BSW HRT Formulary Treatment Options and Pathway

Bath and North East Somerset, Swindon and Wiltshire Together

For healthcare professionals: NICE: Menopause Diagnosis and Management; British Menopause Society (BMS) website HRT Guide ; HRT Practical Prescribing
For patients: Women's Health Concern factsheets ; Pt info leaflets: https://www.menopausematters.co.uk/menopause.php

See end of this document for further references and reading material in addition to the quicklinks above

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

ORAL TREATMENT OPTIONS

Oestrogen Only
(no uterus)
1 prescription charge

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

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)

Herbal medicines are not available on the NHS in BSW and should not be prescribed on FP10. Patients enquiring about OTC 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

Sequential combined
(uterus - monthly bleed)
2 prescripton charges

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

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)
Blissel gel 1 applicator = 50mcg estriol

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
- **Bijuve[5]**
  1mg estradiol + 100mg micronised progesterone (**bioidentical preparation** - useful second line option if adverse effects experienced with synthetic preparations)
- **Tibolone (Livial)**
  (See text overleaf for full guidance)

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 – including off-license use

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- **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[6,7]**. 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[7].
- **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].
- **OFF-LICENSE PRESCRIBING -** Specialists in menopause are increasingly recommending HRT regimens that fall outside current product licenses. Off-license prescribing should not be a first-line option but may be considered, on an individual patient basis, by a specialist in menopause in response to current supply chain issues or where histological assessment, history of adverse effects and risk factors (e.g. for endometrial hyperplasia or breast cancer) are considered prior to recommending off-license use of the estrogen or progesterone component.
  The BMS has guidance on progestogens and endometrial protection[8] which includes information on the limited available evidence for off-license routes of administration of oral micronised progesterone here BMS Progestogens and endometrial protection. There remains debate about what constitutes high dose estrogen and there can be significant individual variation in absorption and metabolism. Our local specialist teams support the information provided in the BMS resource HRT preparations and equivalent alternatives which is based on pharmacokinetics, clinical trials and clinical experience and notes where recommendations are off-license.
  It is up to individual clinicians in primary care to decide whether they take on (either from a private or NHS specialist recommendation) off-license prescribing responsibility of HRT. They should only do so where satisfied that there is sufficient evidence or experience of using the medicine to demonstrate its safety and efficacy given the above guidance. Primary care teams may wish to develop a practice view on this. Informed patient consent and any monitoring and/or follow up treatment should be clearly recorded.

Tibolone – a gonadomimetic[2,9]

- **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

- Requests for prescriptions of testosterone for patients experiencing menopausal symptoms have become increasingly more common. NG23 (Menopause: diagnosis and management 2015)[1] states that off-label use of testosterone can be 'considered' for menopausal women with low sexual desire if HRT alone is not effective. Women should be fully oestrogenised, and any symptoms of vulvovaginal atrophy adequately treated before testosterone is considered.
- **Topical testosterone for the off-label indication of low libido in adult women on HRT is AMBER with Shared Care in BSW.** Our local SCA details roles for primary care/menopause specialist, information on monitoring and practical guidance on prescribing. Read in full here. Testosterone for other indications in adult women e.g. cognitive dysfunction, bone health, well-being or cardiovascular metabolic benefits are **not** approved.
- **'Specialist in menopause'** for the purposes of our BSW SCA is defined as: *a British Menopause Society accredited specialist or equivalent prescriber who can demonstrate that they have received training in and have clinical experience of treating women with testosterone preparations*. This could therefore be a GP working in primary care.
- There are no licensed treatments for women in the UK. The RCGP/RCOG/BMS Position Statement[10] on menopause states some GPs will feel competent and comfortable issuing testosterone prescriptions. It also supports any GP who is not, to seek specialist help if asked to prescribe outside their area of expertise.

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[11].**
  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 BrCa rises with long-term use (use MHRA risk tables[11] 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
- **Women prescribed testosterone** should have an annual blood test, to check Free Androgen Index (FAI) and FBCs. Abnormal results should be reviewed by a Specialist in menopause before continuing with treatment. See SCA here.
- **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 – Rx Charges, Prescribing Intervals, Managing HRT shortages, Private Rxs (cont. overleaf)

- **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*".
- **Prescription charges:**
  From 1st April 2023, patients who pay for their HRT prescriptions will be able to purchase an annual HRT Pre Payment Certificate for £19.30[12,13]. The HRT PPC, valid for 12 months, can be purchased from contractors or online[13] and used against any listed HRT prescription item(s) **licensed** for the treatment of menopause; the list of eligible HRT medicines will be published and updated here[13] and in the Drug Tariff. Further information is expected from DHSC/NHSE detailing changes to exemption status on the reverse of FP10s. Patients with an HRT PPC will continue to pay the prescription charge for any other (non-HRT) medicines (unless another exemption reason applies).
  To support contractors/pharmacists while NHS prescription processing systems are updated, GPs are advised to write HRT items on separate prescriptions. Read more here.
- **HRT – Managing Supply Chain Issues and HRT 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)
  The following resources give guidance on equivalent options with HRT preparations to support switching in primary care where necessary: **BMS HRT Practical Prescribing** and **BMS HRT Preparations and Equivalent Alternatives**

- **Private prescriptions:**
  Some patients may elect to access menopausal services outside the NHS. Responsibility for prescribing rests with the prescriber 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 continued in primary care on FP10 providing: the primary care prescriber agrees the treatment is necessary; the drug is listed on BSWformulary; the drug is normally funded in BSW for that condition. See BSWICB advisory summary on boundaries between NHS/Private treatments www.bsw.icb.nhs.uk. Testosterone initiated by a private provider may be continued on the NHS within BSW but ONLY for the approved indication of low libido in adult women on HRT, where clinically appropriate and where the private Specialist adheres to their responsibilities in the BSW Shared Care Agreement for testosterone - low libido in adult women on HRT .

References and useful links: [accessed Feb and March 2023]

1. Menopause: diagnosis and management. NICE guideline [NG23] Published: 11/2015 Last updated: 12/2019. https://www.nice.org.uk/guidance/ng23 *note that a partial update to NG23 is currently in development, expected publication Feb 2024. Read more here https://www.nice.org.uk/guidance/indevelopment/gid-ng10241/*
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 09/2022. https://cks.nice.org.uk/topics/menopause/
5. SMC assessment of estradiol/micronized progesterone (Bijuve) 08/2022 https://www.scottishmedicines.org.uk/media/7098/estradiol-micronised-progesterone-bijuve-abb-final-aug-2022-for-website.pdf
6. FSRH Clinical Guideline: Intrauterine Contraception. Published 04/2015. Amended 09/2019 Via https://www.fsrh.org/standards-and-guidance/
7. SPC for Mirena 20 mcg/24 hrs IUS https://www.medicines.org.uk/emc/product/1132
8. British Menopause Society. Tool for clinicians: Progestogens and endometrial protection. Published: 10/2021. https://thebms.org.uk/publications/tools-for-clinicians/
9. British National formulary. https://bnf.nice.org.uk/
10. RCGP, RCOG and BMS Position Statement on the Menopause 05/2022 https://www.rcgp.org.uk/policy/rcgp-policy-areas/menopause-position-statement
11. MHRA: (HRT): further information on the known increased risk of breast cancer with HRT and its persistence after stopping. MHRA DSU September 2019
12. PSNC Press release 03/03/2023 https://psnc.org.uk/our-news/new-regulations-to-accompany-the-introduction-of-hrt-prepayment-certificates-hrt-ppcs/
13. NHSBSA: NHS Hormone Replacement Therapy Prescription Prepayment Certificate (HRT PPC). https://www.nhsbsa.nhs.uk/help-nhs-prescription-costs/nhs-hormone-replacement-therapy-prescription-prepayment-certificate-hrt-ppc

The RCGP, BMS and PCWHF have educational materials to support primary care in updating knowledge of the menopause:

- RCGP Learning – Women's Health Hub https://elearning.rcgp.org.uk/course/index.php?categoryid=57
- BMS Tools for Clinicians https://thebms.org.uk/publications/tools-for-clinicians/
- Primary Care Womens Health Forum https://pcwhf.co.uk/resources

For patients:

- Menopause Matters https://www.menopausematters.co.uk/menopause.php
- Women's Health Concern https://www.womens-health-concern.org/help-and-advice/factsheets/ (aimed at patients)