BSW HRT Formulary Treatment Options and Pathway

NHS
Bath and North East Somerset, Swindon and Wiltshire
Clinical Commissioning Group

See the British Menopause Society (BMS) website for further advice on the following:

For healthcare professionals: NICE: Menopause Diagnosis and Management – Guideline Summary ; HRT Guide ; HRT Practical Prescribing
For women: Women's Health Concern factsheets ; Pt info leaflets: https://www.menopausematters.co.uk/menopause.php

TRANSDERMAL OPTIONS

Oestrogen Only
(no uterus)
1 prescription charge

- **Patches.** Change TWICE per week
  Evorel 25, 50, 75, 100mcg estradiol
  Estradot 25, 37.5, 50, 75, 100mcg estradiol
- **Gel - Oestrogel** 0.75mg estradiol/pump.
  Gel - Sandrena 500mcg, 1mg estradiol/sachet
  Spray - Lenzetto 1.53 mg estradiol/spray.

Sequential combined
(uterus - monthly bleed)
2 prescripton charges

- **Evorel Sequi** patches
  Change TWICE per week
  50mcg estradiol + 170mcg norethisterone

Continuous combined
(uterus - no bleed) not suitable for perimenopause or within 12 months of last menstrual period
1 prescription charge

- **Evorel-Conti** patches
  Change TWICE per week
  50mcg estradiol + 170mcg norethisterone

Options for progestogenic opposition of topical oestrogen if woman has uterus:
- Levonorgestrel Intrauterine System (**Mirena coil**) see overleaf
- Micronised progesterone (**Utrogestan 100mg oral capsules**) see overleaf

The transdermal route should be considered as first choice route of estradiol administration, particularly in women with risk factors, including those with a BMI >30 kg/m2. Transdermal administration of estradiol is unlikely to increase the risk of VTE or stroke above that in non-users and is associated with a lower risk compared with oral administration of estradiol[1,2]. See NICE menopause guidance & BMS recommendations on HRT for details.

ORAL TREATMENT OPTIONS

Oestrogen Only
(no uterus)
1 prescription charge

- **Elleste Solo** - 1mg or 2mg estradiol

Sequential combined
(uterus - monthly bleed)
2 prescripton charges

- **Femoston** 1mg or 2mg estradiol + dydrogesterone 10mg
- **Elleste Duet** 1mg or 2mg estradiol + norethisterone 10mg

Continuous combined
(uterus - no bleed) not suitable for perimenopause or within 12 months of last menstrual period
1 prescription charge

- **Femoston Conti** 1mg estradiol + 5mg dydrogesterone
  OR Femoston Conti (low dose) 0.5mg estradiol + 2.5mg dydrogesterone (lowest effective dosed HRT preparation)
  OR Indivina 1mg or 2mg estradiol + 2.5mg or 5mg medroxyprogesterone acetate
- **Kliofem** 2mg estradiol + 1mg norethisterone
- **Elleste Duet Conti** 2mg estradiol + 1mg norethisterone
- **Tibolone (Livial)** (See text overleaf for full guidance)

Low oestrogen options

Women ≥60yrs plus should be offered transdermal preparations first line and may require less oestrogen[2] as found in the following low dose preparations:

- Oestrogen only
  - Evorel 25 patch 25mcg/24hrs
  - Oestrogel (estradiol 0.75mg per pump. 1 pump = low dose)
- Continuous combined
  - Femoston Conti low dose (0.5mg estradiol + 2.5mg dydrogesterone)
  - Kliovance (estradiol 1mg and norethisterone acetate 500mcg)

Modifiable lifestyle factors - *ensure these are addressed:*
- Advise a healthy balanced diet, to maintain a healthy BMI, ensure sufficient dietary calcium (700mg/day) and undertake regular weight-bearing exercise.
- Ensure a discussion occurs with the patient in order to address stopping smoking, reducing alcohol intake.
- Ensure optimum treatment of conditions such as diabetes and blood pressure as applicable.

Urogenital Atrophy [listed in ascending cost order[3] – patient preference may influence choice of formulation]
Ovestin cream 1 applicator = 500 mcg estriol
Vagirux vaginal tabs 1 tab = 10mcg estradiol
Imvaggis pessary 1 pessary = 30 mcg estriol
Estring 7.5mcg /24hrs (vaginal ring worn for 3 months)

Progestogenic side effects‡: *e.g. PMS type symptoms, Breast tenderness, Lower abdominal pain, Backache, Depressed mood, Acne/greasy skin, headache*

Non-hormonal vaginal moisturisers/lubricants (e.g. Replens MD®, Yes VM®) can be used alone or in addition to vaginal oestrogen.
These are available to purchase OTC and online and may be cheaper than the cost of a prescription charge[3].
Also see CKS Scenario: Managing women with menopause, perimenopause, or premature ovarian insufficiency available here[4]

Progestogenic opposition of oestrogen HRT in women with intact uterus

- **Levonorgestrel Intrauterine System (LNG-IUS) (Mirena®),** inserted after appropriate gynaecological/menstrual history and after appropriate assessment/investigation, can be a useful option if progestogenic side effects are an issue with systemic treatment[4]. Mirena is licensed as a contraceptive, to treat menorrhagia and to give endometrial protection as part of HRT. In a HRT regime, Mirena® has a 4 year license but FSRH guidance (2019)[5] p11 currently supports the use of the Mirena® for endometrial protection in conjunction with estrogen therapy (tablet/patch/gel etc**) for up to 5 years – note this is outside the product licence[5,6]**. Other LNG-IUS products (Jaydess® and Levosert®) are not licensed for use as part of a HRT regime. Irregular bleeding is common in first few months of use. Once in situ, periods may reduce by >95% at 6 months and ~20% of users may be amenorrheic[6].

- **Oral Micronised Progesterone (Utrogestan 100mg oral capsule)** is an option if LNG-IUS is unsuitable or has been declined. Licensed dose is 200 mg taken **orally** once daily on days 15–26 of each 28-day cycle (sequential combined) OR 100 mg OD on days 1–25 of each 28-day cycle (continuous combined)[3]. Note that Utrogestan 200mg **vaginal** capsules are available in the UK but vaginal progesterone is only included on the BSW formulary for the licensed indication (fertility) with RED TLS. Vaginal capsules should not be prescribed in primary care or for HRT.

- The BMS has detailed guidance on progestogens and endometrial protection[7] which includes information on the available evidence for off-label routes of administration of oral micronised progesterone here BMS Tools for Clinicians - British Menopause Society (thebms.org.uk)

Tibolone – a gonadomimetic[2,8]

- **Tibolone 2.5mg oral tablets taken once daily**. Tibolone is a synthetic steroid with oestrogenic, progestogenic and androgenic activity so is a type of continuous combined HRT (no bleed) preparation.
- Unsuitable for use in the premenopause (unless being treated with gonadotrophin-releasing hormone analogue). Also unsuitable for use within 12 months of last menstrual period (may cause irregular bleeding).
- If transferring from cyclical HRT, start at end of regimen; if transferring from continuous-combined HRT, start at any time.
- Because of its androgenic activity, it has been shown to have a positive effect on libido. Tibolone has been shown to be as/or more effective than oestradiol in controlling menopausal symptoms.
- In younger women, the risk profile of tibolone is broadly similar to that for conventional combined HRT. For women older than ~60 years, the risks associated with tibolone start to outweigh the benefits because of the increased risk of stroke.

Topical testosterone for low libido in menopause in adult women on HRT

- NG23 (Menopause: diagnosis and management 2015)[1] states that the off-label use of testosterone supplementation can be 'considered' for menopausal women with low sexual desire if HRT alone is not effective. There are no licensed treatments for women in the UK.
- **Topical testosterone for this off-label indication is AMBER with Shared Care in BSW.** Our local SCA details roles for primary/secondary care, information on monitoring and practical guidance on prescribing and can be read in full here.

Herbal medicines for managing menopausal symptoms

- **Herbal medicines are not available on the NHS in BSW and should not be prescribed on a FP10**. Patients enquiring about herbal medicines can be directed to www.menopausematters.co.uk/remedies.php for information. Remind patients these are largely unregulated products lacking consistency between the constituents.

Cautions, Contra-indications and Risks of HRT

- **For full list of cautions and contra-indications**: see individual product Summary of Product Characteristics found here
- **Risks of HRT: The MHRA have produced tables to aid communication about risks and benefits[9].**
  Table 1 Summarises HRT risks and benefits during current use and current use plus post-treatment from age of menopause up to age 69 years, per 1000 women with 5 years or 10 years use of HRT Note that menopausal symptom relief is not included in this table but is a key benefit of HRT and will play a major part in the decision to prescribe HRT.
  Table 2 Detailed summary of relative and absolute risks and benefits during current use from age of menopause and up to age 69, per 1000 women with 5 years or 10 years use of HRT.
  See also NICE CG23 - Menopause (2015, updated 2019)[1] Section 1.5 (p11)

Follow up/Annual Review/Duration of Treatment[1,4]

- **Follow up after 3/12 of starting or changing treatment** to assess effect, enquire about side effects & bleeding pattern **and then at least annually**, unless clinical indications for earlier review (e.g. treatment ineffectiveness or adverse effects).
- In women with a uterus, unscheduled vaginal bleeding is a common side-effect of HRT within the first 3 months of treatment, but should be reported promptly if it occurs after the first 3 months (see recommendations on endometrial cancer in NICE guideline [NG12] Suspected cancer: recognition and referral https://www.nice.org.uk/guidance/ng12
- **At annual review**, reinforce lifestyle measures, check efficacy, side-effects, ensure correct dose, optimal route of delivery and compliance. Also check:
  - Pros & cons of continuing. Risk of breast cancer rises with long-term use (use MHRA risk tables[9] to inform discussion)
  - Check BP, encourage engagement with national screening programmes (breast/bowel/cervical) as appropriate
  - Assess osteoporosis risk & consider the need for investigation/monitoring
  - Enquire about symptoms of urogenital atrophy
- **Duration of treatment**: There are no reasons to place mandatory limitations on duration of HRT. Treatment review should include a well-informed discussion and should consider specific goals and objective estimate of risks and benefits. When stopping HRT, offer a choice of gradually reducing or immediately stopping treatment:
  - gradually reducing HRT may limit recurrence of symptoms in the short term
  - gradually reducing or immediately stopping HRT makes no difference to their symptoms in the longer term.

Practical Prescribing – Prescription Charges, Prescribing Intervals, Private Prescriptions, Medicines Shortages

- **Prescription charges:**
  In Oct 2021, the government proposed action to cut the cost of repeatable HRT prescriptions, see here. As yet, no changes have been implemented and the NHS prescription charge for England is currently **£9.35 per item** (and reviewed annually in April). Sequential preparations e.g. Elleste Duet 1mg or 2mg, Evorel Sequi patches, Femoston 1/10mg or 2/10mg will incur two prescription charges. Further information here PSNC Dispensing Factsheet: Multi-charge items
- **Duration of prescriptions:**
  BSW CCG supports the Wessex LMC position "*the appropriate duration of a prescription should be decided by the prescriber, in conjunction with the patient, taking into account the medicine being prescribed, its monitoring requirements, the condition being treated and the individual patient's needs. A shorter duration is appropriate when a new medicine is first started or when a patient's condition or medicines regimen is likely to change. The quantities on a prescription should reflect the required frequency of dispensing. The quantity (and cost) of wasted medicines is significant and the duration of prescriptions is one factor that affects this*".
- **Private prescriptions:**
  Some patients may elect to access menopausal services outside the NHS. The responsibility for prescribing rests with the doctor who has clinical responsibility for a particular aspect of the patient's care. Further/ongoing treatment with a drug, recommended by a private consultant can be prescribed by a GP in BSW on an FP10 as long as: The GP considers it necessary; the drug is listed on the BSWformulary; the drug is normally funded in primary care for that condition. When the consultant retains clinical responsibility, for example, when he/she continues to administer any treatment or the treatment is recognised to be specialist in nature (e.g. Red Drugs/Unlicensed), he/she should issue the prescriptions. See BSW CCG advisory summary on boundaries between NHS/Private care www.bswccg.nhs.uk
- **Medicines shortages:**
  Historic HRT supply shortages (due to Brexit, increased demand, Covid pandemic and manufacturing processes) are largely improving. The BMS website regularly issues updates on HRT supply in its newsfeed News - British Menopause Society (thebms.org.uk) and these updates additionally give guidance on equivalent options with HRT preparations.

References and useful links: [all accessed 02/2022]

1. Menopause: diagnosis and management. NICE guideline [NG23] Published: 11/2015 Last updated: 12/2019. https://www.nice.org.uk/guidance/ng23
2. Hamoda H, Panay N et al. The British Menopause Society & Women's Health Concern 2016 recommendations on hormone replacement therapy in menopausal women. Post Reproductive Health. 2016;22(4):165-183. https://doi.org/10.1177/2053369116680501
3. https://www.mims.co.uk/
4. CKS Menopause. Last revised 11/2020. https://cks.nice.org.uk/topics/menopause/
5. FSRH Clinical Guideline: Intrauterine Contraception. Published 04/2015. Amended 09/2019 Via https://www.fsrh.org/standards-and-guidance/
6. SPC for Mirena 20 mcg/24 hrs IUS https://www.medicines.org.uk/emc/product/1132
7. British Menopause Society. Tool for clinicians: Progestogens and endometrial protection. Published: 10/2021. https://thebms.org.uk/publications/tools-for-clinicians/
8. British National formulary. https://bnf.nice.org.uk/
9. MHRA: (HRT): further information on the known increased risk of breast cancer with HRT and its persistence after stopping. MHRA DSU September 2019

Also see:

- BMS Tools for Clinicians - British Menopause Society (thebms.org.uk) ; WHC factsheets and other helpful resources - Women's Health Concern (womens-health-concern.org)
- Menopause Symptoms - what happens and when : Menopause Matters