

Tyne and Wear Guidance - Management of the Menopause

DIAGNOSIS^{1,2}

The following can be diagnosed without laboratory tests in otherwise healthy women aged over 45 years with appropriate menopausal symptoms:

- Perimenopause - in woman with vasomotor/ non-vasomotor symptoms and changes in the menstrual cycle
- Menopause - in women who have had no period for at least 12 months and are not using hormonal contraception or with menopausal symptoms without a uterus. The average age for the menopause is 51.

Follicular Stimulating Hormone (FSH) to diagnose menopause should only be done in women^{2,3}:

- Age <40 years where premature ovarian insufficiency is suspected with elevated serum FSH levels (more than 30 IU/L) on two blood samples taken 4–6 weeks apart.
- Age 40-45 years with menopausal symptoms, including a change in their menstrual cycle
- Age >45 years exhibiting atypical symptoms (include anything other than classic menopausal symptoms)

Levels greater than 30 IU/L indicates a degree of ovarian insufficiency but not necessarily sterility. Isolated levels taken in the perimenopause can be misleading. Restrict the measurement of serum FSH to support advice about stopping hormonal contraception in women **over 50** who have no periods. FSH can be measured in those using all progestogen only methods. Normal practice is to continue contraception until age 55 years.³

Information and advice^{1,2}

Ensure patients (family or carers) are given information to include:

- Symptoms include irregular/cessation of periods, hot flushes, sweats, difficulty sleeping, aches and pains, vaginal dryness, mood changes/swings, anxiety, brain fog
- Explanation of the stages of the menopause
- Common symptoms and diagnosis
- Lifestyle changes and interventions to help general health and well being
- Benefits and risks of the treatments for menopausal symptoms (see page 4)
- Long term health implications of the menopause
- Useful information for patients look up 'menopause' on nhs.uk website

Address modifiable lifestyle factors to reduce menopausal symptoms^{2,4}:

- Normalise weight with healthy balanced diet
- Consume adequate vitamin D (10mcg or 400 IU/day) and calcium (700mg/day). Useful information on the Royal Osteoporosis Society website look up 'calcium'
- Undertaking regular weight bearing exercise
- Advise/support women in smoking cessation
- Reduce alcohol intake
- Ensure other long term conditions are managed appropriately
- Avoiding triggers for hot flushes if experiencing them (spicy foods, caffeine, alcohol etc.)
- Good sleep hygiene (Pzizz app, Sleepio app)
- Brain exercise (crosswords, sudoku), socializing, hobbies

Hormone Replacement Therapy (HRT)

Indications¹:

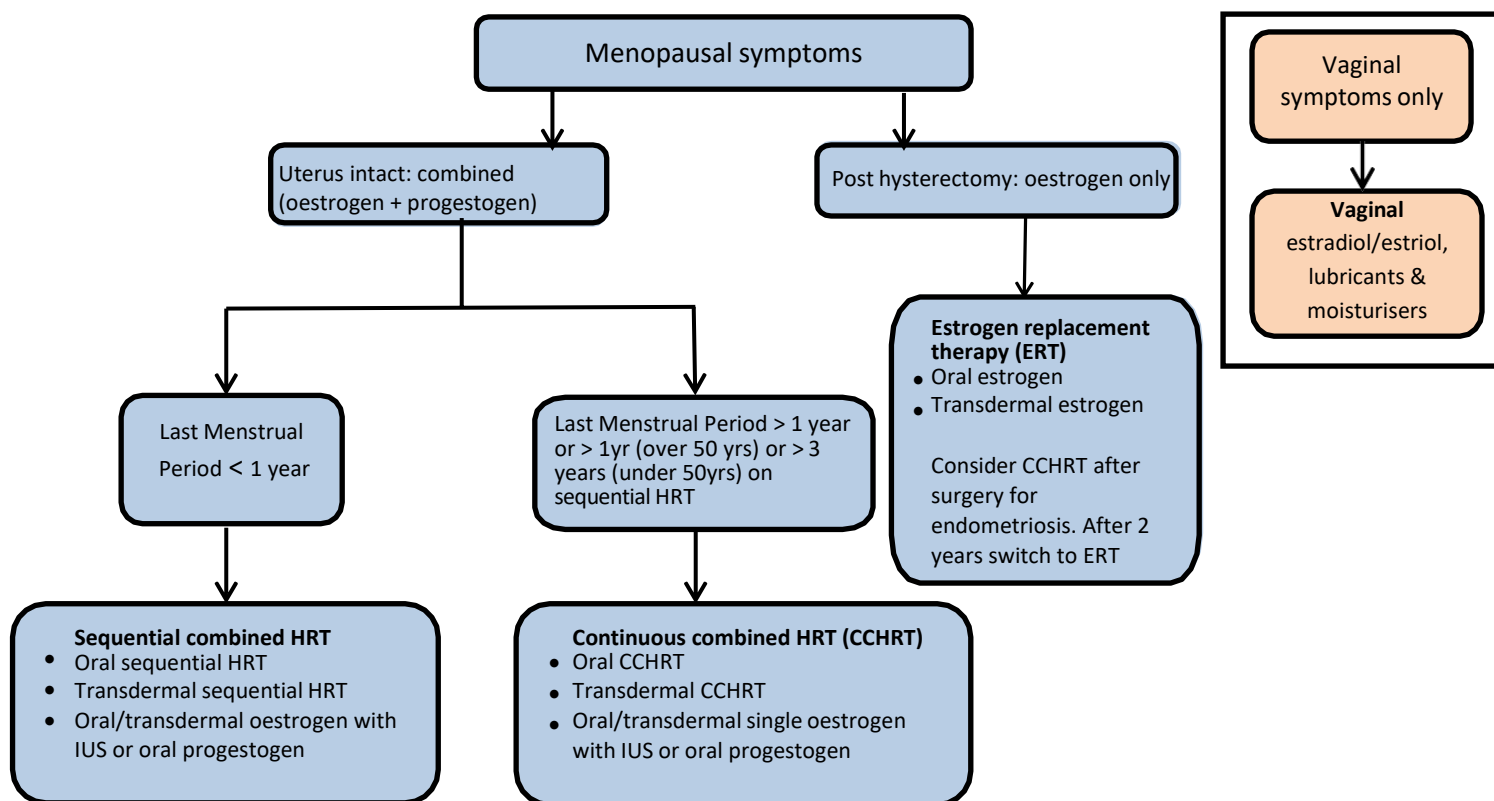
- Short term relief of hot flushes, night sweats
- Prevention of osteoporosis (long term)
- Premature ovarian insufficiency (including surgical menopause)
- Relief of other menopausal symptoms e.g. sleep disturbance, anxiety/depression, and sexual function.

Contraindications²:

- Pregnancy
- Undiagnosed abnormal vaginal bleeding
- Active thromboembolic disorder or acute myocardial infarction
- Suspected or active breast or endometrial cancer
- Active liver disease with severely abnormal LFTs
- Caution with porphyria

Flow chart for Hormone Replacement Therapy (HRT) prescribing^{1,2}

(Refer to table overleaf for formulary choices)



Prescribing considerations²

HRT is available as oral or transdermal depending on women's preferences

In women over 60 years, use lower HRT doses, either 0.5mg estradiol orally or transdermal estradiol +/- progestogen.

Consider transdermal HRT in women with:

- *BMI >30
- *poor control or side effects on oral HRT
- *uncontrolled hypertension
- *hypertriglyceridaemia
- *history of, or risk of venous thromboembolism (VTE), consider referring to specialist for advice
- *history of, or risk of cardiovascular disease, consider referring to specialist for advice
- *bowel disorder which may affect absorption of oral therapy
- * history of migraine (benefit from steady hormonal levels)
- *taking interacting drugs (hepatic enzyme inducers) e.g. anticonvulsants
- *lactose sensitivity
- *history of gallstones

When to refer²:

- Persistent side effects despite changing HRT
- Inadequate control of menopause symptoms despite changes in HRT
- Complex medical history
- In women with hormone dependent tumours who have troublesome menopause symptoms
- Premature ovarian insufficiency (see separate box)
- Bleeding problems (refer to Newcastle Approach to Gynaecology Problems in Primary Care <https://portal.gpteamnet.co.uk/Login?returnUrl=%2F>)
 - during sequential HRT – if irregular bleeding continues after first 6 months, if there is a change in bleeding pattern after 6 months including increased duration, frequency and/or heaviness, irregular bleeding and associated pain
 - during CCHRT or tibolone – if bleeding continues after first 6 months or if bleeding occurs after 6 months of no bleeding

Premature ovarian insufficiency (POI)²

In POI (menopause < 40 years old) it is important to start treatment with either HRT or a combined hormonal contraceptive (CHC). Treatment should continue until the age of natural menopause (unless contraindicated) to protect against increased risks of dementia, cognitive decline, cardiovascular disease and osteoporosis.

Counsel women that:

- HRT has no effect on blood pressure and beneficial effects on metabolic parameters, when compared with CHC but is NOT a contraceptive
- Both HRT and CHC offer bone protection.

Refer all women with POI under age 35.

Consider referring women >35 and <40 with POI to a specialist for help and support in the physical and psychosocial aspects of their diagnosis

HRT formulary

Clinicians can prescribe off formulary in the event of supply issues

	Type of HRT	Sequential combined HRT	Continuous combined HRT	Unopposed oestrogen (ERT)	Progestogen (See box below for features)
	Criteria for use	<ul style="list-style-type: none"> Intact uterus Perimenopausal – had at least one natural period in last year 	<ul style="list-style-type: none"> Intact uterus – had no period for 1 year Over 50 and >1 yr on sequential HRT or under 50 and > 3 years on sequential HRT 	<ul style="list-style-type: none"> Post hysterectomy 	<ul style="list-style-type: none"> As adjunct to transdermal oestrogen if not had a hysterectomy
ORAL TREATMENT OPTIONS	1 st line	Elleste Duet tablets 1mg or 2mg estradiol & 1mg norethisterone	Elleste Duet Conti 2mg estradiol & 1mg norethisterone	Elleste Solo 1mg or 2mg estradiol	Medroxyprogesterone acetate (Provera) 10mg Days 14-28 or 5mg daily
	2 nd line	Femoston 1/10 or 2/10 tablets 1mg or 2mg estradiol & 10mg dydrogesterone	Femoston Conti 0.5/2.5 = 0.5mg estradiol & 2.5mg dydrogesterone OR 1/5 = 1mg estradiol & 5mg dydrogesterone		Micronised Progesterone 100mg daily or 200mg days 14-28
	3 rd line		Tibolone 2.5mg tablets		Levonorgestrel IUS 52mg
TRANSDERMAL	1 st line	Evorel Sequi patches 50micrograms estradiol & 170micrograms norethisterone Change patch TWICE a week	Evorel conti patch 50micrograms estradiol & 170micrograms norethisterone Change patch TWICE a week	Evorel/Estradot patch 25, 50, 75, 100mcg estradiol Change patch TWICE a week	Testosterone supplementation <ul style="list-style-type: none"> Testogel sachet, 40.5mg/2.5g sachet, 1/8th sachet a day Testim 50mg/5g tube, 1/10th tube a day Tostran (2% testosterone gel in a canister containing 60g) starting dose 1 metered pump on alternate days
				Topical gels: option where skin irritation occurs with patch <ul style="list-style-type: none"> Oestrogel: 0.06% oestradiol gel, 1-4 measures (2.5g) oestradiol daily Lenzetto (1.53mg/spray), 1-3 sprays daily 	

Monitoring²

Started on HRT or HRT changed— review at 3 months
Established on HRT—review annually unless there are clinical indications for earlier review. At each review assess efficacy and side effects to assess ongoing risk/benefit balance.

Stopping HRT²

There is no arbitrary limit on HRT duration. In women with POI, HRT should be continued until normal menopause age. Withdraw HRT slowly to reduce risk of recurrent symptoms. If symptoms do recur then recommence treatment.

Urogenital atrophy²

Ovestin cream (0.1% estriol vaginal cream) OR Vagiflex (10 microgram vaginal tablet)

- Use every night for 14 nights then twice weekly.
- Start early before irreversible changes have occurred. Can be taken with systemic HRT.
- If symptoms not relieved consider dose increase, after seeking advice from specialist.
- Explain that symptoms may come back when treatment is stopped, adverse effects are rare.
- Moisturisers and lubricants (**OTC purchase**) can be used alone or in addition to vaginal oestrogen for vaginal dryness.
- Report any unscheduled bleeding promptly.

If preparation exists at lower dose reduce dose for 4 weeks then stop. If already on lowest dose or no lower strength exists then stop.

Progestogens (features)

Synthetics

	Progestogen	Features
C19	Norethisterone, Norgestrel, Levonorgestrel	Better cycle control, androgenic (may be good for libido). Unfavourable effect on lipids.
	Medroxyprogesterone acetate	Can be added to oral or transdermal oestrogen, mildly androgenic (may be good for libido). Unfavourable effect on lipids.
C21	Dydrogesterone	Non androgenic. Not available as single Preparation.
	Levonorgestrel (IUS) 52mg	Replace after 5 years as per FSRH guidance. Provides bleed-free option for perimenopause

Body identical

Micronised progesterone (Utrogestan)	Fewer progestogenic S/Es, no androgenic or glucocorticoid activity. No lipid effects. Less effective cycle control.
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Benefits and risks of HRT

Benefits of HRT ^{1,2}	
<ul style="list-style-type: none"> ➤ Reduction in vasomotor symptoms ➤ Improved sleep, joint pain & QOL ➤ Potential improvement in psychological symptoms e.g. depression & anxiety 	<ul style="list-style-type: none"> ➤ Relief of vaginal dryness ➤ Improved sexual function ➤ Improved bone mineral density, reduced fracture risk

Managing side effects ²	
Encourage women to persist with treatment for 3 months (as adverse effects may resolve)	
Oestrogen-related	Progestogen-related
Fluid retention, bloating, breast tenderness or enlargement, nausea, headaches, leg cramps, and dyspepsia. They may occur continuously or randomly throughout the cycle.	Fluid retention, breast tenderness, headaches or migraine, mood swings, depression (similar to PMS), acne. They tend to occur in a cyclical pattern during the progestogen phase of sequential HRT).
Management strategies	
<ul style="list-style-type: none"> ◦ Change route of delivery. ◦ Dose reduction. ◦ Leg cramps may improve with lifestyle changes e.g. exercise, stretching calf muscles. ◦ Nausea – switch to transdermal or adjust the timing of the oestrogen dose, or take with food. ◦ Breast tenderness may be alleviated by a low-fat diet. ◦ Migraine – switch to transdermal. 	<ul style="list-style-type: none"> ◦ Changing the progestogen type (see Progestogen features table). ◦ Change route of delivery. ◦ Dose reduction. ◦ Reducing the regimen of progestogen administration. Progestogens can be taken for 10–14 days of each monthly sequential regimen, so swapping from a 14-day to a 10-day product may provide benefit. ◦ Changing to a product with a lower dose of progestogen (doses are preparation dependent). ◦ Reducing the frequency of progestogen dosing. This can be achieved by switching to a long-cycle regimen of administering progestogen for 14 days every 3 months (but only in women <u>without natural regular periods</u>). ◦ Changing to continuous combined therapy or tibolone often reduces progestogenic adverse effects with established use. However, this option is only suitable for postmenopausal women.

Cardiovascular and cerebrovascular disease^{1,2} <ul style="list-style-type: none"> • HRT does not increase coronary heart disease (CHD) risk when started in women aged under 60 yrs old, and does not affect the risk of dying from cardiovascular disease. • CVD co-morbidities are not a contra-indication to HRT as long as they are optimally managed. • ERT is associated with no increased risk of CHD. • Transdermal combined HRT is associated with no increased risk of CHD. • Oral oestrogen is associated with small increase in risk of stroke. As the baseline risk of stroke in women under 60 yrs is very low, the increased risk is small (1 extra woman per 1000 using HRT). • In women with past history of CVA or TIA, discuss with local specialist.
Venous thromboembolism (VTE)² <ul style="list-style-type: none"> • Risk is increased 2-fold with oral HRT compared to baseline population risk. • No increased risk with transdermal HRT given at standard therapeutic doses (under 50mcg/24hr) compared to baseline population risk. • Consider transdermal rather than oral HRT in women with an increased risk of VTE, e.g. BMI over 30.
Type 2 diabetes² <ul style="list-style-type: none"> • There is no increased risk of developing type 2 diabetes with any type of HRT. • HRT is not associated with an adverse effect on blood glucose control in diabetics.
Osteoporosis² <ul style="list-style-type: none"> • Give women advice on bone health and discuss any risk factors for osteoporosis. • Risk of fragility fractures is decreased whilst taking HRT but increases once treatment is stopped, and the benefit varies depending on the length of HRT use.
Loss of muscle mass and strength² <ul style="list-style-type: none"> • Limited evidence suggests HRT improves muscle mass or strength, which normally decreases after the menopause. Muscle mass/strength is maintained through weight bearing exercise and where relevant smoking cessation and avoiding excessive alcohol intake should be advised.
Breast cancer^{1,2} <ul style="list-style-type: none"> • All types of ERT associated with a small increased risk of breast cancer (extra 3 per 1000 taking ERT for 5 years in 50s). • Combined HRT is associated with an increased risk of breast cancer (8 extra cases per 1000 taking HRT for 5 years in their 50s) and reduces back to background rate after 5 years. • In women who have had breast cancer, non-hormonal options should be discussed. Local vaginal oestrogen is an option in those taking tamoxifen if moisturisers/lubricants produce no relief.
Ovarian cancer^{1,2} <ul style="list-style-type: none"> • ERT or HRT has little effect on the incidence of ovarian cancer (1 extra case per 1000 taking HRT in their 50s).

Testosterone supplementation⁵

- Androgen deficiency symptoms include lethargy, loss of muscle mass and strength, loss of libido, lack of motivation, low wellbeing and lowered mood. More common in women with POI, over 60s and where both ovaries have been removed.
- Consider psychosexual counselling.
- Consider tibolone.
- Consider testosterone. Takes 10-12 weeks before benefit is felt.

Non-hormonal options²

- Limited evidence to support use of 'over the counter' remedies.
- Evidence suggests that the following may be helpful:
 - Clonidine slowly increased from 25mcg twice a day for 2 weeks to a maximum dose of 50mcg three times a day. Side effects include dizziness, dry mouth and constipation. Do not stop suddenly as this can cause rebound hypertension.
 - Venlafaxine 37.5mg slowly increased up to 150mg a day, Paroxetine 10mg or Citalopram 10mg-30mg a day, side effects include dry mouth, constipation, and nausea are more likely with higher doses.

Title	Menopause – Guidance on management and prescribing
Document reference	
References	1 NICE guidelines [NG23] Menopause: diagnosis and management, last revised December 2019 https://www.nice.org.uk/guidance/ng23 2 NICE Clinical Knowledge Summaries Menopause, last revised March 2022 http://cks.nice.org.uk/menopause 3 FSRH Clinical Guideline: Contraception for women aged over 40 years, amended September 2019 https://www.fsrh.org/documents/fsrh-guidance-contraception-for-women-aged-over-40-years-2017/ 4 NICE Guidelines Vitamin D deficiency in adults, last revised January 2022 https://cks.nice.org.uk/topics/vitamin-d-deficiency-in-adults/management/prevention/ 5 British Menopause Society Guidelines Testosterone replacement in menopause https://thebms.org.uk/publications/tools-for-clinicians/testosterone-replacement-in-menopause/ 6 Menopause matters guidelines. Hormone replacement therapy. https://www.guidelines.co.uk/menopause-matters/hrt
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