

SEL Gynaecology Network: Primary Care Guidelines

10.10.23

Due for review date: TBC

Table of Contents

1	Menopause Guidelines
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DRAFT

Introduction

Purpose:

- Greater consistency over the workup of patients referred to secondary care
- To reduce the disparity of care for women living in South East London
- To provide education and information on the options that can be tried in primary care, while patients wait for appointments in secondary care
- Assurance that secondary care does not return referrals to primary care which might be above a GP's ability to confidently manage
- Receipt of the best possible care as quickly as possible for patients being referred

Background:

The guidelines provided set out the commonly accepted pathways for management and referral that are based on existing pathways within South East London (SEL).

This guide has been produced utilising published guidance and in collaboration with clinical and non-clinical staff across the Acute Provider Network, South East London Integrated Care Board, South East London Primary Care representatives and the South East London Integrated Care Board Medicines Optimisation Teams.

It is intended to be a guide to assist Primary care colleagues in decision making and does not replace clinical judgement .

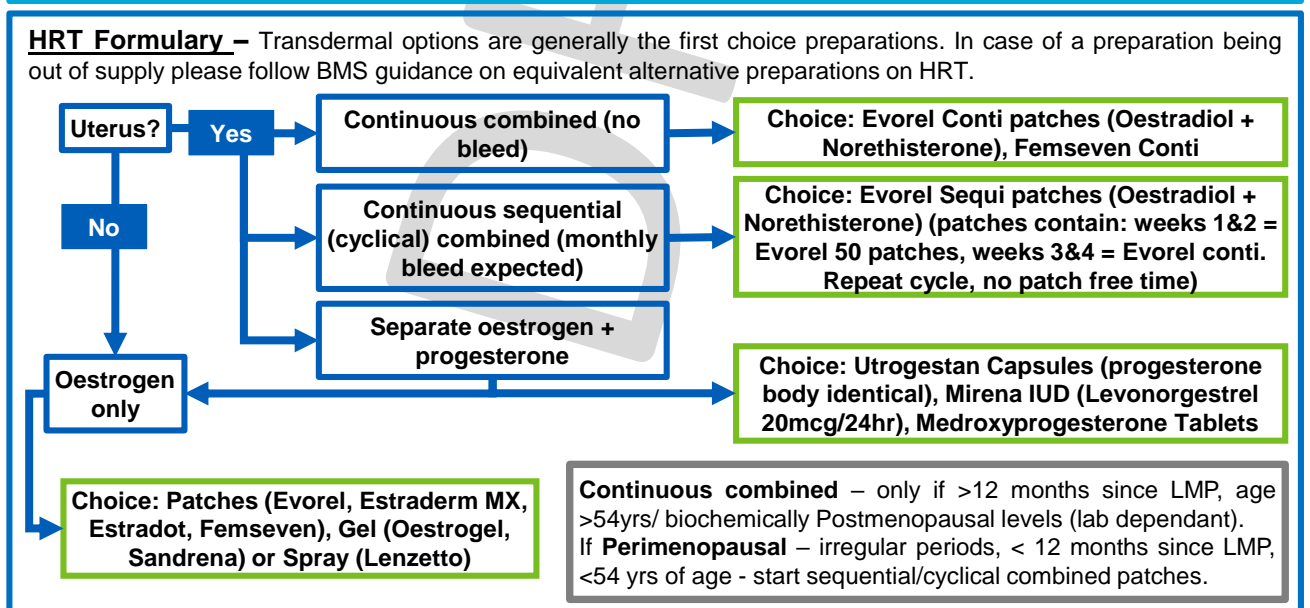
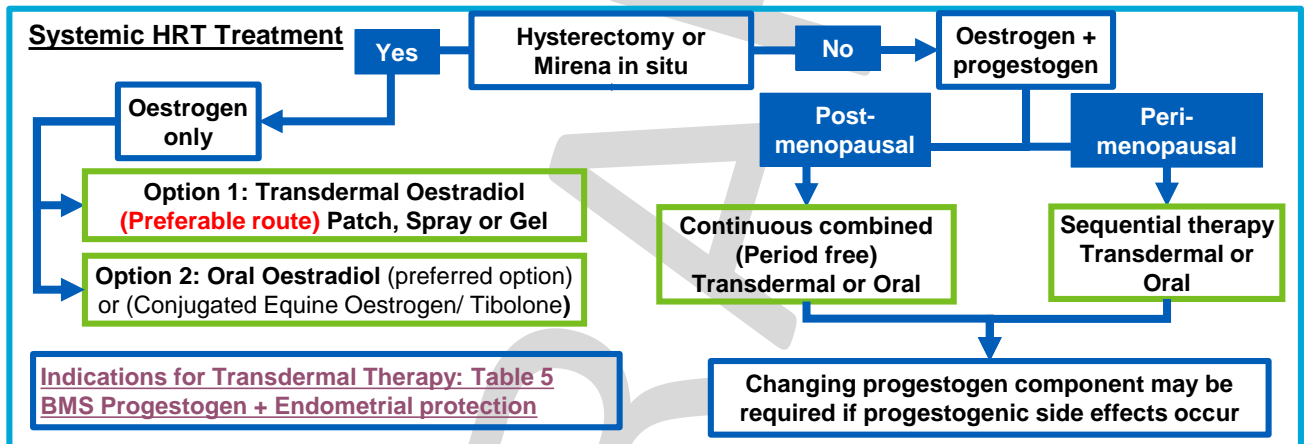
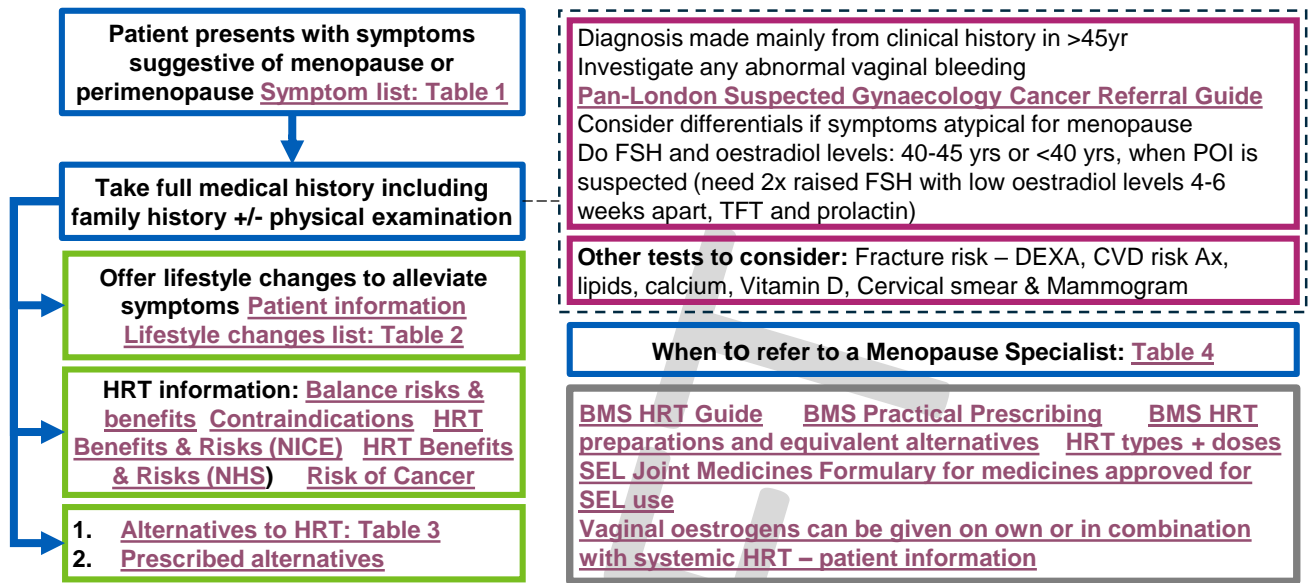
Please refer to the appropriate guidelines which have been hyperlinked into this documents of any drug considered. The guidelines give all available medication options supported by links to the applicable guidelines but should not be interpreted as a prescriptive list; rather, these must be prescribed based on the local formulary.

We encourage users of this document to seek advice from primary or secondary care colleagues when they are unsure, the later using established communication channels such as Advice and Guidance.

Shortages of medicines are becoming a frequent issue that hinders patients getting access to their medicines in a timely manner.

Please note, when medicines used in the management of menopause are subject to shortages, clinicians may recommend an alternative which is not on the SEL JMF. Please see the medicines supply tool, which can be accessed from the SPS website. The tool provides up to date information on medication shortages, and also includes advice on the prescribing of alternative products.

Guidelines for HRT in Menopause



Guidelines for HRT in Menopause

Preparations for atrophic vaginitis and other genitourinary syndrome of menopause (GSM):

1. Vaginal lubricants 2. Vaginal moisturisers: water based & oil based. 3. Vaginal oestrogens: creams, pessaries or ring (not suitable for women on aromatase inhibitors).

Other medication which can be prescribed after specialist input: Ospemifene, DHEA pessary (Prasterone) - [SEL IMOC Formulary recommendation](#).

Avoid vaginal oestrogens with history of hormone dependent cancers. Seek specialist advice in such patients.

Vaginal oestrogens can be-

- Prescribed with or without systemic oestrogen
- Used long term (no known increased cancer or VTE risks)
- Prescribed without progesterone - minimal systemic absorption
- Inserted (pessary) or applied topically to vulva

Prescribe daily for first two weeks, reduce gradually to maintenance of twice weekly. Maximum benefit usually around 1-3 months. Approximately 1 year supply of topical vaginal therapy is equivalent to one tablet of oral HRT.

If using condoms or diaphragm for contraception – advise to use tablet or vaginal ring as creams can damage condoms and diaphragms. [HRT & Contraception: Table 6](#)

Preparations-

- Blissel® Gel- (50mcg/g) 50 mcg/ 1g applicator dose- Not on formulary
- Oestradiol 10mcg vaginal Tablets.
- Gynest® cream- (Oestriol 100mcg/g Cream) 500mcg/ 5ml applicator dose
- Ovestin® Cream-(Oestriol 1000mcg/g)-500mcg/0.5g applicator dose
- Invaggis® Pessaries-(Oestriol 30mcg) 30mcg per pessary dose
- Estring® Vaginal ring- (Oestradiol 2mg) 7.5mcg/24 hours- Replace every 3 months
- Intrarosa® DHEA Pessary 6.5mg daily and only to be used after failure of vaginal oestrogen

HRT for specific clinical conditions

HRT + previous Endometrial ablation: Combined HRT regimen (either sequential or continuous regimen) should be used to reduce the risk of endometrial hyperplasia in any residual endometrial tissue.

Subtotal hysterectomy + HRT: E+P sequential for 3 months, if no bleeding then E only continuous, if bleeding need E+P

HRT + Premature Ovarian Insufficiency: Where there is a loss of ovarian activity under the age of 40 years either spontaneously or iatrogenic:

- Offer HRT or combined hormonal contraceptive to patient, unless contraindicated.
- Continue HRT until natural age of menopause (average 51 years). Reassess need for ongoing therapy after that.
- Assess fragility risk (DEXA scan/FRAX scoring).

HRT + Endometriosis: Hysterectomy for endometriosis may need progestogens despite removal of uterus to avoid reactivation of microdeposits of endometriosis elsewhere which can cause pain. This needs discussion regarding risks of oestrogen only (reactivation of microdeposits of endometriosis elsewhere causing pain) vs risk of adding in progestogen (increases risk of breast cancer). Seek advice from menopause specialist if unsure. [BMS article](#)

HRT + Migraine: Migraine with aura is not a contraindication for HRT but use non-oral body identical oestrogen like gel or patch at the lowest possible dose. Mirena IUD preferable option for progestogens as less hormone fluctuation [BMS article](#)

HRT + Breast Cancer: In women with a history of breast cancer offer non-hormonal alternative therapies first. Refer to menopause specialist if poor symptom control [BMS article](#) [Risks & Benefits of HRT with Breast Cancer](#)

Testosterone replacement:

Transdermal therapy may be useful for women with **low sexual drive** when maximum effective dose of HRT has not helped with low libido symptoms. In SEL this medication has been approved for formulary use as AMBER 2. If clinically appropriate referral can be made to menopause clinic for assessment and initiation. However, this can be initiated in primary care by specialist GPs or any primary care clinician if they feel confident in initiating this. In this case, please use A&G (baseline testosterone levels need to be done prior to referral or advice and guidance). There are many issues affecting libido, ensure to rule out other causes that affect libido.

Testosterone implants and patches have now been withdrawn. Testosterone gels are now commonly used in women who require androgen replacement due to the lack of available alternatives. In UK, these products are licensed only for use in men and their use in women is an out of licence use for the product. The preparations currently available are: *Option 1* - Testogel (40.5 mg/2.5mg) sachet used over 8 days. *Option 2* - Testim gel 1% in 5ml tubes- one tube used over 10 days. *Option 3* - Tostran 2-3 measures a week (each application 10 mg testosterone).

Monitoring: (advise patient not to have a blood test shortly after using testosterone gel)

- Total testosterone (and FAI) at baseline to ensure baseline levels not above the normal reference range.
- Re-assess 2-3 months after starting: to ensure levels remain within reference range. Continue if improvement in symptoms. It can take 4-6months to evaluate the full efficacy of the treatment.
- Yearly review in primary care to ensure risk/benefit and to check total testosterone (and FAI) and side effects (unwanted hair, frontal baldness, deepening of voice).

[Testosterone replacement in menopause](#) [BMS Testosterone explained](#) [BMS statement on testosterone](#)
[Testosterone for women factsheet](#) [BMS Update on HRT Supplier Availability](#)

[Topical testosterone risk of harm to children following accidental exposure.](#)

Guidelines for HRT in Menopause

Management of side effects

Suspected problem	Advice
Compliance	Allow 3-6 months on treatment for full effect & counsel on importance of compliance.
Oestrogen dose	Review correct application before increasing dose. Increase dose or change administration route if the patients has an incomplete symptom response. Blood test to check oestrogen levels may also be considered.
Poor patch adhesion / skin irritation	Ensure that patient is rotating application site. Switch to alternative brand or oestrogen gel for poor patch adhesion.
Incorrect diagnosis	Review indications (e.g. thyroid disease)/ refer
Poor absorption	Consider change to route of administration
Unlikely expectations	Counsel patient
Drug interactions	Enzyme inducers (e.g. phenytoin) lower the circulating hormone levels -change to non-oral routes. Mirena IUD are not affected.

Oestrogen-related adverse events (may occur continuously or randomly throughout cycle)

Side effects	Management
Breast tenderness or enlargement	<ul style="list-style-type: none"> • Evening primrose oil or starflower oil purchased OTC • Wearing a well fitted bra or sports bra • Topical or oral Non-steroidal anti-inflammatory if not contra-indicated • Can be alleviated by a low-fat, high carbohydrate diet • Reduce the dose of oestrogen
Nausea, bloating, or dyspepsia	<ul style="list-style-type: none"> • May be helped by adjusting timing of oestrogen dose or taking with food • Change the route of administration to a non-enteral formulation.
Headaches or migraines	<ul style="list-style-type: none"> • Can be triggered by fluctuating oestrogen levels – try switching to a transdermal route as this produces more stable oestrogen levels.
Angioedema	<ul style="list-style-type: none"> • Oestrogens can cause or exacerbate angioedema symptoms. Especially for patients with hereditary angioedema. Consider menopause expert referral.

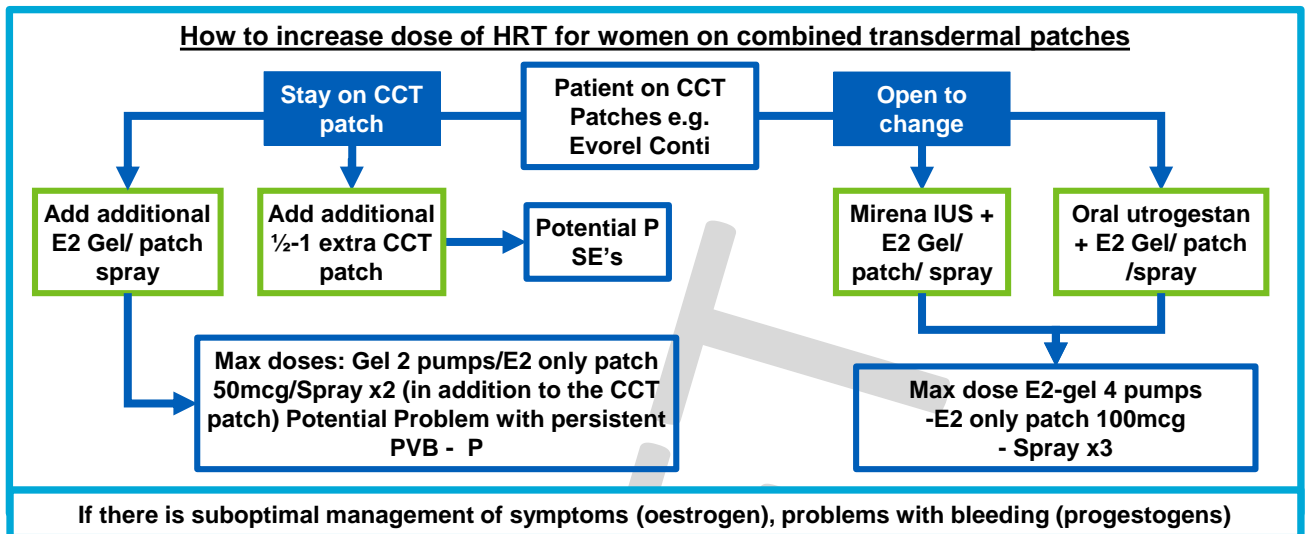
Progestogen adverse events (may occur in cyclical pattern during cyclical HRT's progestogen phase)

Side effects	Management
Fluid retention Breast tenderness Lower abdominal pain Back pain Headaches or migraines Mood swings Depression Acne	<ul style="list-style-type: none"> • Type: Change progestogen type (e.g. from more androgenic nortisterone to Utrogestan) • Route: Change route of progestogen delivery (e.g. from oral to transdermal, vaginal, or Mirena IUD). May benefit women experiencing nausea/bloating or dyspepsia with oral preparations. 100mg vaginal progesterone tablets (Lutigest) or 200mg vaginal pessaries (utrogestan or cyclogest) or utrogestan oral tablets can be used off-license vaginally in same dosage regimen. • Regimen: Reduce the progestogen admin regimen. Progestogens can be taken for 10-14 days of each monthly sequential regimen, so swapping from 14 to 10 days product may have benefit • Product: changing to a product with lower dose of progestogen • Frequency: reduce progestogen dosing frequency by either switching to a long term regimen of administering progestogen for 14 days every 3 months (only suitable for women without natural regular periods) or continuous progestogen- provides better long-term protection than cyclical. • Changing to continuous combined therapy often reduces progestogenic adverse effects with established use. Only suitable for postmenopausal women.

When to stop HRT: Stop HRT when risks outweigh benefits and patient agrees to stop. Consider gradual withdrawal of HRT to limit a recurrence of symptoms (depend on clinical judgement, pending investigation). Consider stopping HRT temporarily if the following occur:

- Sudden breathlessness or cough with blood-stained sputum
- Hepatitis, jaundice, or liver enlargement
- Sudden severe chest pain (even if not radiating to left arm) or unexplained swelling/severe pain in calf of 1 leg
- Blood pressure above systolic 160mmHg or diastolic 95mmHg
- New contraindication to treatment e.g a recent diagnosis of hormone dependent cancer.
- Serious neurological effects, including unusually severe, prolonged headache, especially: If it is the first time, or getting progressively worse, There is sudden partial or complete loss of vision, Sudden disturbance of hearing or other perceptual disorders, Dysphasia, Vasovagal episode or collapse, First unexplained epileptic seizure, Weakness, motor disturbances, or very marked numbness suddenly affecting one side/part of body
- Prolonged immobility after surgery or leg injury – if on oral HRT- switch to transdermal preparation.

Guidelines for HRT in Menopause



Unscheduled Bleeding on HRT

- Common in the first 3 months and will usually settle. Counsel women about bleeding issues which can happen in the first few months of HRT initiation during first consultation to manage expectations.
- Exclude 2ww criteria ([refer to local guidelines](#)). For a significant majority of patients bleeding on HRT does not need 2 week wait referral. Patient can continue using the HRT.
- [Pan-London Suspected Gynaecology Cancer Referral Guide](#)
- If continues beyond 3 months consider alteration of progestogen dose or type (see below section).
- Rule out other causes-Check smear history, Vaginal examination, STI screen, Exclude local vaginal causes.
- Detailed history-Type of HRT sequential or continuous combined, Is she on the correct type, Severity and extent of bleeding, Compliance with medication.
- Continued bleeding after 6 months -assess endometrium with scan +/- refer for endometrial sampling/hysteroscopy, exclude 2WW criteria. Consider further adjusting the progestogen at this stage.

HRT Continuous combined

- Increase dose of progestogen
- Consider adding Utrogestan 100mg PO to regime (off license)
- If using micronized progesterone increase to 200mg daily (off license), if using Medroxyprogesterone acetate increase from 5-10mg PO daily
- Change type of progestogen
- Change the progestogen component to an alternative oral preparation or to a Levonorgestrel 52mcg IUD
- Change to a preparation with a different progestogen component
- Add Desogestrel 75mcg PO to regime (off license)
- Change to a sequential preparation for a further 12 months

HRT Sequential

- Increase dose of Progestogen- if using Utrogestan increase to 300mg po (off license)
- If using Medroxyprogesterone acetate increase to 20mg po 12-14 days per cycle (off license)
- Increase duration of cyclical progestogen to 14 or 21/7 of a 28/7 HRT cyclical preparation
- Change to a preparation with an alternative progestogen including consideration of 52mcg Levonorgestrel IUD

Progestogens in HRT regimes and doses

- Utrogestan 200mg orally 14 days per cycle (2 weeks on, 2 weeks off) for sequential, 100mg PO daily for continuous combined
- Dydrogesterone 10mg PO for 14 days per cycle, 5mg daily -continuous combined
- Medroxyprogesterone acetate 10mg for 14 days per cycle, 5mg daily- continuous combined (In SEL formulary as medroxyprogesterone - not Provera which is branded preparation)
- Northisterone 5mg PO for 14 days per cycle (*dose different to BNF), 0.5-1mg PO daily
- Levonorgestrel IUD -Mirena has a license for 4 years but can be used for 5yrs off license

Guidelines for HRT in Menopause

Table 1: Symptoms of the menopause (women may experience 1 or more symptoms)

Vasomotor	Psychological	Urinary/vaginal	Others
Hot flushes	Nervousness	Vaginal infections	Skin itching/crawling sensation
Night sweats	Anxiety/panic attacks	Painful sex	Change in bleeding pattern
Sweating	Anger/irritability	Post coital bleeding	Joint pains
Shivering	Confusion	Irritation/itching	Weigh gain
Increased pulse	Depression	Decreased libido	Headaches
Feeling faint	Forgetfulness	Dysuria	Tiredness
Weakness	Difficulty concentrating	Atrophic vagina	
Vertigo	Energy fatigue/loss	Urinary frequency	
Nausea	Low self esteem	Urinary urgency	
Insomnia	Memory deterioration	Post micturition bleeding	
Palpitations	Psychosexual dysfunction	Urge/ Stress incontinence	
	Decreased libido		
	Poor sleep		
	Tearfulness		

Table 2: Lifestyle recommendations to alleviate symptoms

Symptom	Lifestyle Modification
Hot flushes + night sweats	Regular exercise, healthy BMI, wearing lighter clothing, sleeping in a cooler room with silk pillows, using a fan, reducing stress & avoiding possible triggers (e.g. smoking, caffeine, spicy foods, alcohols)
Sleep disturbances	Avoiding exercise late in the day, maintain regular bedtime, mindfulness and sleep apps. NHS recommended wellbeing apps (headspace , calm , Sleepio .)
Mood + anxiety disturbances	Adequate sleep, regular physical activity and relaxation exercises, mindfulness
Cognitive symptoms	Exercise and good sleep hygiene Self Care Forum leaflet

Table 3 - Alternatives to HRT

Can be helpful in women who do not want to/cannot take hormonal medication. However, there is limited research available for these products and the research that does exist is related to short term symptoms. None of these can be prescribed (**BOUGHT OTC - DO NOT PRESCRIBE**), can be expensive and generally have no impact on CVD or osteoporosis prevention or managing vaginal issues.

Phyto-oestrogens like soy and red clover contain plant like oestrogen that may be beneficial in reducing short term symptoms

- Black cohosh can improve vasomotor menopausal symptoms but can have side effects such as liver toxicity and interactions with tamoxifen- **not recommended for women with history of hormone dependent cancers**
- Acupuncture - women should be advised that no scientific evidence exists that this works any better than a placebo, but that all placebos work to some degree or other. They should be advised to find a registered practitioner
- CBT for hot flushes and night sweats- [patient advice](#)

PRESCRIBABLE ALTERNATIVES TO HRT – [bms advice](#)

Table 4: When to refer to Menopause Specialist or seek advice and guidance

- Complex medical history (e.g endometriosis)
- Carriers of faulty genes such as BRCA1/2 or Lynch, known to increase risk of cancer
- Current, past or suspected hormone dependent cancers.
- Ineffectiveness or persistent side effects despite following treatment pathway.
- Recurrent bleeding which has been fully investigated, no abnormality detected but not resolved.
- Low libido not improving on maximum effective dose of oestrogen – specialist advice for considering testosterone therapy.
- Women with suspected POI -baseline tests required prior to referral for POI: Pelvic ultrasound, DEXA, FSH/LH and Oestradiol levels x2 (raised FSH>30, oestradiol<92) done 4-6 weeks apart, TFT and prolactin.

Table 5: Indication for transdermal HRT

Preferred route in most patients as it avoids first pass metabolism and have no impact on the clotting cascade and can be especially useful if there are other risk factors. It should be the only route to be considered in these patients- *Individual preference, *Poor symptom control with oral HRT, *GI disorders affecting oral absorption, *Previous or family history of VTE, *BMI>30, *Variable blood pressure control, *Migraine, *Current use of hepatic inducing enzyme medication, *Gall bladder or liver disease

Table 6: HRT and Contraception

A woman is potentially considered to be fertile for 2 years after her last menstrual period if <50 years of age, and for 1 year if >50 years of age. In patients requiring contraception and free of all contraindications consider offering the following HRT/contraceptive options: *Oestrogen only pill, patch or gel and Mirena® coil (other IUDs are not licensed for endometrial protection) • Combined hormonal contraception (if eligible but only up until age 50) • Sequential combined HRT (pill or patch) and progestogen-only contraception (tablet, implant, injection) • If hormonal contraception is declined: advise barrier methods with sequential combined HRT.

When to stop contraception:

- >50 years - 1 year after LMP
- < 50 years- 2 years after LMP
- 45- 55 years - Mirena® inserted after 45 years can stay in till age 55 for contraception but only for 5years if used as part of HRT also (unlicensed use for 5years for HRT)
- Stop hormonal contraception at 55 years of age.
- Do not check FSH or oestradiol if on HRT / combined hormonal contraception
- If >50 years with amenorrhea due to progestogen only method- check FSH: if FSH level >30 IU/L stop after 1 year.

Abbreviations

Abbreviation	Definition
2WW	2 Week Wait Pathway
A&G	Advice and Guidance
Ax	Assessment
BMI	Body Mass Indicator
BMS	British Menopause Society
BRCA 1	Breast Cancer gene 1
BRCA 2	Breast Cancer gene 2
BSO	Bilateral Salpingo-Oophorectomy.
CBT	Cognitive Behaviour Therapy
CCT	Continuous Combined Therapy
CVD	Cardiovascular disease
DEXA	Dual energy x-ray absorptiometry
DHEA	Dehydroepiandrosterone sulphate
E2 Gel	Oestradiol Gel
E + P	Oestrogen and Progestogen
FAI	Free Androgen Index
FRAX	Fracture Risk Assessment Tool
FSH	Follicle-stimulating hormone
GI Disorder	Gastrointestinal Disorder
GSM	Genitourinary Syndrome of Menopause
HRT	Hormone Replacement Therapy
IUS/IUD	Intrauterine System/Device
LH	Luteinizing Hormone
LMP	Last Menstrual Period
OTC	Over the Counter
P + SEs	Progesterone and Side Effects
POI	Premature Ovarian Insufficiency
TAH	Total Abdominal Hysterectomy
TFT	Thyroid Function Test
VTE	Venous Thromboembolism