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# BNSSG Hormone Replacement Therapy Prescribing Pathway

## MENOPAUSAL SYMPTOMS

### NO UTERUS*
or Mirena® Coil in situ

### INTACT UTERUS

Sequential HRT
Perimenopause
<54 years
Last menstrual period <12m

Continuous Combined HRT
≥54 years
LMP >12m
5 years on sequential HRT
Following certain gynaecological procedures

***Endometriosis**
should be managed with a continuous combined HRT regimen.
See Remedy: Gynaecological conditions and HRT

HRT brands within each drug class listed below are in ascending order according to cost and the brand with the lowest acquisition cost should be offered where possible.[1]
Aim for the lowest effective dose in all women. The route of HRT administration should be individualised to the patient.

| OESTROGEN ONLY | SEQUENTIAL COMBINED | CONTINUOUS COMBINED |
|---|---|---|
| **Elleste Solo**<br>Estradiol 1mg or 2mg | **Elleste-Duet**<br>1mg or 2mg Estradiol +<br>1mg Norethisterone | **Kliovance**<br>1mg Estradiol + 0.5mg Norethisterone<br>**Kliofem**<br>2mg Estradiol + 1mg Norethisterone |
| | **Femoston**<br>1mg or 2mg Estradiol +<br>10mg Dydrogesterone | **Femoston Conti**<br>0.5mg Estradiol +<br>2.5mg Dydrogesterone<br>1mg Estradiol +<br>5mg Dydrogesterone<br>**Bijuve**<br>1mg Estradiol +<br>100mg Micronised Progesterone |

or

**Tibolone** (Synthetic steroid)
2.5mg daily
Androgenic, positive effect on low libido & energy.
Less stimulatory effect on fibroids & endometriosis.
Oestrogen effect is often suboptimal in managing menopausal symptoms in POI or surgical menopause.

### WHEN TO OFFER TRANSDERMAL HRT [4,5]

Offer transdermal HRT when oral HRT is **contraindicated, not tolerated** or **ineffective**.

Indications for transdermal HRT as **first line** are as follows:

- Aged≥60 years
- Increased VTE risk
- Obesity (BMI >30kg/m$^2$)
- Gall bladder disease
- Hypothyroidism
- Migraine
- Variable blood pressure and hypertension
- Increased cardiovascular risk
- Current use of hepatic enzyme inducing medication
- Malabsorption syndromes

### PROGESTOGENS AND ENDOMETRIAL PROTECTION

- Unopposed estrogen replacement is associated with a significant increase in the risk of endometrial hyperplasia that is both dose and duration dependent. See BMS guidance on the management of unscheduled bleeding.[2]
- The dose of progestogen should be proportionate to the dose of estrogen. Women who require high dose estrogen intake should have a balanced dose of progestogen dose to ensure endometrial protection.
- See Appendix 1: Licensed estrogen dose and proportionate progestogen dose[2]

### PROGESTOGEN
**Adjunct** to oestrogen only if uterus intact

**Norethisterone tablets**

or

**Medroxyprogesterone acetate tablets**

or

**Micronised progesterone capsules**

**Gepretix is the BNSSG preferred brand due to cost effectiveness**

See BMS guidance on Progestogens and endometrial protection[3]

See Remedy: Hormone Replacement Therapy for progestogen doses per licensed oestrogen dose

See BMS guidance on Unscheduled Bleeding on HRT(p16)[2]

For women with uterus requiring endometrial protection +/- contraception

**Evorel®**
Estradiol patch 25, 50, 75 and 100 mcg/24 hrs.
To be applied twice weekly.
Initiate with Evorel 50; increase or decrease as necessary.

**Estradot®**
second line brand option for patients where Evorel patch reported to lack adhesion, be poorly absorbed or where localised reactions to the glue are reported.
Estradot patch 25, 37.5, 50, 75 and 100 mcg/24 hrs.
To be applied twice weekly.
Initiate with Estradot 50; increase or decrease as necessary.

**Oestrogel® gel**
Two pumps (1.5 mg) OD continuously.
Increase if necessary up to 3 mg OD after 1 month.

**Sandrena® gel**
Initiate 1mg OD,
can adjust after 2-3 cycles to 0.5-1.5mg OD.

**Lenzetto® Transdermal Spray**
Estradiol 1.53mg/spray
Initiate 2-3 sprays daily
Reserved for patients where non-oral treatment is indicated but patches/gel are not tolerated

**Evorel® Sequi**
Estradiol 50mcg + Norethisterone 170mcg / 24 hrs
To be applied twice weekly.

**Evorel® Conti**
Estradiol 50mcg + Norethisterone 170mcg / 24 hrs
To be applied twice weekly.

**FemSeven Conti**
Estradiol 50mcg + Levonorgestrel 7mcg / 24hrs
To be applied once weekly.

Alternatively, a **COMBINATION** of topical oestrogen + Mirena® Coil or oral progestogen

### or Mirena® Coil

- Other IUS products are not licensed for use as part of a HRT regimen
- Change 5 yearly, even if postmenopausal
- Lower VTE risk

### PROGESTOGENS FEATURES

**Norethisterone & Medroxyprogesterone** (synthetics)
Better for cycle control, androgenic (may be good for libido); unfavourable effect on lipids

**Micronised Progesterone** (Body-identical)
Lower VTE risk, fewer progestogenic side effects, non-androgenic or glucocorticoid activity. No effect on lipids. Less effective cycle control. Lower breast effects.

**Dydrogesterone** (in Femoston, body-similar)
Lower VTE and breast risk

### UNSCHEDULED BLEEDING

Refer on 2WW pathway:
- Heavy/prolonged bleed or risk factors for hyperplasia
- Women with no risk factors for endometrial hyperplasia in women with unscheduled bleeding ≥ 6 months since starting HRT or ≥3 months since change in dose / preparation[2,6]

See Remedy for more information on unscheduled Bleeding on HRT

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# VAGINAL SYMPTOMS

## UROGENITAL ATROPHY

**Vaginal oestrogen can be used alone or in addition to systemic HRT**

NB Vaginal oestrogen does not increase endometrial hyperplasia or VTE risk in a low risk population. Vaginal oestrogen does not increase breast cancer risk in women who do not take aromatase inhibitors.

See Remedy: Urogenital Symptoms and Management

**Vaginal moisturisers +/- lubricants**
Advise patients to buy **over-the-counter**

**Yes! Vaginal Moisturiser** (Restricted)
Can be offered on prescription to women with oestrogen-sensitive conditions for whom topical oestrogens are unsuitable.

**Estriol 0.1% cream (generic)**
Apply 1 applicatorful nightly by vagina for up to 4 weeks, then reduce based on relief of symptoms to a maintenance dose e.g. once to twice weekly

**Vagirux® or Vagifem® Pessaries**
**Estradiol**
One nightly for 2 wks, then alternate nights for 2 wks, then twice weekly

**Estring®**
*Estradiol Vaginal Ring*

Reserved for women who are either:

- unable to use vaginal pessaries e.g. lack of dexterity or dementia *or;*
- for those who have tried vaginal creams/ pessaries for several months without benefit

**Imvaggis®**
*Lower dose estriol*

**2nd line** after vaginal moisturisers for women with oestrogen -sensitive conditions following discussion with oncologist or menopause specialist

**4th line** for women who have not tolerated other formulary options

**Ospemifene**
*Non-oestrogen oral tablets*

Reserved for women with

- history of breast for whom low dose estriol (Imvaggis) is unsuitable **or;**
- Significant local allergy to vaginal oestrogens **or;**
- for those who have failed to respond to all other formulary options after several months of treatment

**Prasterone (Intrarosa® gel)**
*DHEA*

Reserved for women on aromatase inhibitors;

**or;**

Last line option for those intolerant to all other formulary options e.g. allergy or issues with oral absorption

# TESTOSTERONE GEL

Testosterone is not a third component of HRT.

Management of low libido in menopause requires a biopsychosocial approach and clinicians should consider contributory factors such as vulvovaginal atrophy and relationship issues.

Tostran® 2% gel and Testogel® 40.5mg/2.5g gel sachets should only be considered in postmenopausal women who meet the following criteria:

1. libido causing distress **and**
2. Ongoing symptoms despite optimised oestrogen and progesterone HRT **and**
3. All other causes (biopsychosocial approach) have been excluded **and**
4. total testosterone <1.5nmol/L.

Testosterone gel is amber 3 months which means it must be initiated by a menopause specialist. See testosterone shared care protocol[7]

A qualified menopause specialist in primary care may initiate testosterone for women who meet this criteria and according to the shared care protocol.

See the Formulary for the definition of a specialist in menopause.

**Referral criteria**
If referring to the specialist menopause clinic for consideration of testosterone replacement, ensure:
- HRT is optimised e.g. oestrogen dose is sufficient – consider increasing oestrogen dose and assessing response after 3 months.
- Baseline blood test is taken including total testosterone levels (<1.5nmol/L) and sex hormone binding globulin (SHBG)

See Remedy: Testosterone

# MONITORING HRT

## FOLLOW UP 3 MONTHS AFTER INITIATING OR CHANGING HRT

- Assess symptom control
- Bleeding pattern (See **'Unscheduled Bleeding'** box)
- Side effects. Encourage women to persist with treatment for 3 months if possible as side effects may resolve. (See **'Managing Side Effects'** box)

## ANNUAL REVIEW

- Assess efficacy
- Medication review including dose, preparation, compliance and side effects.
- If uterus intact and taking oestrogen only HRT, ensure Mirena® Coil is in date and in situ. If Mirena® Coil is removed, ensure an appropriate combination of oestrogen and progesterone is prescribed.
- Discuss risks vs benefits of continuing HRT
- Discuss breast awareness, mammography & cervical screening attendance
- Ask about symptoms of urogenital atrophy
- Check BP, weight, CVD risk factors

## WHEN TO STOP HRT

See Remedy: Hormone Replacement Therapy

- Consider weaning dose down after 5 years of HRT (5 years after reaching average menopausal age in POI).
- Withdraw HRT slowly to reduce risk of recurrent symptoms. If symptoms do recur, then recommence treatment.

## MANAGING SIDE EFFECTS

| | | |
|---|---|---|
| **Oestrogen related** | Fluid retention, bloating, breast tenderness or enlargement, nausea, headaches, leg cramps, and dyspepsia.<br><br>*They may occur continuously or randomly throughout the cycle.* | X Change formulation if intolerable<br>X Dose reduction<br>X Leg cramps may improve with lifestyle changes (exercise, stretching calf muscles)<br>X Nausea - adjust the timing of the oestrogen dose or taking with food.<br>X Breast tenderness - may be alleviated by a low-fat, high-carbohydrate diet<br>X Migraine - switch to transdermal |
| **Progestogen related** | Fluid retention, breast tenderness, headaches or migraine, mood swings, depression, acne, lower abdominal pain, and back pain.<br><br>*They tend to occur in a cyclical pattern during the progestogen phase of cyclical hormone replacement therapy (HRT).* | X Change the progestogen type<br>X Change formulation if intolerable<br>X Dose reduction / change to a product with a lower dose of progestogen<br>X Reduce the regimen of progestogen administration by swapping from 14-day to a 10-day product.<br>X Change to continuous combined therapy or tibolone **(postmenopausal women only)** |

## HRT AVAILABILITY

There is currently good availability of most HRT products. However if formulary HRT products become unavailable, prescribers should liaise their community pharmacist for the most up to date information regarding Out of Stocks.[9]

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## CLINICAL GUIDANCE ON MENOPAUSE

**Click links below to access guidance on Remedy**

Premature Ovarian Insufficiency
Early Menopause
Diagnosing Menopause
Hormone Replacement Therapy
Genitourinary symptoms
Side Effects and risks of HRT
Testosterone for low libido
Breast Conditions and HRT
Gynaecological Conditions and HRT
Hormone Sensitive Cancers
Cardiovascular Conditions and HRT
HRT over 60 years old
HRT and VTE Risk
Migraines and HRT
Alternatives and Adjuncts to HRT
Contraception
Referrals
Resources for patients

## REFERENCES

All medications included in the HRT Pathway reflect the BNSSG Adult Joint Formulary


1. Drug Tariff prices May 2024
2. BMS Joint Guidelines - British Menopause Society: Management of Unscheduled Bleeding on Hormone Replacement Therapy
3. British Menopause Society: Progestogens and endometrial protection
4. NICE NG23 Menopause: diagnosis and management
5. British Menopause Society Tools for clinicians: HRT—Guide
6. Womb (uterus) cancer - Causes - NHS
7. BNSSG Testosterone shared care protocol
8. BMS Testosterone Replacement in Menopause
9. British Menopause Society further update on HRT supply