Oxford University Hospitals NHS NHS Trust

Oxfordshire HRT formulary and treatment guidance

NHS Oxfordshire Clinical Commissioning Group

Contents

Oral or transdermal HRT—offer choice but avoid oral if

- VTE risks or personal /first degree relative with history
- Poor symptom control with oral
- Bowel disorder /absorption problems /gastric banding
- Lactose intolerance
- History of migraines
- Stroke risks e.g. BMI>30/smoker/sedentary
- History of or concerns of gall stones
- On hepatic enzyme inducing agent including OTC preparations

First treatment option

Second line treatment options

Amber continuation after specialist initiation

Formulary Individual patient needs and treatment problems may require other preparations.

Oestrogen only

Hysterectomy, 1 prescription charge

HRT Product	Oestrogen	Delivery	Dose	Indication for use
Elleste solo	Oestradiol	Oral tablets	1 mg, 2mg daily	First line oral treatment option
Premarin	Conjugated equine oestrogen	Oral tablets	300mcg, 0.625mg, 1.25mg daily	Consider if previously well on conjugated equine oestrogen.
Evorel	Oestradiol	Transdermal patches	25,50,75,100 mcg twice weekly	First line transdermal option
Elleste Solo Mx	Oestradiol	Transdermal patches	40, 80mcg twice weekly	Skin allergy /poor absorption with Evorel, alternative adhesives
Estradot	Oestradiol	Transdermal patches	25, 37.5, 50, 75, 100mcg twice weekly	Smaller sized patches consider for higher doses and petite women
Sandrena	Oestradiol	Transdermal gel	0.5, 1, 1.5 mg/g daily	Patient preference, skin allergy to patches or side effects

Sequential/cyclical combined HRT

Uterus present, perimenopausal women, 2 prescription charges, monthly bleed

HRT Product	Oestrogen/progestogen	Delivery	Dose Oestrogen/ progestogen	Indication for use
Elleste duet	Oestradiol /norethisterone	Oral tablets	1mg/1mg 2mg/1mg daily	First line oral treatment option
Femoston	Oestradiol/dydrogesterone	Oral tablets	1mg/10mg 2mg/10mg daily	If cyclical side effects to norethisterone or other progestogen
Prempak C	Conjugated equine oestrogen/norgestrel	Oral tablets	0.625mg/150mcg 1.25mg/150mcg daily	Consider if previously well on conjugated equine oestrogen.
Evorel Sequi	Oestradiol/norethisterone	Transdermal patches	50mcg/170mcg twice weekly	First line transdermal treatment option
FemSeven Sequi	Oestradiol/levonorgestrel	Transdermal patches	50mcg/10mcg once weekly	Skin allergy /poor absorption with Evorel, alternative adhesives
Oestradiol tablet/ patch/gel as above plus adjunctive progestogen/ progesterone	Oestradiol plus proges-togen/progesterone of choice (see table below)			Side effects with other progestogens, bleeding problems, contraceptive needs

Continuous combined HRT

Uterus present, postmenopausal women, 1 prescription charge, cycle free

HRT Product	Oestrogen/progestogen	Delivery	Dose Oestrogen/ progestogen	Indications for use
Kliovance	Oestradiol/norethisterone	Oral tablets	1mg/0.5mg	First line oral treatment option
Femoston Conti	Oestradiol/dydrogesterone	Oral tablets	1mg/5mg 0.5mg/2.5mg	If side effects to other progestogen
Premique low dose	Conjugated equine oestrogen/ medroxyprogesterone acetate	Oral tablets	0.3mg/1.5mg	Consider if previously well on conjugated equine oestrogen.
Indivina	Oestradiol/ Medroxyprogesterone acetate	Oral tablets	1mg/5mg	Continued irregular bleeding with other oral continuous combined HRT with no uterine pathology
Angeliq	Oestradiol/drospirenone	Oral tablets	1mg/2mg	Bloating, breast tenderness, acne with other progestogens
Tibolone	Tibolone (synthetic molecule with oestrogen, progestogen and androgenic properties)	Oral tablets	2.5mg	Low libido (also consider post hysterectomy and/or BSO if libido low)
Evorel Conti	Oestradiol/norethisterone	Transdermal patches	50mcg/170mcg twice weekly	First line transdermal treatment option
FemSeven Conti	Oestradiol/levonorgestrel	Transdermal patches	50mcg/10mcg once weekly	Skin allergy /poor absorption with Evorel, alternative adhesives
Oestradiol only tablet/ patch/gel (see page 1) plus adjunctive progestogen/progesterone	Oestradiol plus progestogen/ progesterone of choice (see table below)			Side effects with other progestogens or bleeding problems
Duavive	Conjugated oestrogens and bazedoxifene	Oral tablets	0.45mg/20mg	Amber continuation. Specialist initiation only. If intolerant to progestogens.

Topical vaginal oestrogen

HRT product	Oestrogen	Delivery	Dose	Indications for use
Vagifem	Oestradiol	Vaginal tablet	10mcg as directed	First line topical treatment option
Gynest/Estriol 0.01%	Oestriol	Vaginal cream	Using applicator as directed	Patient or clinician preference
Estring	Oestradiol	Vaginal ring	7.5mcg daily over 90 days	Allergies to other topical products, dexterity problems with applicators, patient preference

Testosterone—Amber continuation. Only on initiation by Oxford Menopause Service. See page 8

<u>Adjunctive progestogen in HRT</u>—use alongside either oral or transdermal oestrogen for women with uterus to provide endometrial protection.

Intrauterine system (Mirena) - NB Licensed for 4 years for HRT use

Medroxyprogesterone acetate (provera) tablets

- cyclical regime—10mg for 12 days each 28 day cycle
- continuous combined HRT—2.5-5mg daily continuously

Utrogestan (micronized progesterone) capsules

- Cyclical regime—200mg orally at bedtime for 12 days each 28 day cycle
- Continuous combined HRT—100mg orally daily continuously at bedtime

Treatment guidance

Adopt an individualised approach to diagnosis, investigation and management of menopause

Diagnosing menopause and need for treatment—both short and long term

- Diagnosis of menopause should be based on the woman's symptoms and age
  - Healthy women > 45 years with menopausal symptoms, diagnose without laboratory tests if
    - the woman has vasomotor symptoms and irregular periods.
    - the woman has not had a period for at least 12 months.
    - or based on symptoms in woman without a uterus.
  - Consider using FSH if
    - the woman is between 40–45 years with menopausal symptoms, including a change in menstrual cycle.
    - the woman is younger than 40 years in whom premature menopause is suspected.
- A pelvic examination should be performed only if clinically indicated and to exclude other possible causes of symptoms.
- FSH level over 30 IU/L is diagnostic of ovarian decline. Fluctuations of FSH in perimenopause limit its value. FSH should not be done if taking combined oestrogen and progestogen contraception or high dose progestogen.
- Consider HRT to manage menopause symptoms including vasomotor symptoms, psychological symptoms (including low mood that arises as result of menopause), altered sexual function and urogenital atrophy.
- The benefits of HRT are likely to outweigh the risks for women with disruptive symptoms below the age of 60 years or within 10 years of menopause.
- In women with premature ovarian insufficiency (premature menopause), systemic HRT is recommended, if not contraindicated, until at least the average age of natural menopause (51-52 years) to prevent the early onset of osteoporosis, CVD, Alzheimer's disease, Parkinsonism and cognitive decline.
- HRT may be appropriate for prevention of osteoporosis related fractures in women below the age of 60 years or within 10 years of menopause in symptomatic women or if other bone protection medication is contraindicated.
- There is no clear evidence that SSRIs or SNRIs ease low mood in menopausal women who have not been diagnosed with depression.

Initiating and managing HRT

- The option of taking HRT is an individual decision made after a consultation with the woman that addresses quality of life, health priorities, risks (including age and time since menopause), benefits and her personal preference.
  - Consider HRT, if not contraindicated, for treatment of vasomotor symptoms, low mood in menopausal women, urogenital atrophy (either topical alone or alongside systemic) and altered sexual function. It will also provide osteoporosis protection.
  - Discuss effectiveness of HRT, risks, benefits, bleeding patterns, side effects.

• **Patient assessment includes**
History of menopause and other symptoms Menstrual history Contraceptive needs (HRT is not contraceptive)
Personal and family medical problems, patient risk factors cancer—breast, bowel, ovarian osteoporosis venous thromboembolism, CV risks other medical problems including migraine
Concomitant medication including alternative/OTC therapies
Patient preference for treatment
Check blood pressure, height, weight, BMI

- **Choice of route**

  Offer patient choice of oral or transdermal. Avoid oral if
  - VTE risks or personal /first degree relative with history of VTE (both provoked and unprovoked)
  - Poor symptom control with oral
  - Bowel disorder /absorption problems /gastric banding,
  - Lactose intolerance
  - History of migraines
  - Stroke risks e.g. BMI>30/smoker/sedentary
  - History of or concerns of gall stones
  - On hepatic enzyme inducing agent including OTC preparations

- **Treatment regimes.**

Non-hysterectomised		Hysterectomised	Urogenital atrophy only
Perimenopausal	Postmenopausal	Oestrogen only	Low dose topical vaginal oestradiol or oestriol
Combined cyclical (sequential) regime	Continuous combined regime		
Continuous oestrogen/ cyclical progestogen for 10-14 days in 28 day cycle, giving cyclical progestogen withdrawal bleed Consider changing to continuous combined HRT when postmenopausal or 54 years	Cycle free HRT, continuous oestrogen and progestogen / progesterone	Prescribe continuous combined oestrogen & progestogen • If history of severe endometriosis • Occasionally after subtotal hysterectomy, the decision is made by the surgeon • TCRE	Can also be added alongside systemic HRT

  - The dose and duration should be consistent with safety issues and treatment goals. Generally the lowest effective dose is advised for symptom control (see bone protective doses below).
  - Review after 3 months as symptom control and side effects (including bleeding) can take time to be effective and/or settle, then annually or earlier if concerns.
  - Encourage women to maintain healthy diet and life style, invite them to seek information at www.menopausematters.co.uk and www.nos.org.uk.

- **Topical oestrogen for urogenital atrophy**
  - All topical products are low dose oestradiol or estriol. They include oestradiol vaginal tablets (Vagifem), oestradiol vaginal ring (Estring), estriol creams (Gynest/oestriol 0.01%, Ovestin) and estriol pessaries (Ortho-Gynest).
  - Low postmenopausal oestrogen levels can cause vaginal atrophy and an increased incidence of UTIs. Vaginal oestrogen treats vaginal atrophy and can also prevent recurrent UTI type symptoms in postmenopausal women.
  - Caution is required for women with a history of oestrogen receptor positive breast cancer. Estriol 0.01% cream may be prescribed in women with oestrogen receptor positive breast cancer whilst taking tamoxifen, after checking with the oncologist but not in women taking aromatase inhibitors.
  - All topical vaginal oestrogen can be used in the long term without adjunctive progestogens and endometrial monitoring.
  - Creams and pessaries may affect condom integrity.

- **Dose, duration and weaning off HRT**
  - As women get older, generally lower oestrogen doses are sufficient for symptom control. Consensus advice is that the lowest effective dose should be used.
  - Gradually reducing HRT may limit recurrence of symptoms in short term but will not make a difference to symptoms in long term. (10% of women flush for more than 12 years and some have symptoms in the very long term).
  - Consider reducing the oestrogen dose if changing a woman to a continuous combined HRT from a cyclical, reducing again 1-2 years later . Avoid being prescriptive about when doses are reduced and encourage reductions as menopause symptoms permit (menopause symptoms /poor quality of life are a criteria for continuing to take HRT). Lower the dose to the minimal instead of extending dosing frequency.
  - Ask women to address trigger factors for flushes prior to dose reduction (suggest patient visits menopause matters website at www.menopausematters.co uk).
  - Offer topical vaginal oestrogen when discontinuing systemic HRT in women with history of urogenital problems or who are still sexually active.
  - Matrix patches can be cut so that the dose can be reduced slowly and cautiously.

- **Tibolone**

This is a synthetic steroid compound, derived from soy. An amenorrhoea regime for primarily postmenopausal women, it has oestrogenic, progestogenic and androgenic actions. It conserves bone mass and treats vasomotor, psychological and libido problems (due to its androgenic effects). There is an increased risk of breast cancer and venous thromboembolism, broadly similar to combined HRT. Its use in women over 65 years needs to be cautious because of increased stroke risk.

Contraindications, cautions and risks of HRT

- **Contraindications**
  - Current, past, or suspected breast cancer.
  - Known or suspected oestrogen-sensitive cancer.
  - Undiagnosed abnormal vaginal bleeding.
  - Untreated endometrial hyperplasia.
  - Current venous thromboembolism (deep vein thrombosis or pulmonary embolism), unless the woman continues on anticoagulant treatment.
  - Active or recent arterial thromboembolic disease (for example angina or myocardial infarction).
  - Untreated hypertension.
  - Active liver disease with abnormal liver function tests.
  - Porphyria cutanea tarda.
  - Pregnancy.
  - Dubin-Johnson and Rotor syndromes (or monitor closely).

- **Cautions for HRT use**
  - A personal or first degree relative with any history of venous thromboembolism (whether provoked or unprovoked) see local guidelines on HRT and venous thromboembolism http://orh.oxnet.nhs.uk/Gynaecology/Pages/Guidelines.aspx .
  - Migraines (transdermal preparation starting low dose is advised with dose gradually increased to control symptoms without exacerbating migraines).
- **Risks**

For complete NICE guidelines visit: https://www.nice.org.uk/guidance/ng23/chapter/Recommendations#long-term-benefits-and-risks-of-hormone-replacement-therapy .

- Venous thromboembolism (VTE)
  - The risk of VTE is increased by oral HRT, particularly in the first year of use.
  - The risk associated with transdermal HRT with standard doses is no greater than baseline population risk.
  - Consider transdermal HRT if woman has VTE risk factors including BMI>30.
  - If high risk of VTE including family history consider referring to specialist service. See also local guidelines at http://orh.oxnet.nhs.uk/Gynaecology/Pages/Guidelines.aspx .
- Cardiovascular disease (CVD)
  - HRT does not increase CVD if started under 60 years or risk of dying of CVD.
  - The presence of CVD risk factors is not a contraindication to HRT if they are optimally managed.
  - The risk of coronary heart disease and stroke for women around menopause varies according to her risk factors.
  - Oestrogen-alone HRT does not increase risk of coronary heart disease.
  - HRT with oestrogen and progestogen is associated with little or no increased risk of coronary heart disease.
  - Oral, not transdermal oestrogen is associated with a small increased risk of stroke but in women <60 years the risk is very low.
- Diabetes
  - HRT is not associated with an increased risk of developing type 2 diabetes.
  - HRT is not generally associated with adverse effect on blood glucose in women with type 2 diabetes.
  - Consider HRT symptoms in women with type 2 diabetes after considering comorbidities and/or seeking specialist advice.
- Breast cancer
  - Oestrogen-only HRT is associated with little or no increased risk of breast cancer.
  - Oestrogen and progestogen HRT can be associated with an increased risk of breast cancer, generally the risk is considered low.
  - Any increase in risk is related to duration of HRT and reduces after stopping.
- Ovarian cancer
  - NICE did not discuss the risk of ovarian cancer in women taking HRT. However, evidence suggests that HRT use may be associated with a small increased risk of ovarian cancer with both oestrogen only and combined HRT but the risk falls after cessation of HRT.

Considerations associated with HRT

- **Bleeding patterns on HRT**
  - Cyclical (sequential) HRT (*Bleeds should start towards end of progestogen or first week of oestrogen only phase)*
    - Usually heavier initially but get lighter after 2-3 months.
    - Bleeds generally similar to patient's natural periods i.e. length and menstrual symptoms.
    - 5-10% of women do not bleed on cyclical HRT due to atrophic endometrium, if there is good symptom response then of no concern, otherwise consider possible poor absorption as reason for amenorrhoea.
    - Strategies for bleeding problems with cyclical regimes include
      - Consider causes e.g. compliance, drug interactions, GI or other absorption problems, pelvic pathology.
      - Heavy or prolonged bleeding – increase or change type of progestogen or reduce oestrogen dose.
      - Bleeding early in progestogen phase – increase dose of progestogen or change type.
      - Painful bleeding – change type of progestogen.
      - Irregular bleeding – change regime or increase progestogen.
  - Continuous combined (COCO) HRT
    - Unpredictable irregular bleeding common for 3-6 months, if settling continue HRT.
    - If heavy or continuing after 6/12 consider investigating.
    - Investigate if new bleeding after 1 year amenorrhoea .
    - Bleeding patterns generally better with low oestrogen dose HRT & as women get older.
    - Strategies for bleeding problems with COCO therapies
      - Bleeding patterns better with lower oestrogen dose.
      - Good compliance essential.
      - Increase progestogen dose.
      - Some women bleed despite atrophic endometrium/normal uterine pathology.

- **Lack of efficacy**

Causes
Consider the following causes - Too soon for symptom response - Oestrogen dose not high enough - Patient compliance poor - Limited absorption/metabolism - Woman anxious about taking HRT - Symptoms not menopausal

How long does HRT takes to work?

Vasomotor symptoms—some improvement after one month, maximum by 3 months

Urogenital symptoms— some improvement by 3 months, but may take 6 months

Psychological symptoms—variable response

- **Side effects**
  - Oestrogen and progestogen can both cause side effects, the cause is more difficult to distinguish in continuous combined preparations.
  - Generally progestogen side effects are more problematic than oestrogen, note the two groups of progestogens (see below) as some women may tolerate one type better than the other.
  - There is no evidence that HRT causes weight gain. However on average women gain 10kg between 40-60 years independently of menopause.

Oestrogen side effects	
Breast tenderness Nipple sensitivity Bloating Leg cramps Nausea/heartburn Headaches	Wait—side effects generally settle <3 months If side effects severe, lower dose Change route i.e. from oral to transdermal
Progestogen side effects	
PMS type symptoms Mood changes Breast tenderness Bloating Headaches Mood changes Acne/greasy skin	Change type of progestogen Change route e.g. oral to transdermal Change regime - consider long cycle HRT or continuous combined HRT , perhaps with IUS to provide progestogen Ask advice from Oxford Menopause Service

Types of progestogens

Progestogens are synthetic forms of progesterone, there are two main groups derived from either

- **testosterone** *(norethisterone, levonorgestrel, norgestrel)*
- **progesterone** *(dydrogesterone, medroxyprogesterone acetate)*
- **other options**
  drospirenone—only available in Angeliq
  micronized progesterone (Utrogestan)

Comparative doses

These are a rough guide as absorption varies

1mg oral oestradiol=25mcg patch=0.5g Sandrena gel

2mg oral oestradiol=50mg patch=1g Sandrena gel

4mg oral oestradiol=100mcg patch=Sandrena licenced to 1.5g

Equivalent doses of conjugated equine oestrogen to oestradiol are not clear

NB The right dose is the lowest to control symptoms/provide bone protection. Younger women tend to need higher doses.

Minimum bone protective doses	
HRT	**Dose**
Oestradiol oral	1-2mg
Oestradiol patch	25-50mcg
Oestradiol (Sandrena gel)	1g
Conjugated equine oestrogens	0.3-0.625mg

- **Contraception, IUS and HRT**
  - HRT is not contraceptive and will not prevent spontaneous ovulation in perimenopausal women.
  - Women >50 years, use contraception for 1 year after last spontaneous period.
  - Women <50 years, continue contraception for 2 years following last spontaneous period.
  - Fit, healthy, non-smoking, normotensive women may continue the COCP until 50 years. The POP can be used alongside cyclical HRT.
  - Barrier methods become safer in older women as fertility declines, and have a lower failure rate.
  - The intra-uterine system (IUS) can be used as the progestogen component of HRT alongside oestrogen to provide contraception, control perimenopausal bleeding problems and provide endometrial protection.
  - The IUS is only licensed for 4 years in HRT use.

Premature ovarian insufficiency (POI) / Premature menopause

- Premature menopause is before the age of 40 years (however menopause before 45 years is still considered early)
- Diagnose premature menopause on symptoms, menstrual changes and 2 raised FSH levels over 30 IU/L taken 4-6 weeks apart. Other tests - prolactin, testosterone, SHBG, TFTs, autoimmune screen (specifying ovarian, thyroid and adrenal), chromosome analysis and FMR1 gene (especially for women under 30 or if desiring pregnancy). Consider baseline bone density measurement.
- If there is doubt about the diagnosis of premature menopause, consider referral for specialist advice.
- If no contraindication treat premature menopause (and also early menopause) with hormone replacement, offering the choice of HRT or a combined oral contraceptive pill as appropriate. Explain to these young women the importance of hormone replacement at least until the average age of natural menopause (51-52 years) to prevent early onset of osteoporosis, cardiovascular disease, Alzheimer's disease, Parkinsonism and cognitive decline.
- Young women often need higher doses of HRT for symptom control (oral oestradiol 3-4mg or transdermal 75-100mcg patches) and to ensure bone and other long term protection.
- Discuss contraception. HRT is not contraceptive. If conception is desirable, less than 5% will spontaneously become pregnant after diagnosis.
- In women < 50 years, HRT is not associated with an increased risk of breast cancer compared to normally menstruating women.

When to refer to specialist service

- Premature ovarian insufficiency/menopause. It is likely that most women <40 years will need referral to specialist clinic.
- Complex medical history
- Concerns about the safety of HRT in a particular patient
- Persistent treatment problems e.g. side effects, lack of efficacy
- Bleeding problems despite following logical changes in bleeding management section above.
- History of hormone dependent cancer and patients with BRCA genes

Patient resources

Menopause Matters website – excellent general menopause information www.menopausematters.co.uk

National osteoporosis Society – excellent information on all areas of bone health and treatments www.nos.org.uk

Early menopause group- www.daisynetwork.org.uk

Health talk on line – interviews with women, including young women, discussing menopause issues www.healthtalk.org

NICE Menopause—Information for the public November 2015 www.nice.org.uk/guidance/ng23/ifp/chapter/menopause

Women's Health Concern—Benefits and risks of HRT December 2015 www.womens-health-concern.org/help-and-advice/factsheets/hrt-know-benefits-risks/

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Testosterone transdermal gel for low libido in menopause / post-menopause (Testim 50mg/5g, Testogel 50mg/5g)

Initiated by Menopause clinic only

Background

There is strong evidence that androgens influence female sexual function and that testosterone therapy may be useful for women who have experienced loss of sexual desire and/or arousal. NICE NG23 2015, Menopause, does recommend consideration of testosterone if HRT is ineffective for short term symptoms in menopausal women.

Testosterone treatment should be initiated by OUH Menopause Clinic specialist only. Menopause clinic retain prescribing until effectiveness is assessed and the patients stabilised. Usually treatment takes up to 3 months to be effective, so a 3 month telemed follow up is arranged and then 3 monthly follow up appointments continue until a woman is established on treatment. The clinic will recheck the free androgen index (FAI) if testosterone side effects occur

Testim or testogel are preferred by the OUH Menopause Clinic and one tube/sachet is prescribed to be used over 10 days. A new tube/sachet is started on the 1st, 11th and 21st of each calendar month. The female dose is one tenth of the male dose.

Patients criteria:

Women with menopause symptoms on HRT where there has not been an improvement in altered sexual function with HRT only.

Before initiating the treatment the clinic will

- Investigate other causes of low libido and if necessary treat first. Testosterone should only be prescribed if libido continues to remain low and where there is no other obvious cause of low libido.
- Carry out blood tests to check sex hormone binding globulin (SHBG) and testosterone to show that FAI (free androgen index) is within the normal range before treatment is started.
- Ensure that women are on oestrogen HRT before and while taking testosterone

Testosterone treatment

Initiation

- Initiated by OUH Menopause Clinic specialist only
- Testim (Testosterone 50mg/5g gel unit dose 30 tubes £32)or Testogel (Testosterone 50mg/5g gel unit dose 30 sachets £31.11) are preferred brands (Sep 17 DT prices)
- Testosterone therapy should be considered as a clinical trial, which should not be continued if a woman has not experienced a significant benefit by 6 months.
- Administered by the patient herself, onto clean, dry, healthy skin on the sites indicated by the manufacturer. Applied immediately onto the skin. Allow drying for at least 3-5 minutes before dressing. Wash hands with soap and water after applications.
- the menopause clinic will retain prescribing until effectiveness is assessed and the patients stabilised. Usually treatment takes up to 3 months to be effective, so a 3 month follow up is arranged and then 3 monthly telemed follow up appointments continue until a woman is established on treatment. The clinic will recheck the free androgen index (FAI) if testosterone side effects occur
- Sometimes women need to continue under the clinic but usually if all is well, the clinic request the GP to take over the follow up care.

GP continuation and follow-up

- The annual review can be carried out by the GP. GP will assess effectiveness and adverse effects i.e. low libido or altered sexual function has improved and that there is no other problems impacting libido, intercourse or the relationship which would suggest that testosterone was no longer appropriate e.g. partners health, relationship difficulties, painful intercourse and life stresses
- ADRs include: application site irritation, headache, acne, worsened hypertension, dizziness, paraesthesia, amnesia, hyperaesthesia, mood disorders, diarrhoea, haematocrit increase, alopecia, urticaria, pruritis, hot flushes
- Androgenic side-effects of testosterone therapy are dose-related and avoidable with the use of formulations and doses appropriate for women.
- women should be reviewed in the menopause service again after 5 years of testosterone treatment
- testosterone should be discontinued first before HRT is finally discontinued

2016 IMS Recommendations on women's midlife health and menopause hormone therapy
http://www.imsociety.org/manage/images/pdf/4429e3dd302aac259ad68c3be7f60599.pdf
NICE NG23 Menopause, November 2015
https://www.nice.org.uk/guidance/ng23/chapter/Recommendations#managing-short-term-menopausal-symptoms