Hormone replacement therapy: A prescribing guide

*Updated January- March 2025 to reflect minor updates to NG23 and *new* Oestrogen dose dependent progesterone guidance from the British Menopause Society. (approved at PMOC section 1&2 March 2025)*

This guideline is designed to support HRT decision making for Doncaster and Bassetlaw prescribers; It does not cover the initial diagnosis or non-pharmacological management of the menopause. Evidence based information on these topics can be found in NICE Guideline NG23: Menopause: Diagnosis and Management (1) and the BMS website. (2)

Reference to terminology used throughout the guideline:

Transdermal Oestrogen: Oestrogen patch, Oestradiol gel or Lenzetto® Spray

Oral Oestrogen: Oestrogen in a tablet form

Topical Oestrogen: An oestrogen preparation such as cream, pessary or ring applied locally to the vagina and vulva.

Contents

In the updated NICE Guidance, emphasis is put on the increasing evidence for Cognitive Behavioural Therapy, in particular menopause specific CBT in the management of the menopause which is not covered in this prescribing guideline.

Prescribing considerations

- Hormone replacement therapy is licensed for the vasomotor symptoms of the menopause. There is no absolute age for when cessation of therapy should be mandated, but women should be aware that risks increase after age 60 or 10 years after the beginning of menopause.
- It is advisable to use the lowest dose of oestrogen that controls the patient's symptoms. Especially in the perimenopause and in younger women this may vary significantly.
- Blood pressure and BMI should be measured before commencing therapy.
- Treatment should be reviewed after 3 months and then annually using the Arden's template.
- Blood tests to check Oestrogen levels are often unreliable, and symptom control should guide dose escalation.

Pre-payment Certificates

A pre-payment certificate is now available for women to obtain their HRT prescriptions. It should be noted that not all HRT regimes are included, and women should be advised to check if their preparation is covered. https://health-charge-exemptions.nhsbsa.nhs.uk/buy-hrt-ppc/start.

Risks and benefits of HRT

- NICE have updated the guidelines to include a decision aid that can be used when discussing risk with patients.
- https://www.nice.org.uk/guidance/ng23/resources/incidence-of-medical-conditions-with-and-without-hrt-a-discussion-aid-pdf-13553199901

- The risk of VTE is increased 2-4-fold when using oral oestrogen preparations. Some Progesterone's can also increase VTE risk (3). Low risk women are not at increased risk of VTE when using transdermal preparations. Also note that Micronised Progesterone and IUS are considered "breast friendly" progesterones. (3) Consider seeking specialist menopause and/or haematology advice for high-risk women or those with a previous unprovoked DVT.
- Consider transdermal HRT for women who are at increased risk of VTE, including those with BMI >30.
- HRT does not increase CVD risk when started in women aged <60. The presence of CV risk factors is not contraindication to HRT if they are optimally managed. HRT with oestrogen alone is associated with no or reduced risk of CHD. HRT with oestrogen and progesterone is associated with little or no increase in the risk of CHD. Taking oral oestrogen is associated with a small increase in the risk of stroke (baseline population risk of stroke in women <60 is very low.) Specialist advice should be sought when considering HRT use in patients with established cardiovascular disease (1).

- HRT is not associated with an increased risk of developing type 2 diabetes. HRT is not generally associated with an adverse effect on blood glucose control and the risks and benefits should be discussed with patients
- Long term use of sequential combined HRT for more than 5 years may be associated with a small increased risk of endometrial hyperplasia and endometrial cancer. (4)
- HRT with oestrogen alone is associated with little or no change in the risk of breast cancer. HRT with oestrogen and progesterone can be associated with a small increase in the risk of breast cancer compared to women who have never taken HRT. Any increase in the risk of breast cancer is related to treatment duration and reduces after stopping HRT however studies have shown that after 5 years of use, there is an association with a small increased risk that does not return to baseline after stopping treatment. (5)
- The risk of fragility fracture is decreased while taking HRT and this benefit is maintained during treatment but decreases once treatment stops. The benefits of weight bearing exercise on the reduction in osteoporotic risk should be discussed with patients.

Transdermal vs Oral preparations

Transdermal preparations would usually be considered as 1st line therapy (patch, gel or spray) as they have favourable risk profile from a VTE, and stroke risk perspective compared to oral oestrogen therapies.

The following should be considered:

- Patient preference for body identical products (e.g., Oestradiol and Micronised progesterone) Note *Bioidentical* compound products are NOT recommended as there is concern related to purity, potency and safety of these products.
- Contraceptive requirements – Until age 55 except:
    - If patients have had 2xFSH blood tests at least 6 weeks apart in the post-menopausal range, they can cease contraception 1 year afterwards if aged over 50
    - If patients have had 2xFSH blood tests at least 6 weeks apart in the post-menopausal range, they can cease contraception 2 years afterwards if aged under 50.
- Risk factors for VTE including BMI >30kg/m2, age >60
- Preference for application method
- Compliance with therapy
- Availability of products
- Urogenital symptoms of the menopause
- Family history of breast or ovarian cancer
- Family history of thrombophilia

Continuous vs Sequential therapy

- Continuous combined preparations are not usually suitable for use in the perimenopause or within 12 months of the last menstrual period due to the increased risk of irregular bleeding. If HRT was initiated in the perimenopause, consideration should be given to switching from cyclical regimens to continuous combined regimens after the woman becomes postmenopausal. Women who have been using a cyclical preparation for a minimum of 1 year or are aged over 54 should be transferred to a continuous regime. If a patient has had a total hysterectomy, they are suitable for Oestrogen only therapy.
- If the indication for the hysterectomy was endometriosis, it may be advisable to discuss with the patient's consultant as they may also require progesterone therapy as well on a case-by-case basis to prevent re-activation of residual disease. However, there is limited evidence available on this to guide clinical practice. (4)

Information on Bijuve®

- Bijuve® is an oral product containing 1mg of Estradiol and 100mg Micronised progesterone. It is a continuous combined therapy suitable for post-menopausal women only. It is included in the Sheffield formulary but note "Consultants and GPs with a specialist interest in Menopause in Sheffield advise transdermal oestrogen and oral micronised progesterone as 1st line choice" as there is no published data comparing Bijuve® to transdermal oestrogen and oral micronised progesterone.

An approach to HRT prescribing-Flowchart

All progesterone only methods can be used in addition to sequential HRT for contraception.

Patient wishes to be prescribed HRT

NO → Clinician to signpost patient to other resources e.g. Women's Health Concern website.

YES

Patient has a uterus?*

YES → Patient requires a COMBINED regime

NO → Patient requires an OESTROGEN ONLY regime

*Seek specialist advice if hysterectomy secondary to severe endometriosis

**Or on sequential regime for 1 year or more

More than 12 months since last period?**

YES

Prescribe a continuous regime

Choice of oestrogen AND IUS e.g Mirena® (4 year license but accepted 5 year use)

OR

Choice of oestrogen AND Micronised progesterone 100mg to be taken at night (off license accepted use)

OR

Evorel Conti® Patches to be changed twice weekly

NO

Prescribe a sequential regime

Choice of oestrogen AND IUS e.g Mirena® (4 year license but accepted 5 year use)

OR Choice of oestrogen AND Micronised progesterone 200mg days 14-28 of cycle (2*100mg tablets)

OR

Evorel Sequi® Patches to be changed twice weekly (Pack contains two different patches)

Patient accepts topical oestrogen?

YES

Topical oestrogen

Patch -Evorel® 25-50 micrograms*** or Oestradot ®25, 37.5 or 50 micrograms***

OR

Gel -Oestrogel® 1-2 pumps or Sandrena® 1 sachet daily (half each arm)***

OR

Spray-Lenzetto® 1 spray daily***

NO

Oral Oestrogen

Prescribe Ellest Solo® 1mg tablets once daily***

***Starting doses of oestrogen

Urogenital symptoms of the menopause

Topical vaginal oestrogens can be prescribed if required *in addition* to transdermal or oral HRT specifically for vaginal dryness and can be used long term.

- 1st choice: Generic Estriol 1mg/G Vaginal Cream. Use each night for 3-4 weeks and then twice weekly thereafter.

- Intravaginal tablet therapy: Vagirux® Insert 1 tablet daily per vagina for 2 weeks, then twice weekly ongoing. Box of 24 contains single re-usable applicator.

- Alternative choice: Vagifem® which has individual applicators. Insert 1 tablet daily per vagina for 2 weeks, then twice weekly ongoing.

Note – Estradiol 0.06% transdermal gel (Oestrogel Pump Pack®) is licenced only for transdermal use for menopausal symptoms. It is not to be used on the vagina or vulva for urogenital symptoms.

2nd Line therapy considerations

2024 update -NICE section 1.5.9 -Consider vaginal Prasterone 6.5mg Pessary Interosa® for moderate-severe symptoms not responsive to vaginal oestrogens. Prasterone is DHEA, broken down in vulval tissue to oestrogen and androgen metabolites. It should be reviewed 6 monthly. Common side effects include an increase in vaginal discharge and cervical smear changes. Traffic lighted as GREEN.

Section 1.5.10 suggests considering oral Ospemifene 60mg if local treatments are impractical e.g. due to a disability – Currently traffic lighted AMBER for specialist initiation only-Seek advice from menopause clinic.

Formulary Product Choices

- If the formulary products are unavailable, please choose the most cost-effective alternative and prescribe on an acute prescription while formulary products are unavailable and switch back when supply problems are resolved. This document is a helpful reference guide to dose equivalence between different products. https://thebms.org.uk/wp-content/uploads/2024/02/15-BMS-TfC-HRT-preparations-and-equivalent-alternatives-JAN2024-B.pdf

- **Doses prescribed should be within the licensed doses as per BNF.**

Oestrogen products

Oestrogen only		Brand	Dose	Considerations
Topical	**Patch**	Evorel ®	25, 50, 75, 100 microgram patches	Change patch twice weekly apply to abdomen/buttocks
Alternative	**Patch**	Oestradot®	25, 37.5, 50, 75, 100 microgram patches	Smaller, sticker than Evorel® change twice weekly apply to abdomen/buttocks
	Gel	Oestrogel® 0.06%	2-4 pumps daily	Needs to dry for 5 minutes before dressing apply to thigh or arms (1/2 dose each side)
Alternative	**Gel**	Sandrena®	500micrograms/0.5g 1mg/1g 1 sachet	Needs to dry for 5 minutes before dressing apply to thighs or arms (1/2 dose each side) Usual dose 0.5-1.5mg daily
	Spray	Lenzetto® 1.53mg/dose	1-3 squirts daily	Quick drying
Oral		Ellest solo®	1mg, 2mg tablets	2nd line unless patient choice/issues with absorption

Progesterone options for sequential/continuous regimes in women with a uterus

NEW for 2024: See further guidance on progesterone dosing for low/moderate/high dose oestrogen regimes- Appendix 1.

Key: Prescribed estrogen dose for ultra-low, low, standard, moderate and high dose regimens

	Ultra-low dose	Low Dose	Standard dose	Moderate dose	High dose
Oestrogel	½ pump	1 pump	2 pumps	3 pumps	4 pumps
Sandrena	0.25 mg	0.5 mg	1 mg	1.5-2 mg	3 mg*
Lenzetto spray	1 spray	2 sprays	3 sprays	4-5 sprays*	6 sprays*
Patch	12.5 µg	25 µg	50 µg	75 µg	100 µg
Oral estradiol	0.5 mg	1 mg	2 mg	3 mg^	4 mg^

* Off-license use
mg = milligrams
^ Off-license use – rarely required to achieve symptom control
µg = micrograms

https://thebms.org.uk/wp-content/uploads/2024/12/01-BMS-GUIDELINE-Management-of-unscheduled-bleeding-HRT-NOVEMBER2024-A.pdf

Progesterone products

Progesterone	Sequential	Combined	Information
52mg IUS – Mirena is licensed, other 52mg IUS can be used off license but in BMS guidelines.	For 5 years	For 5 years	Licensed for 4 years but BMS guidelines recommend use for 5 years. Also, can be used for contraception.
Micronised progesterone **Micronised progesterone on higher dose oestrogen regimes**	200mg (2x100mg) tablets to be taken orally for 12-14 days of the cycle WITH oestrogen of choice 300mg (3x100mg) tablets taken for 12-14 days	100mg to be taken each night* 200mg (2*100mg)	*BNF suggests day 1-25 so off label dosage but accepted by BMS guidelines The BMS defines "high dose oestrogen" as 100mic patch/4 pumps Oestrogel/3mg Sandrena/6 sprays Lenzetto/4mg oral oestradiol.

Combination products:

	Sequential regime	Dose	Combined regime	Dose	Information
Transdermal	Evorel ®Sequi (Two separate patch types)	Estradiol 50mics/24 hours +Norethisterone 170mics/24 hours 2 weeks Estradiol 50mics/24 hours alone 2 weeks	Evorel Conti®	Estradiol 50mics/24 hours +Norethisterone 170mics/24 hours	Change patches TWICE weekly
Alternative choice	Fem7 Sequi® (Two separate patch types)	2 weeks 50micrograms estradiol/7mics Levonorgestrel. 2 weeks 50micrograms estradiol alone	Fem7 Conti®	50micrograms estradiol/7mics Levonorgestrel	Apply below the waist change patches ONCE weekly
Oral therapy	Ellest duet® (Two separate tablets)	1mg or 2mg estradiol 1mg Norethisterone	Ellest duet Conti®	2mg Estradiol 1mg Norethisterone	
Alternative	Femoston® (Two separate tablets)	1mg or 2mg estradiol 10mg Dydrogesterone	Femoston conti®	Estradiol 0.5mg/Dydrogesterone 2.5mg or Estradiol2mg/Dydrogesterone 5mg	

Testosterone therapy

- There are currently no licensed products for testosterone replacement in women in the UK. Available preparations that may be used (out of licence/ 'off label') include: Testogel® gel sachet 40.5mg/2.5mg and Testim® gel tube 50mg/5g.
- Please refer to the Sheffield guidelines that can be found here: https://medicinesmanagement.doncasterccg.nhs.uk/wp-content/uploads/2022/02/SCP_testosterone_HRT_women.pdf
- Testosterone gel is Amber for women if referred to a specialist
- But can be initiated in primary care (Green) if a GP has a specialist interest, training and confidence in HRT/testosterone prescribing.

References

1. **NICE NG23 – Menopause: diagnosis & management . [Online] November, 2015 updated November 2024. https://www.nice.org.uk/guidance/ng23.**

2. society, British Menopause. Tools for clinicians. [Online] https://thebms.org.uk/publications/tools-for-clinicians.

3. *Hormone replacement therapy in women with history of thrombosis or a thrombophilia.* Morris G, Talaulikar V. 2023, Post Reproductive Health, pp. 29(1):33-4.

4. *Progestogens and endometrial protection.* BMS. 2022.

5. Hormone replacement therapy (HRT): further information on the known increased risk of breast cancer with HRT and its persistence after stopping. *MRHA Drug Safety Update.* [Online] August 2019.

6. MRHA. Safety information drug safety update. [Online] http://www.mhra.gov.uk/Safetyinformation/DrugSafety Update/CON079163.

7. FSRH Guidance: Contraception for women aged over 40 years. [Online] 2017 . https://www.fsrh.org/documents/fsrh-guidance-contraception-for-women-aged-over-40-years-2017/.