Newson Health
Menopause & Wellbeing Centre

HRT Easy Prescribing Guide

The menopause affects all women yet only the minority receive evidence-based care, advice and treatment. The life expectancy of women has increased over the past century, this means that on average, women spend over a third of their lives being postmenopausal.

Many suffer in silence and do not realise how effective hormone replacement therapy (HRT) can be at dramatically improving not only their symptoms but their future health too.

Managing symptoms

Managing people with symptoms of perimenopause and menopause is a very rewarding aspect of clinical practice. There are now excellent guidelines available, both national and international, for healthcare professionals on the management of the menopause[1–3]. However, worldwide, only a minority of perimenopausal and menopausal people are prescribed HRT despite these guidelines stating that for the majority of women the benefits of HRT outweigh any risks.

It is estimated that around 75% of menopausal women experience symptoms and around 25% of women experience severe symptoms that have a negative effect on their lives, often affecting their family and performance at work.

The vasomotor symptoms of the menopause are the ones that are most obvious when thinking about menopause, but these are not the symptoms that affect women the most. It is the symptoms of low mood, anxiety, reduced self-esteem, poor memory and concentration, reduced libido, joint pains and vaginal dryness that usually affect women and some non-binary people the most.

Benefits and risks of HRT

There are numerous potential benefits to be gained by women taking HRT. Symptoms of menopause such as hot flushes, mood swings, night sweats, and reduced libido improve. In addition, taking HRT has also been shown to reduce future risk of cardiovascular disease, osteoporosis, type 2 diabetes, osteoarthritis and cognitive decline [4-7]. Most benefit is afforded when women start HRT within 10 years of their menopause. HRT can be given to perimenopausal women and continued for as long as benefits outweigh the risks (usually forever). Older women who start HRT usually also gain benefit.

The type of HRT also affects a woman's benefits and risks. HRT containing micronised progesterone is associated with a lower risk of breast cancer, cardiovascular disease, and thromboembolic events compared with synthetic progestogens [8-9]. In addition, the mode of delivery of oestrogen is also important because, in contrast with oral oestrogen, transdermal oestrogen is not associated with an increased risk of venous thromboembolism (VTE) [10].

Most women and healthcare professionals are concerned about the possible risks of breast cancer in women taking HRT. However, the risk is far lower than many realise. Women who take oestrogen only HRT (women who have had a hysterectomy) have a lower future risk of breast cancer [10]. Women who take oestrogen and a progestogen who are over 51 years old may have a small increased risk of breast cancer. However, this increased risk is a lower magnitude to the risk of breast cancer for women who are overweight or drinking a glass or two of wine each night. Telling them this often helps to put this risk into perspective. This risk with synthetic progestogens has not been shown to be statistically significant in any studies. Studies have shown that women who take micronised progesterone have an even lower risk of breast cancer than other women who take other progestogens. There has not been a good quality study showing that there is a risk of breast cancer at all in women who take oestrogen with micronised progesterone.

Women with a history of cancer can still take HRT safely, in most cases. Many cancers are not associated with oestrogen, including cancers of the cervix, vagina, vulva, malignant melanoma and bowel. Most types of endometrial and ovarian cancer are also not associated with hormones. Women with a family history of cancer — including breast cancer — can still usually take HRT due to the bene fits taking it provides.

There is no good evidence regarding giving HRT to women with a history of an oestrogen receptor positive cancer. Some women with a history of these cancers choose to take HRT for the health benefits and improvements to the quality of their lives. Women with oestrogen receptor negative cancers can usually take HRT.

How to prescribe HRT: Firstly, keep it simple

There is robust evidence demonstrating that transdermal oestrogen in association with micronised progesterone represents the optimal HRT regimen, particularly in women at risk of cardiovascular events [11]. This combination should ideally be initiated by healthcare professionals at a primary care level.

Considerations when prescribing combination products:

- There is less flexibility if you want to alter the oestrogen dose
- They all contain older progestogens, except Bijuve®.

Considerations when prescribing oral oestrogen first line:

- There is VTE risk with oral oestrogen
- Oral oestrogen increases sex hormone binding globulin (SHBG) so reducing free androgen index (can lower libido even more)
- There is less reliable absorption
- There are more contraindications (for example obesity, diabetes, gallbladder disease, migraine and so on).

1. The most important hormone in HRT is oestrogen (best is 17 beta-oestradiol)

The optimal dose for each woman should be given to improve symptoms and also to optimise bone and heart health. Women can continue taking HRT for as long as the benefits outweigh any risks, which usually means for ever. They should have an annual review.

Transdermal oestrogen has no clot risk associated with it. It can be given to women with a history of clot and women with an increased risk of clot or stroke including women with migraines. It can also be given to women with hypertension and cardiovascular disease.

Patches – pros:

- Usually stick well and easy to use
- Can swim, shower, bath with them on
- Constant level given so can be better in women with migraines
- Can use more than one which is useful for women with early menopause / primary ovarian insufficiency (POI) who may need higher doses

Gel – pros:

- Easy to alter dose so women have more control
- Usually absorb really easily
- Can be used with patches to 'top up'
- Women with cyclical symptoms (including PMS) can use more on the days with worse symptoms

Spray – pros:

- Light preparation and small volume
- Is absorbed easily
- Can be used with patches to 'top up'
- Women with cyclical symptoms (including PMS) can use more on the days with worse symptoms

Patches – cons:

- Some women do not like to have something stuck to their skin
- Can lead to local irritation
- Some women find they do not stick on well or they crinkle (therefore reduced absorption)
- Some women find they have high absorption in hot climates
- Plaster mark on bottom – can be removed with baby oil and dry flannel!

Gel – cons:

- Young women needing higher doses need to use large quantities
- Harder to remember as needed once or twice a day
- Sachets can be hard to open

Spray – cons:

- Young women needing higher doses need to use large quantities
- Harder to remember as needed once or twice a day
- Appears to have unreliable absorption in some women

Commonly prescribed preparations:

- Evorel 25 / 50 / 75 / 100mcg patches, twice a week
- Estradot 25 / 50 / 75 / 100mcg patches, twice a week
- Oestrogel 2-4 pumps a day
- Sandrena gel 0.5 / 1mg sachets

Some women may choose an oral preparation or may not absorb transdermal oestrogen adequately. The safest progestogen (after micronised progesterone) with respect to breast cancer and clot risk is dydrogesterone.

The following are the available preparations containing dydrogestodene:

- **Femoston 1/10 (1mg oestradiol and 10mg dydrogesterone) – cyclical preparation**
- **Femoston 2/10 (2mg oestradiol and 10mg dydrogesterone) – cyclical preparation**
- **Femoston Conti 0.5/2.5 (0.5mg oestradiol and 2.5mg dydrogesterone) – continuous preparation**
- **Femoston Conti 1/5 (1mg oestradiol and 2.5mg dydrogesterone) – continuous preparation**

Dose Equivalents of Various Preparations

Patch	Half a 25 microgram patch	25 micrograms	50 micrograms	75 - 100 micrograms
Gel - pump	1/2 pump	1 pump	2 pumps	3 - 4 pumps
Gel - sachet	1/2 of a 0.5mg sachet	0.5mg sachet	1mg	1 - 2mg
Spray*		1-2 spray	2-3 sprays	>3 sprays

* These doses are approximate as absorption of the spray is very variable with many women finding they need to use large quantities for symptomatic benefit.

2. Women with a uterus need progesterone or a progestogen too

A few tips:

- Give cyclical HRT for first 6-12 months if they are having periods
- Continuous progestogens are better for endometrial protection
- Any age woman can take continuous HRT but it may cause erratic bleeding if given too early

The evidence supports the use of micronised progesterone (Utrogestan) as the most favourable progestogen. Can be prescribed cyclically, 200mg each evening, for 2 out of 4 weeks OR continuously, 100mg each evening. The dose can be increased (to 200mg each evening) if women are experiencing breakthrough bleeding with the continuous dose of 100mg.

Pros:

- Fewer side effects so better tolerated
- Can improve cardiovascular risk / lipids
- Neutral effect on BP / may reduce BP
- No VTE risk
- No good quality evidence it increases breast cancer risk
- Studies have shown some positive effect on bone strength
- Can often reduce anxiety
- Can be used vaginally (off label) usually at half the oral dose in women who cannot tolerate oral progesterone
- Can be considered by some as a contraceptive, if taken continuously and no periods (off label)

Cons:

- Can result in more breakthrough bleeding than synthetic progestogens
- Can cause some sedation — is taken at night time (though many women like this side effect). Needs to be taken on an empty stomach (eating food increases absorption, however this is not detrimental)
- Not licensed as a contraceptive

If Utrogestan is not available or not tolerated then consider Evorel Conti or Evorel Sequi (50mcg oestradiol). Some women need additional oestradiol which can be given as an oestradiol patch or as the gel or spray.

Mirena Coil (IUS)

Pros:

- Contraception
- Less risk of bleeding
- Can be safely used for 5 years as endometrial protection as recommended by FSRH[12] (actually licensed for 4 years)

Cons:

- Systemic side effects can occur in first 3-6 months
- Spotting and irregular bleeding can occur in first 3-12 months
- Not every woman's choice
- Sometimes difficult to access because of local commissioning arrangements

Explanation of why various doses are prescribed to different people

The optimum dose and duration of HRT treatment is decided according to the severity of a woman's symptoms, her response to treatment and how the HRT is absorbed and metabolised in her body. Every woman is different so a "one-size-fits-all" approach to HRT is not the best for women.

The dose of hormones – oestrogen, progesterone and testosterone - can vary between women and often women find that their doses need to change (either increase or decrease) with time. For example, a woman may start on a low dose during the perimenopause and then increase as her own hormones decline with time.

Some women need higher doses of oestrogen than other women to achieve the same benefits, especially as oestrogen can often be absorbed differently through the skin. Absorption can be affected by both modifiable and non-modifiable factors such as gender, age, ethnicity, hydration, skin temperature, metabolism, and site of application

There is no robust evidence that higher doses of oestrogen are associated with a greater risk to a patient as there have been no randomised controlled trials undertaken in this area.
An explanation of why various doses are prescribed to different people is in ***this article***

3. Testosterone is often beneficial

Adding testosterone to HRT can improve sexual function and general wellbeing. Testosterone can improve libido [14]. In addition, testosterone can improve mood, energy, stamina and concentration. Many women notice that their brain fog and memory improve.

A significant problem with prescribing testosterone is that there are currently no available licensed preparations for women in the UK. GMC guidance on the prescription of unlicensed medication should be consulted when prescribing. It is important to ensure that women are adequately oestrogenised before adding in testosterone; this is usually the case when they are no longer experiencing vasomotor symptoms.

Blood results are a guide and are not a reliable way of assessing need for testosterone.

It can sometimes take several weeks, even months for a woman to notice the beneficial effects of testosterone. If they have not noticed an improvement after six months, then it is unlikely to be beneficial. Clinical improvement in symptoms is more important than aiming for a specific level on treatment.

- Baseline blood tests are optional as most women will have low testosterone and FAI – treatment is often based on symptoms
- Ensure no other cause for her symptoms
- Ensure the woman does not have a specific treatable cause for her low FAI (e.g. oral oestrogens)

Commonly used testosterone replacement for women:

- Testogel ® (1% testosterone gel in 2.5g sachets, containing 50mg testosterone): Starting dose 1/8 of a sachet/day = 5mg/day i.e. each sachet should last 8 days. You should avoid washing the area for 2-3 hours after. The gel should be applied to the outer thighs, lower abdomen or bottom.
- AndroFeme ® (1% testosterone cream in 50ml tubes with screw cap, only available privately): Starting dose 0.5ml/day = 5mg /day i.e. each tube should last 100 days.

Vaginal oestrogens

Although vaginal oestrogen is not actually HRT it is important to know the following:

- Vaginal oestrogen is safe to give with HRT (about 20% of women need both)
- Vaginal oestrogen can be given as a pessary, cream, gel or vaginal ring
- Vaginal oestrogen should be prescribed in the long term (i.e. on repeat prescriptions)
- The dose of vaginal oestrogen is very low (using 10mcg oestrogen pessaries regularly for one year is an equivalent dose to just one 1mg oestradiol HRT tablet)
- Women with a history of any type of cancer, including an oestrogen receptor positive cancer, can still usually use vaginal oestrogen and continue using this in the long term[15]
- Evidence does not show an increased risk of cancer recurrence among women currently undergoing treatment for breast cancer, or those with a personal history of breast cancer, who use vaginal oestrogen to relieve urogenital symptoms
- GPs and primary care healthcare professionals can safely prescribe vaginal oestrogen
- Theoretically, women taking aromatase inhibitors should not use vaginal oestrogen preparations, however, these preparations can still usually be given to these women and they can really have a beneficial effect on their localised symptoms
- Many women using vaginal oestrogen should also be recommended to use non-hormonal vaginal moisturisers and lubricants too

Intrarosa (prasterone) is a daily pessary treatment containing DHEA (dehydroepiandrosterone) and is converted intracellularly to androgens and oestrogens. It has been shown to be associated with improvements in symptoms without significant changes in serum oestrogen or androgen levels.

Useful resource: **British Society for Sexual Medicine (2023) Position Statement for Management of Genitourinary Syndrome of the Menopause (GSM)**

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Newson Health

Menopause & Wellbeing Centre

Our clinicians provide individualised consultations,
with a holistic approach to the perimenopause and menopause.

We have clinics nationwide so whether you come to see one of our clinicians face-to-face or prefer to sit in the comfort of your own home and have your consultation virtually, you will be given time with an experienced health care professional who specialises in the perimenopause and menopause.

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