NHS South Yorkshire Integrated Care Board Doncaster Place

NHS Nottingham and Nottinghamshire Bassetlaw Place-Based Partnership

Hormone replacement therapy: A prescribing guide

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 and the BMS website.

https://thebms.org.uk/publications/tools-for-clinicians/

https://www.nice.org.uk/guidance/ng23

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. If possible "stopping and starting" HRT should be avoided, as this theoretically can contribute to destabilisation of cardiovascular plaques.
- It is advisable to use the lowest dose of oestradiol 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.
- At present due to ongoing supply issues prescriptions for HRT should be issued on a 3 monthly basis. A single annual pre-payment certificate for HRT is due to be introduced in April 2023.
- The British Menopause Society has issued an update on HRT supply to provide guidance to BMS members and clinical practitioners on the current availability of HRT products. https://thebms.org.uk/news/british-menopause-society-update-on-hrt-supply/

Benefits and Risks

- The risk of VTE is increased by oral HRT. The risk associated with transdermal HRT given standard therapeutic doses (<50 microgram patch) is no greater than baseline population risk. 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 <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)
- 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.

- 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 an increase in the risk of breast cancer. Any increase in the risk of breast cancer is related to treatment duration and reduces after stopping HRT. HRT taken for less than 5 years does not significantly increase the risk of breast cancer, but 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. (MRHA 2019)
- The risk of fragility fracture is decreased while taking HRT and this benefit is maintained during treatment but decreases once treatment stops.

Transdermal vs Oral preparations

The following should be considered:

- Patient preference for body identical products (e.g., estradiol and micronised progesterone)
- Contraceptive requirements – Until age 55
- 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

- **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.**

Continuous vs Sequential therapy

- Continuous combined preparations are not suitable for use in the perimenopause or within 12 months of the last menstrual period as this increases the 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. In women who are more than a year post-last period or have used a cyclical preparation for 2 to 3 years this can be transferred to a continuous regime using micronised progesterone 100 mg daily, which should keep women amenorrhoeic.

- If a patient has had a total hysterectomy, they are suitable for Oestrogen only therapy. However, 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.

A note on Bijuve®

Bijuve® is a new oral product to the market containing 1mg of Estradiol and 100mg micronised progesterone. It is a continuous combined therapy suitable for post-menopausal women. It is included in the Sheffield formulary but "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.

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An approach to HRT prescribing

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 2-3 years or more

More than 12 months since last period?**

YES

NO

Prescribe a sequential regime

Choice of oestrogen AND Mirena® Coil (5 year license)
OR
Choice of oestrogen AND Utrogestan® (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)

Prescribe a continuous regime

Choice of oestrogen AND Mirena® coil (5-year license)
OR
Choice of oestrogen AND Utrogestan® 100mg to be taken at night
OR
Evorel Conti® Patches to be changed twice weekly

Patient accepts topical oestrogen***?

YES

NO

Topical oestrogen

Patch -Evorel® 25-50 micrograms or Oestradot ®25, 37.5 or 50 micrograms
OR
Gel -Oestrogel® 2 pumps or Sandrena® 1 sachet daily (half each arm)
OR
Spray-Lenzetto® 1 spray daily

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: Estriol (Ovestin® 0.1%) 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®.

Note – Estradiol 0.06% transdermal gel (Oestrogel Pump Pack®) is licenced only for transdermal hormone replacement therapy for oestrogen deficiency symptoms in postmenopausal women. It is not to be used locally for vaginal atrophy.

Formulary 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.

Oestrogen only

Oestrogen only		Brand	Dose	Considerations
Topical	**Patch**	Evorel ®	25, 50, 75, 100 microgram patches	Change patch twice weekly apply to abdomen/buttocks
		Estradot®	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)
		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

Progesterone	**Sequential**	**Combined**	**Information**
Mirena® coil	For 5 years	For 5 years	Licensed for 4 years but BMS guidelines can be used for 5 years. Also, can be used for contraception.
Micronised progesterone	200mg (2x100mg) tablets to be taken orally for 14 days of the cycle WITH oestrogen of choice	100mg to be taken each night*	*BNF suggests day 1-25 so off label dosage but accepted by BMS guidelines
Medroxyprogesterone Climanor®	10mg day 14-28 WITH oestrogen of choice	2.5mg daily (with 1mg PO or 25mic patch of oestrogen) or 5mg daily with 2mg PO or 50mic patch	

Patient prefers combined therapy:

	Sequential regime	**Dose**	**Combined regime**	**Dose**	**Information**
Transdermal	Evorel ®Sequi (Two separate patches)	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 patches)	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 choice	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.

- Testosterone replacement in woman is traffic lighted as Amber- shared care

- Please refer to the Sheffield's shared care protocol that can be found here: https://medicinesmanagement.doncasterccg.nhs.uk/wp-content/uploads/2022/02/SCP_testosterone_HRT_women.pdf

Sources of further information for Healthcare Professionals

1.NICE NG23 – Menopause: diagnosis & management https://www.nice.org.uk/guidance/ng23 Nov 2015, updated Dec 2019 (under review – due August 2023)
2.Women's Health Concern – Factsheets for patients https://www.womens-health-concern.org/help-and-advice/factsheets/menopause/
3.NICE CKS clinical topic: Menopause http://cks.nice.org.uk/menopause
4.MHRA Drug Safety Update Hormone replacement therapy (HRT): further information on the known increased risk of breast cancer with HRT and its persistence after stopping. (Aug 2019) https://www.gov.uk/drug-safety-update/hormone-replacement-therapy-hrt-further-information-on-the-known-increased-risk-of-breast-cancer-with-hrt-and-its-persistence-after-stopping http://www.mhra.gov.uk/Safetyinformation/DrugSafety Update/CON079163
5.British Menopause society – tools for clinicians https://thebms.org.uk/publications/tools-for-clinicians
6.FSRH Guidance: https://www.fsrh.org/documents/fsrh-guidance-contraception-for-women-aged-over-40-years-2017/