterone 5 mg orally daily (unlicensed use)** (1mg would be sufficient but not available in stand-alone preparations)<br>*OR*<br>**Micronised Progesterone (100 mg and 200 mg (200mg Gepretix® brand only)) oral capsules**<br>Sequential regimen: 200 mg for last 12-14 days of each 28-day cycle **(14 days use is off label)** |

| | | | | | |
|---|---|---|---|---|---|
| Preferred | **Femoston®**<br>**1/10 or 2/10 tablets:**<br>1 mg or 2 mg estradiol tablets for days 1-14, then 1 mg or 2 mg estradiol & 10 mg dydrogesterone tablets for days 15 to 28. | **Indivina® tablets:** Estradiol / Medroxyprogesterone acetate; strengths: 1 mg/2.5 mg; 1 mg/5 mg; 2 mg/5 mg; 1 tablet daily<br>*OR*<br>**Conjugated oestrogens 300microgram / Medroxyprogesterone 1.5 mg modified-release tablets**; 1 tablet daily<br>*OR*<br>**Femoston Conti® tablets:**<br>0.5/2.5 = 0.5 mg estradiol & 2.5 mg dydrogesterone OR 1/5 = 1mg estradiol & 5mg dydrogesterone; 1 tablet daily<br>*OR*<br>**Bijuve® capsules:** 1 mg estradiol & 100mg progesterone capsules; 1 capsule daily (Body identical oral option; alternative when other HRT not tolerated OR replaces HRT regimens where separate oestrogen & micronised progesterone are used (single hormone products in combination are more expensive) | **Progynova® tablets:** Estradiol valerate 1 mg or 2 mg tablets; 1 tablet daily<br><br>**Generic Conjugated Oestrogens tablets** 300 micrograms / 625 micrograms / 1.25 mg strength tablets; 1 tablet daily | | Continuous regimen: 100 mg capsule daily (at bedtime) **(off label)** (**licensed use** is 100 mg capsule daily on days 1-25 of 28-day cycle)<br>**Medroxyprogesterone acetate 2.5, 5, 10mg oral tablets**<br>Sequential regimen: 10 mg daily for 12-14 days every month (days 15-26 or days 15-28 of each therapeutic cycle (sequential) **(Off-label)**<br>Continuous regimen: 2.5 or 5mg daily **(Off-label)**<br><br>*OR*<br>**Norethisterone brand unlicensed, off-label:** Continuous regimen: **Noriday®** (Norethisterone brand) **(unlicensed)** in progestogen only contraceptive pill **dose for regimen:** 3 tablets of 350 micrograms (1.05 mg) daily of **Noriday®**<br>*OR*<br>**Drospirenone 4mg brand oral tablets**<br>Continuous regimen: **Drospirenone 4 mg (Slynd®)** 1 active hormonal tablet 4 mg can be taken daily on a continuous basis (omitting the 4 hormone free pills in the pack) **Off licence use** of this progestogen-only contraceptive pill can be considered as an equivalent alternative for women experiencing progestogenic side effects with other preparations<br>*OR*<br>**Desogestrel 75 and 150 microgram oral tablets**<br>Earlier studies have reported that desogestrel 150 micrograms is effective as the progestogen component of HRT with no increase in the risk of endometrial hyperplasia. There is lack of evidence on the use of desogestrel 75 micrograms as the progestogen component of HRT. If desogestrel 75 micrograms is used as contraception in women receiving HRT, it would be recommended to add further progestogen (e.g. micronised progesterone 100 mg daily or 200 mg for 12 days a month) to provide adequate endometrial protection<br>*OR*<br>**Nalvee (dydrogesterone) 10 mg tablets**<br>Sequential regimen: 10 mg dydrogesterone during the last 14 days of each 28-day cycle. Depending on the clinical response, the dosage may be adjusted to 20 mg dydrogesterone daily in the course of the treatment. |
| 2nd line | | **Tibolone 2.5 mg tablets (prescribe as generic as more cost effective)** (synthetic gonadomimetic with oestrogen, progestogen & some androgenic properties), Low libido (also consider for women with endometriosis post hysterectomy &/or BSO who may have endometriosis deposits remaining, if libido low) (See box on page 8 for features). Note: in those 60 years or over, the increased risk of stroke in older women should be taken into account in prescribing decisions. See MHRA Drug Safety Update. | | | |

**Topical Vaginal Oestrogen for Urogenital Atrophy: check individual SPCs for specific product licensing**

| HRT product | Oestrogen | Delivery | Strength | Indications for use |
|---|---|---|---|---|
| Estradiol (1st line) | Estradiol | 10 micrograms Intravaginal Pessary | 10 micrograms daily for 2 weeks then twice weekly for as long as necessary. | First line topical treatment option Consider cost effective brand, **Vagirux®** (environmentally friendly option as 1 applicator per pack of 24) **/ Vagifem®** brand less cost effective |
| Estriol 1 mg/g (1st line) | Estriol | Intravaginal cream | 0.1% (1 mg/g) (0.5mg estriol per app) daily for 2- 4 weeks (max), then twice weekly | First line most cost-effective topical HRT. Can also be applied externally to the vulva in addition to using vaginal Estradiol or Estriol. More cost-effective compared to Estriol 0.01%. |
| *Estriol 0.01% (Non formulary)* | *Estriol* | *Intravaginal cream* | *0.01% (0.1 mg/g) (0.5 mg estriol per app) daily for 2 – 4 weeks (max), then twice weekly* | *Patient or clinician preference. Note Estriol 0.01% is ++ more expensive compared to Estriol 0.1%. Contains arachis oil and is not suitable for those with peanut allergy. Should also avoid in patients with soya allergy.* |
| Blissel® gel (2nd line) | Estriol | Intravaginal gel | 0.005% (50 micrograms/g) (50 micrograms estriol per app) daily for 3 weeks, then twice weekly. Review after up to 12 weeks. | Reduced potency estriol, Prescribing should be **RESTRICTED** to patients with side effects/ sensitivity to other topical preparations |
| Imvaggis® (2nd line) | Estriol | Intravaginal 0.03mg estriol pessary | 0.03 mg daily for 3 weeks and then twice weekly | Less potent estriol where other preparations not tolerated/ side effects or difficulty in using other preparations |
| Estring® (2nd or 3rd line) | Estradiol | Intravaginal ring | 7.5 mcg/24hrs over 90 days | Allergies to other topical products, dexterity problems with applicators, patient preference |
| Intrarosa® (2nd line) | Prasterone (DHEA)<br><br>(Prasterone is metabolised to oestrogens and androgens, hence, not to be prescribed for patients unsuitable for topical oestrogens) | 6.5 mg prasterone Vaginal pessary | 6.5 mg once daily at bedtime | Prescribing should be **RESTRICTED** to patients who have already tried several other topical vaginal estriol / estradiol preparations but found them to be unsuitable due to lack of efficacy or intolerance / side effects. |
| Senshio® (Specialist Advised) | Ospemifene<br><br>(Ospemifene is a selective oestrogen receptor modulator that has an oestrogen-like effect in the vagina, increasing the cellular maturation and mucification of the vaginal epithelium). | Oral tablet | 60 mg once daily | Only prescribeable on specialist recommendation, specifically for those patients where local application of vaginal oestrogen may be impractical; e.g. with physical or intellectual disabilities may find it difficult to use local vaginal oestrogen. |

## Use of topical Oestrogen

- Start early before irreversible changes have occurred. Can be taken with systemic HRT. Absorption of local oestrogen therapy, delivered vaginally is minimal, particularly once tissue quality improves as a result of treatment.
- Vaginal oestrogen therapy found to be superior to placebo for overactive bladder (OAB) symptoms. Consider in conjunction with oral antimuscarinics for women with OAB symptoms and/or also for perimenopausal/menopausal/post-menopausal women with recurrent urinary tract infections (UTIs). See APC CG023 - Management of OAB and Recurrent UTIs section of APC CG005 - Primary Care Adult Antibiotic Guidelines.
- If symptoms not relieved consider dose increase, after seeking specialist advice. Report any unscheduled bleeding promptly.
- Explain that symptoms may come back when treatment is stopped, adverse effects are rare.
- Women should be informed that urogenital atrophy can take several months to respond to treatment, particularly in more severely affected women.
- Moisturisers and lubricants (**OTC purchase**) can be used alone or in addition to vaginal oestrogen for vaginal dryness. Lubricants and moisturisers are first line recommended treatment for women for whom oestrogen is contraindicated.

## Prescribed oestrogen dose for ultra-low, low, standard, moderate and high dose regimens

| | No of doses per container | Ultra-low dose | Low dose | Standard Dose | Moderate dose | High dose |
|---|---|---|---|---|---|---|
| **Oestrogel®** | 64 pumps | ½ pump | 1 pump | 2 pumps | 3 pumps | 4 pumps |
| **Sandrena®** | 28 sachets | 0.25 mg | 0.5 mg | 1 mg | 1.5-2 mg | 3 mg* |
| **Lenzetto® spray** | 56 sprays | 1 spray | 2 sprays | 3 sprays | 4-5 sprays* | 6 sprays* |
| **Patch** | | 12.5 micrograms | 25 micrograms | 50 micrograms | 75 micrograms | 100 micrograms |
| **Oral estradiol** | | 0.5 mg | 1 mg | 2 mg | 3 mg^ | 4 mg^ |

*Off-licence use ^Off-licence use – rarely required to achieve symptom control

## Progestogen dose per licensed oestrogen dose in the baseline population

| | Progestogen type | | | | | | |
|---|---|---|---|---|---|---|---|
| **Oestrogen dose** | **Micronised progesterone** | | **Medroxyprogesterone acetate** | | **Norethisterone** | | **52mg LNG-IUD** |
| | continuous HRT | sequential HRT | continuous HRT | sequential HRT | continuous HRT | sequential HRT | |
| **Ultra-low/Low** | 100 mg | 200 mg | 2.5 mg | 10 mg | 5 mg* | 5 mg* | One device – can be used for up to 4 years (SPC), up to 5 years (FSRH) |
| **Standard** | 100 mg | 200 mg | 2.5-5 mg | 10 mg | 5 mg* | 5 mg* | |
| **Moderate** | 100 mg | 200 mg | 5 mg | 10 mg | 5 mg | 5 mg | |
| **High** | 200 mg | 300 mg | 10 mg^ | 20 mg^ | 5 mg | 5 mg | |

*1mg provides endometrial protection for ultra-low to standard dose oestrogen but the lowest stand-alone dose currently available in the UK is 5 mg (off-licence use of three Noriday® Progestogen Only Pills (i.e. 1.05 mg), could be considered if 5mg is not tolerated)
^There is limited evidence in relation to optimal medroxyprogesterone acetate dose with high dose oestrogen; the advised dose is based on studies reporting 10 mg providing protection with up to moderate dose oestrogen.

## Features of Progestogens

| Progestogens (features) | |
|---|---|
| **Synthetics** | |
| **Norethisterone, Norgestrel, Levonorgestrel** | Better cycle control, androgenic (may be good for libido). Unfavourable effect on lipids. |
| **Medroxyprogesterone acetate** | Can be added to oral or transdermal oestrogen, mildly androgenic (may be good for libido). Unfavourable effect on lipids. |
| **Dydrogesterone** | Non androgenic |
| **52mg Levonorgestrel-IUD** | Replace after 4 years as per SPC. Provides bleedfree option for perimenopause |
| **Body identical** | |
| **Micronised progesterone** | Fewer progestogenic sod effects, no androgenic or glucocorticoid activity. No lipid effects. Less effective cycle control. |

## Monitoring of HRT

- Started on HRT or HRT changed— review at 3 months
- Established on HRT—review annually unless there are clinical indications for earlier review.
- At each review, assess efficacy, side effects and ongoing risk/benefit balance

## Stopping HRT

- There is no arbitrary limit on HRT duration. In women with POI, HRT should be continued until normal menopause age. Withdraw HRT slowly to reduce risk of recurrent symptoms
- If symptoms do recur, then recommence treatment

## Management of side effects of HRT

Encourage women to persist with treatment for 3 months (as adverse effects may resolve)

**Oestrogenic side effects**

| System | Side effect | Management |
|---|---|---|
| Breast symptoms | Breast tenderness<br>Breast enlargement | • May be alleviated by a low fat, high carbohydrate diet.<br>• Reduce dose of oestrogen.<br>• Change to transdermal route (more stable oestrogen levels). |
| Gastrointestinal symptoms | Bloating<br>Nausea | • Adjust timing of dose and take with food.<br>• Change route of administration. |
| Other symptoms | Headache / Migraine<br>Leg cramps.<br>Fluid retention | • For headache / migraine – change route of administration.<br>• Leg cramps may improve with lifestyle changes, e.g. exercise and stretching calf muscles. |

**Progestogenic side effects -** tend to occur in a cyclical pattern during the progestogen phase of cyclical HRT.

| System | Side effect | Management |
|---|---|---|
| PMS like symptoms | Fluid retention<br>Breast tenderness<br>Lower abdomen pain<br>Backache | • Change **progestogen type** (see 'Progestogen features' table on page 8).<br>• Change **route of delivery** from oral to transdermal, vaginal, or intrauterine.<br>• **Reduce the regimen** of progestogen administration. Progestogens can be taken for 10–14 days of each monthly sequential regimen, so swapping from a 14-day to a 10- day product may provide benefit but caution as need to ensure adequate endometrial protection.<br>• Reducing **frequency of progestogen dosing** by switching to a long cycle regimen of progestogen for 14 days every 3 months (for women without natural regular periods). |
| | Depression<br>Mood swings | |
| | Acne/greasy skin<br>Headache | |

**Unscheduled bleeding on HRT**

See BMS Guideline 'Management of unscheduled bleeding on HRT'
(https://thebms.org.uk/wp-content/uploads/2024/04/01-BMS-GUIDELINE-Management-of-unscheduled-bleeding-HRT-APRIL2024-F.pdf)

## Transdermal Testosterone Supplementation

See APC Drug Positioning Statement DPS098 and Specialist Initiated Drug Checklist SIDC19

**Patient criteria:** Women with menopause symptoms on HRT where there has not been an improvement in altered sexual function with oestrogen +/- progestogen replacement.

**Local Formulary Status: Specialist Initiation:**
**Initiated by Community Gynaecology Service or equivalent, Secondary Care Menopause Clinic or GPs with extended role in menopause**

Testosterone treatment should be initiated by the Community Gynaecology Service, menopause specialist in secondary care or a GP with Extended Role (GPwER) working in the community who has undergone enhanced menopause training (through an accredited menopause training programme). The prescriber will initiate treatment and prescribe for an initial 3-to-6-month trial to allow optimisation of treatment and demonstrate that the patient's response is consistent. There should be at least an annual evaluation of ongoing usage thereafter.

If secondary care or Community Service has initiated, the GP will take over prescribing at this stage as long as the dose and total testosterone levels are stable. Total testosterone levels should remain in the physiological range for women.

## Contraception

See the Faculty of Sexual and Reproductive Healthcare (FSRH) guidance on *'Contraception for Women Aged Over 40 Years'*

- HRT is not a contraceptive and will not prevent spontaneous ovulation in perimenopausal women.
- Women >50 years, use contraception for 1 year after last spontaneous period.
- Women <50 years, continue contraception for 2 years following last spontaneous period.
- Combined oral contraception (COC) with levonorgestrel or norethisterone should be considered first-line COC preparations for women over 40 due to the potentially lower VTE risk compared to formulations containing other progestogens. Barrier methods become safer in older women as fertility declines and have a lower failure rate.
- COC with ≤30 micrograms of ethinylestradiol should be considered first-line COC preparations for women over 40 due to the potentially lower risks of VTE, cardiovascular disease and stroke compared to formulations containing higher doses of oestrogen.
- Women aged 50 and over should be advised to stop taking CHC for contraception and use an alternative, safer method.
- The FSRH supports extended use of a 52 mg levonorgestrel intrauterine device (LNG-IUD) (Mirena/Benilexa/Levosert) for contraception until the age of 55 if inserted at age 45 or over, provided it is not being used as the progestogen component of hormone replacement therapy (HRT) for endometrial protection. This means that if a woman is using the LNG-IUD solely for contraception and is at least 45 years old when it is inserted, she can continue using it for contraception until age 55, even though the standard license for these devices may be shorter.
- All 52 mg LNG-IUDs are licensed for 8 years for contraception. The FSRH supports use of any 52 mg LNG-IUD for up to 5 years for endometrial protection in individuals using oestrogen as part of HRT. This recommendation is an off-label use, as the Mirena LNG-IUD (the only licensed one for this purpose) is only approved for 4 years, though studies show it is effective for 5. Other 52 mg LNG-IUDs like Benilexa One Handed® and Levosert®, while not licensed for HRT, are also recommended for this duration by the FSRH.

## Non-hormonal options: for Specialist Consideration Only

Evidence suggests that the following may be helpful in certain patients only. See also BMS Prescribeable alternatives to HRT and Non-hormonal based treatments for menopausal symptoms. **As many of these are off-label uses, then specialist advice from Community Gynaecology Service or equivalent, Secondary Care Menopause Clinic or GPwER in menopause, would be recommended**:

- Venlafaxine 37.5 mg slowly increased up to 150 mg a day, Paroxetine 10mg or Citalopram 10mg-30 mg a day, side effects include dry mouth, constipation, and nausea are more likely with higher doses. These are all off-label indications.
- Oxybutynin, which is usually used to treat overactive bladder (off label for menopause indications), but has been shown to reduce the incidence of hot flushes. It is being used off licence by some menopause specialists for this purpose. Side effects may include stomach pain, diarrhoea, nausea, headaches, dry mouth and dry eyes. The usual dose is 2.5 mg twice daily, with the option of increasing to 5 mg twice daily.
- Gabapentin at 300 mg daily increasing to 300 mg maximum three times a day or Pregabalin 75-150 mg twice daily shows statistically significant improvement in hot flushes as compared with placebo. Dose dependent side effects limit compliance, the most common side effects being somnolence, dizziness, weight gain and dry mouth. Also Schedule 2 Controlled Drug
- Clonidine is the only non-hormonal drug with a licenced indication for control of hot flushes in the UK but limited effectiveness and notable side effects. Clonidine 25 micrograms is prescribed twice daily for 2 weeks, slowly increased up to a maximum of 50 micrograms three times a day. The evidence base is contradictory. Side effects include dizziness, dry mouth and constipation and sleep disturbances. Withdraw slowly as can cause rebound hypertension.

## Complementary therapies and unregulated preparations

- The efficacy and safety of unregulated compounded bioidentical hormones are unknown and should not be confused with body identical HRT which is licensed and regulated. See BMS Consensus Statement on Bioidentical HRT.

- Limited evidence to support use of 'over the counter' remedies. Herbal preparations, isoflavones and bioidentical hormones are not regulated by the European Medicines Authority and in some instances not subject to any quality control or research studies of sufficient power or quality.
- Some evidence isoflavones and black cohosh may relieve vasomotor symptoms, but the quality, and safety of these products may be unknown; different preparations may vary. Black Cohosh can be associated with major adverse effects such as constipation, arrhythmia, weight gain and abdominal cramps and should be avoided if history of breast cancer.
- Explain to women who wish to try complementary therapies that the quality, purity and constituents of products may be unknown. If a herbal treatment is chosen, patients should look for the Traditional Herbal Remedy (THR) stamp validating strength and quality.
- Advise women with a history of, or at high risk of, breast cancer that, although there is some evidence that St John's wort may be of benefit in the relief of vasomotor symptoms, there is uncertainty about:
    - Appropriate doses
    - Persistence of effect
    - Variation in the nature and potency of preparations
    - Potential serious interactions with other drugs (including tamoxifen, anticoagulants and anticonvulsants)

## Patient Resources

- Menopause Matters website – general menopause information. Available at: www.menopausematters.co.uk
- The Menopause Charity website - general menopause information. Available at: https://themenopausecharity.org/
- Menopause Support – general menopause information. Available at: https://menopausesupport.co.uk/
- Royal Osteoporosis Society –information on all areas of bone health and treatments. Available at: https://theros.org.uk/
- Daisy Network (Early menopause group) Available at: www.daisynetwork.org
- Health talk online – interviews with women, including young women, discussing menopause issues. Available at:
- www.healthtalk.org
- NICE Menopause—Information for the public 2015 (last updated 2024). Available at: https://www.nice.org.uk/guidance/ng23/informationforpublic
- Women's Health Concern. HRT: Benefits and risks. Information for women. Last updated November 2020. Available at: www.womens-health-concern.org/wp-content/uploads/2022/12/11-WHC-FACTSHEET-HRT-BenefitsRisksNOV2022-B.pdf
- Women's Health Concern. Management of unscheduled bleeding on HRT. Information for women. August 2024. Available at: www.womens-health-concern.org/wp-content/uploads/2024/08/33-WHC-FACTSHEET-Management-ofunscheduled-bleeding-on-HRT-AUG2024-D.pdf
- Rock My Menopause. Patient information site. Available at: https://rockmy.com/menopause/

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- FSRH Clinical Guideline: Contraception for women aged over 40 years, amended July 2023. Available at: https://www.fsrh.org/Public/Standards-and-Guidance/Aged-Over-40.aspx
- NICE Clinical Knowledge Summaries: Vitamin D deficiency in Adults, last revised January 2022. Available at: https://cks.nice.org.uk/topics/vitamin-d-deficiencyin-adults/
- British Menopause Society. Various resources. Available at: https://thebms.org.uk/
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- Women's Health Concern. Various resources. Available at: https://www.womens-health-concern.org
- Summaries of Product Characteristics. Available at: www.medicines.org.uk
- British National Formulary. Available at: https://bnf.nice.org.uk/
- Drug Tariff. Available at: https://www.nhsbsa.nhs.uk/pharmacies-gp-practices-and-appliance-contractors/drug-tariff
- ESHRE Guideline: Management of women with premature ovarian insufficiency, Human Reproduction, May 2016. Available at: https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Premature-ovarian-insufficiency



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NHS North East and North Cumbria integrated Care Board. Northern Treatment Advisory Group. Management of the Menopause. October 2024. Available at: https://ntag.nhs.uk/wp-content/uploads/2024/10/NENC-Menopause-guidance-FINAL-Sept-24-approved.pdf