Suffolk and North East Essex (SNEE)
HRT Formulary Treatment Options and Pathway

NHS Suffolk and North East Essex Integrated Care Board

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; https://www.menopausematters.co.uk/menopause.php; HRT prepayment certificate; Alternative therapies
See end of this document for further references and reading material in addition to the quick links above

The transdermal route is often considered as first choice route of estradiol administration, particularly in women with risk factors, including those with a BMI >30 kg/m2 and migraine. 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.

TRANSDERMAL OPTIONS

Oestrogen Only*

Patches. Change TWICE per week
Evorel 25, 50, 75, 100mcg estradiol
Estradot 25, 37.5, 50, 75, 100mcg estradiol

Alternative formulations:
Gel. Oestrogel 0.75mg estradiol per each pump TWO pumps daily
2nd line. Sandrena (gel) 500mcg, 1mg estradiol/sachet ONE sachet daily
Spray. **Lenzetto** THREE sprays DAILY

Sequential combined
with uterus - menstrual period within 12 months

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

Continuous combined
with uterus - suitable if >12months from last bleed i.e. post menopause or amenorrheic due to Mirena

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

***HRT essentially means oestrogen replacement. Progesterone protects uterine tissue from unopposed oestrogen which could otherwise cause proliferation and uterine cancer. Anyone with a uterus requires progesterone. If a hysterectomised patient has residual uterine tissue i.e. from cervical stump post hysterectomy or severe endometriosis they may need consideration of progesterone.**

PROGESTOGEN OPTIONS

PROGESTOGEN PROTECTION OF OESTROGEN HRT IN WOMEN WITH INTACT UTERUS[3]

Levonorgestrel intrauterine system (LNG-IUS) (Mirena®) inserted after appropriate gynaecological/menstrual history and appropriate assessment/investigations, can be a useful option if progestogenic side effects are an issue with systemic treatment. In HRT Mirena® has a 4 year licence but FRSH guidance (2019)[4] currently supports the use of Mirena® for endometrial protection in conjunction with estrogen therapy **for up to 5 years - note this is outside the product licence**[6,7] N.b Mirena for contraception has been extended to 8 years

Oral Micronised Progesterone (100mg oral capsules) Licenced dose is 200mg taken ONCE daily for 14 consistent days of each 28 day cycle (sequential combined) OR 100mg ONCE daily (continuous combined). N.b. High dose oestrogen requires a higher dose of micronised progesterone

Medroxyprogesterone acetate 10mg ONCE daily for 12 days a month (cyclical) OR a minimum of 2.5mg ONCE daily (continuous combined)

Norethisterone 5mg ONCE daily for 12 days a month (cyclical) 0.5mg-1mg ONCE daily (continuous combined)

Changing progestogen component may be required if progestogenic side effects occur e.g. bloating and fluid retention, low mood, breast tenderness, unscheduled vaginal bleeding. For more information see BMS: Progestogens and endometrial protection.

Vaginal dryness, itching and pain during sexual intercourse affects over 70% of perimenopausal women and symptoms are often not volunteered during a consultation so please ask. Any reports should be treated, targeted for local relief in addition to HRT treatment. Perimenopausal symptoms including urogenital atrophy can take several months to respond to treatment and compliance is important. There are many OTC preparations available as well as the products listed below.

UROGENITAL ATROPHY

Urogenital atrophy

Estradiol 10mcg pessaries Vagirux/Vagifem
Insert once daily for TWO weeks then TWICE weekly thereafterN.B Vagirux hasve a reusable applicator

Estriol 0.1% cream Ovestin (oil based)
Insert once daily for TWO weeks then TWICE weekly thereafter

Estring 7.5mcg/24 hours vaginal ring
Reinsert every TWELVE weeks

2nd line: **Estriol** (Imvaggis) 0.03mg pessary Insert once daily for THREE weeks then TWICE weekly thereafter. **Estriol** (Blissell) 50mcg gel Insert once daily for THREE weeks then TWICE weekly thereafter - **water based can be used externally for soreness**

3rd line: **Prasterone** (Intrarosa) 6.5mg pessary ONCE daily. For women who are unable to manage vaginal insertion only: **Ospemifene** 60mg tablets (Senshio) ONCE daily

Non-hormonal vaginal moisturisers/lubricants (e.g. Replens MD®, Yes VM®, Sylk) **available OTC** can be used alone or in addition to vaginal oestrogen. Advise to use moisturisers daily.

ORAL TREATMENT OPTIONS
(Currently considered 2nd line after transdermal route)

Oestrogen Only *

Elleste Solo - 1mg or 2mg estradiol

Sequential combined
with uterus - menstrual period within 12 months

Femoston
1mg or 2mg estradiol + **dydrogesterone** 10mg

Elleste Duet
1mg or 2mg estradiol + **norethisterone** 10mg

Continuous combined
with uterus - suitable if >12months from last bleed i.e. post menopause or amenorrheic with Mirena

Femoston Conti (low dose)
0.5mg estradiol + 2.5mg dydrogesterone (lowest effective dosed HRT preparation)
OR Femoston Conti
1mg estradiol + 5mg dydrogesterone

Bijuve[5]
1mg estradiol + 100mg micronised progesterone (bioidentic preparation - useful second line option if adverse effects experianced with synthetic preparations)

Tibolone

see **Tibolone** section on page 4

TESTOSTERONE

Testosterone gel (Tostran® 2% gel, Testim® 1% gel, Testogel® 40.5mg/2.5mg)
Only those with competence and confidence should prescribe testosterone in Primary Care. Within SNEE, topical testosterone for hypoactive sexual desire disorder in menopause if classified as GREEN for this indication – it can be prescribed in primary care under the recommendation of a specialist in the management of menopause. The specialist can be a primary care prescriber if they feel it is within their scope of practice. For more information on monitoring[6] see BMS: Testosterone replacement in menopause Nice guidance recommends considering testosterone supplementation for women with low sexual desire associated with menopause if HRT **alone** is not effective[1]. Testosterone can be prescribed on the NHS if the prescriber is familiar with it and willing to prescribe it "off licence", Some prescribers may prefer to refer to a specialist for advice before prescribing.

Ensure modifiable lifestyle factors 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.**
- **Discuss cognitive behavioral therapy (CBT)[1] as an option for management of symptoms associated with menopause**



Oestrogen dosing[7]

Ooestrogen dose for ultra-low, low, standard, moderate and high dose regimens					
	Ultra low	Low	Standard	Moderate	High
Oral	0.5milligram	1 milligram	2 milligrams	3 milligrams^	4 milligrams^
Patch	Half 25 microgram	25 micrograms	50 micrograms	75 micrograms	100 micrograms
Gel – pump	½ pump	1 pump	2 pumps	3 pumps	4 pumps
Gel – sachet	¼ sachet (0.25 milligrams)	½ sachet (0.5 milligrams)	1 sachet (1mg)	1.5-2 sachets (1.5-2 milligrams)	3 sachets* (3 milligrams)
Spray	1 spray	2 sprays	3 sprays	4-5 sprays*	6 sprays*

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

Progestogen dosing[7]

Progestogen dose per licenced ooestrogen dose							
Oestrogen dose	Micronised progesterone		Medroxyprogesterone		Northisterone		LNG-IUD (52mg)
	continuous	sequential	continuous	sequential	continuous	sequential	
Ultra/Low	100mg	200mg	2.5mg	10mg	5mg*	5mg*	One for up to 5 years of use
Standard	100mg	200mg	2.5-5mg	10mg	5mg*	5mg*	
Moderate	100mg	200mg	5mg	10mg	5mg	5mg	
High	200mg	300mg	10mg^	20mg^	5mg	5mg	

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

Progestogen opposition of oestrogen HRT in women with intact uterus – including off-licence use

- **OFF-LICENCE PRESCRIBING -** Specialists in menopause are increasingly recommending HRT regimens that fall outside current product licences. Off-licence 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-licence use of the oestrogen or progesterone component.
  The BMS has guidance[3] on progestogens and endometrial protection[8] which includes information on the limited available evidence for off-licence routes of administration of oral micronised progesterone here **BMS Progestogens and endometrial protection**. There remains debate about what constitutes high dose oestrogen and there can be significant individual variation in absorption and metabolism. Our local specialist teams support the information provided[9] 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-licence.
  For more information on prescribing in these situations please see the GMC Prescribing Unlicenced Medicines guidance.

Tibolone – a gonadomimetic[2,10]

- **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 perimenopause (unless being treated with gonadotrophin-releasing hormone analogue).
- 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 estradiol 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

- **Only those with competence and confidence should prescribe testosterone in Primary Care**
- Requests for prescriptions of testosterone for patients experiencing menopausal symptoms have become increasingly more common. NG23 (Menopause: identification and management 2024)[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.
- There are no licenced treatments for women in the UK. **The RCGP/RCOG/BMS position Statement**[11] 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.
- Take baseline bloods: Liver Function Tests (LFT), Total testosterone baseline, 2-3months later and then 6-12 monthly[6]

Management of unscheduled bleeding

- It is normal to for patients to experience some bleeding whilst taking HRT. When bleeding occurs outside of an expected pattern it is described as "unscheduled". For more information[7] see British Menopause Society Management of Unscheduled Bleeding On Hormone Replacement Therapy
- In women with a uterus, unscheduled vaginal bleeding is a common side-effect of HRT within the first 3 months of treatment, but women should be encouraged to report it promptly to their healthcare professional (see recommendations on endometrial cancer in NICE guideline [NG12] Suspected cancer: recognition and referral[12] https://www.nice.org.uk/guidance/ng12

Cautions, Contra-indications and Risks of HRT

- **For 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[13].**

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 2024)[1] and Womens Health Concern Fact Sheet HRT: Benefits and Risks and Womens Health Concern Fact Sheet: Understanding the Risks of Breast Cancer. These factsheets aid communication about risks and benefits.
- Use HRT and the likelihood of some medical conditions: A discussion aid for healthcare professionals and patients to support the discussion with the patient during a consultation.

Follow up/Annual Review/Duration of Treatment[1,14]

- **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).
- **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[13] 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 LFT's, Total testosterone/Free Androgen Index (FAI) and FBCs. Abnormal results should be reviewed by a Specialist in menopause before continuing with treatment. See guidance 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:**
  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". For more information see SNEE position statement.
- **Prescription charges:**
  From 1st April 2024, patients who pay for their HRT prescriptions will be able to purchase an annual HRT Pre Payment Certificate for £19.80[15,16]. The HRT PPC, valid for 12 months, can be purchased from contractors or online[16] and used against any listed HRT prescription item(s) **licenced** for the treatment of menopause; the list of eligible HRT medicines will be published and updated here[16] 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).
- **Private prescriptions:**
  Some patients may elect to access menopausal services outside the NHS. For information on prescribing following a private consultation please see section 4.2 SNEE ICB Defining the boundaries between NHS and privately funded healthcare.

References and useful links: [accessed October and November 2024]

1. Menopause: diagnosis and management. NICE guideline [NG23] Published: 11/2015 Last updated: 11/2024. https://www.nice.org.uk/guidance/ng23
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3. BMS. Progestogens and endometrial protection Published 10/2021 14-BMS-TfC-Progestogens-and-endometrial-protection-APR2023-A.pdf
4. FSRH Clinical Guideline: Intrauterine Contraception. Published 03/2023. Amended 07/2023 Via FSRH Clinical Guideline: Intrauterine contraception (March 2023, Amended July 2023) - Faculty of Sexual and Reproductive Healthcare
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. BMS. Testosterone replacement in menopause Published 12/2022 08-BMS-TfC-Testosterone-replacement-in-menopause-DEC2022-A.pdf
7. BMS. Management of unscheduled bleeding on Hormone replacement Therapy (HRT) Published 04/2024 01-BMS-GUIDELINE-Management-of-unscheduled-bleeding-HRT-JULY2024-A.pdf
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9. BMS. HRT preparations and equivalent alternatives Published 03/2022 15-BMS-TfC-HRT-preparations-and-equivalent-alternatives-JAN2024-B.pdf

10. British National formulary. https://bnf.nice.org.uk/
11. RCGP, RCOG and BMS Position Statement on the Menopause 05/2022 https://www.rcgp.org.uk/policy/rcgp-policy-areas/menopause-position-statement
12. Suspected cancer: recognition and referral. NICE guideline [NG12] Published: 6/2015 Last updated: 10/2023. Overview | Suspected cancer: recognition and referral | Guidance | NICE
13. MHRA: (HRT): further information on the known increased risk of breast cancer with HRT and its persistence after stopping. MHRA DSU September 2019
14. CKS Menopause. Last revised 09/2022. https://cks.nice.org.uk/topics/menopause/
15. PSNC Press release 03/03/2023 https://psnc.org.uk/our-news/new-regulations-to-accompany-the-introduction-of-hrt-prepayment-certificates-hrt-ppcs/
16. 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)

N.B The term woman is used to include anyone born with ovaries

This guidance has been adapted with permission from guidance from Bath, North East Somerset, Swindon and Wiltshire ICB