Initiating hormone replacement therapy (HRT) / menopausal hormone therapy (MHT)

Dr Sonia Davison
Jean Hailes Consultant Endocrinologist

Before you prescribe

- Ensure there are no contraindications to HRT/MHT
  - Breast cancer (hormonally sensitive)
  - Thrombophilia/past venous thrombo-embolic event (VTE)
  - Undiagnosed vaginal bleeding
  - Active liver disease
  - Uncontrolled hypertension
  - CVD risk or disease
- Ensure screening is up to date
- Start with a mid-range dose (can be titrated up or down at first review) and use for the shortest duration for symptom control

Oestrogen only vs. oestrogen + progestogen

- **oestrogen only** if the woman has had a hysterectomy or has a levonorgestrel IUD in situ
- Women who have undergone an endometrial ablation will still require a progestogen if prescribed systemic oestrogen

Systemic HRT/MHT vs. vaginal oestrogen

Vaginal oestrogen

- appropriate if the woman has vaginal atrophy symptoms only
- urogenital syndrome of the menopause

Systemic MHT for symptoms such as:

- flushes/night sweats
- insomnia
- joint aches and pains etc.
- (will also be beneficial for genito-urinary symptoms)

Continuous combined vs. sequential HRT/MHT

This is a decision based on the likelihood of bleeding

Continuous combined

- if more than 12 months post menopause
- (if use it earlier there is a risk of erratic bleeding which can be inconvenient or confusing)

Sequential

- if perimenopausal or within 12 months of menopause
- or if ongoing bleeding despite being >12 months after menopause (NB. any new bleeding that occurs in a postmenopausal woman who has been bleed-free for some time needs to be investigated)

Perimenopausal vs. postmenopausal

Perimenopausal

- will potentially need contraception
- will need a sequential regimen of MHT or will have bleeding issues
- Levonorgestrel IUD is a good option for both of these and will provide the progestogen for up to 5 years

Postmenopausal

- can use continuous combined therapy

Types of HRT

- PBS vs. non PBS - will be a financial consideration for some women
- oral vs. transdermal vs. vaginal oestrogen
- combined products (oestrogen and progestogen) vs. combination of separate oestrogen and progestogen products vs. oestrogen only (if hysterectomy or Levonorgestrel IUD in situ)
  - MHT is not contraceptive
  - resources - AMS guide to equivalent doses / Jean Hailes info sheet on MHT for patients

Oral or transdermal?

Oral

- Convenient, daily dosing
- Reliably absorbed
- May have nausea
- Undergoes first-pass metabolism – larger effective dose
- May have more tendency for weight gain / fluid retention / breast tenderness or enlargement
- Increase in VTE risk (not tibolone)

Transdermal

- Convenient, twice weekly dosing (if patch; daily if gel)
- Lower effective dose as avoids first-pass metabolism (dose is delivered straight into the bloodstream)
- Less tendency for weight gain / breast tenderness or enlargement
- No increase in VTE risk

Tibolone?

- Appropriate if ≥1 year postmenopause
- Synthetic HRT/MHT
- Oestrogenic / progestogenic / androgenic properties
- Does not increase breast density
- Less VTE risk vs. oral oestrogen + progestogen combination
- Consider if low libido a predominant symptom

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AUSTRALASIAN MENOPAUSE SOCIETY
NEW DIRECTIONS IN WOMEN'S HEALTH

INFORMATION SHEET

AMS Guide to Equivalent HRT/MHT Doses

This Information Sheet has been developed as a guideline only to approximately equivalent doses of the different HRT/MHT products available Jan 2016. HRT is now referred to as Menopausal Hormone Therapy (MHT). The intention is to help physicians change their patients to higher or lower approximate doses of HRT /MHT if needing to tailor therapy, or remain within the same approximate dose if needing to change brands of HRT/MHT. Products which are underlined are Australia only; products in *italics* are NZ only. Products with an * meaning Private/non PBS script.

Oestrogen and progestogen combination MHT

Cyclical oestrogen and progestogen combinations use these at peri-menopause or if less than 12 months amenorrhoea

Low Dose		
Product	Presentation	Composition
Femoston	tablet	1mg oestradiol/10mg dydrogesterone
Medium dose		
Trisequens*	tablet	1 and 2mg oestradiol/1mg norethisterone
Femoston	tablet	2mg oestradiol/10mg dydrogesterone
Estalis sequi 50/140	transdermal patch	50mcg 17 B oestradiol/140mcg norethisterone acetate (twice weekly application)
Estalis sequi 50/250 (same oestrogen, more progestogen than Estalis sequi 50/140)	transdermal patch	50mcg 17 B oestradiol/250mcg norethisterone acetate (twice weekly application)

Continuous oestrogen and progestogen combinations

Should be used if 12 months since LMP or after 12 months cyclical MHT

Low dose		
Product	Presentation	Composition
Angeliq1/2*	tablet	1mg oestradiol/2mg drospirenone
Femoston-conti	tablet	1mg oestradiol/5mg dydrogesterone
Kliovance*	tablet	1mg oestradiol/0.5mg norethistrone
Livial*, Xyvion* (generally suitable for women under 70 yrs at least 1 year post-menopause)	tablet	2.5mg tibolone
Medium dose		
Kliogest*	tablet	2mg oestradiol/1mg norethistrone
Premia 2.5 continous*	tablet	0.625mg conjugated equine oestrogens/ 2.5mg medroxyprogesterone acetate
Premia 5 continous* (same oestrogen, more progestogen than Premia 2.5 continuous)	tablet	0.625mg conjugated equine oestrogens/ 5mg medroxyprogesterone acetate
Estalis continuous 50/140	transdermal patch	50mcg 17 B oestradiol/140mcg norethisterone acetate (twice weekly application)
Estalis continuous 50/250 (same oestrogen, more progestogen than Estalis continuous 50/140)	transdermal patch	50mcg 17 B oestradiol/250mcg norethisterone acetate (twice weekly application)

Oestrogen only therapy

Only use these if patient has had a hysterectomy or in combination with a progestogen or Mirena if intact uterus

Low dose		
Product	**Presentation**	**Composition**
Estrofem*	tablet	1mg 17 B oestradiol
Progynova	tablet	1mg oestradiol valerate
Premarin*	tablet	0.3mg conjugated equine oestrogen
Climara 25	transdermal patch	25mcg/24hrs 17 B oestradiol (weekly application)
Estradot 25 or 37.5	transdermal patch	25 or 37.5mcg/24hrs 17B oestradiol (twice weekly application)
Estraderm 25 MX	transdermal patch	25mcg/24hrs 17B oestradiol (twice weekly application)
Medium dose		
Estrofem*, Zumenon	tablet	2mg 17B oestradiol
Progynova	tablet	2mg oestradiol valerate
Premarin*	tablet	0.625mg conjugated equine oestrogens
Climara 50	transdermal patch	50mcg/24hours 17B oestradiol (weekly application)
Estradot 50, Estraderm 50 MX	transdermal patch	50mcg/24 hours 17B oestradiol (twice weekly application)
Sandrena	gel	1mg oestradiol (daily application)
High dose		
Climara 75	transdermal patch	75mcg/24hours oestradiol (weekly application)
Estradot 75, Estradot 100	transdermal patch	75 or 100mcg/24 hours (twice weekly application)
Climara 100	transdermal patch	100mcg/24hours oestradiol (weekly application)
Estraderm 100 MX	transdermal patch	100mcg/24hours 17B oestradiol (twice weekly application)
Oestradiol implants - No longer available		
Oestrogen only vaginal therapy		
Product	**Presentation**	**Composition**
Ovestin	cream	1mg/g oestriol
Vagifem Low	pessary	10mcg oestradiol

Progestogen

Suggested alternative doses for use with the oestrogen preparations above where fixed dose therapy is not suitable

Low dose for use with low dose oestrogen		
Product	**Presentation**	**Composition**
Provera (1/2 of 5mg tablet)	tablet	2.5mg medroxyprogesterone acetate
Provera 2.5mg tablet*	tablet	2.5mg medroxyprogesterone acetate
Primolut N (1/4 of 5mg tablet)	tablet	1.25 mg norethisterone
Mirena* (PBS indication for contraception/menorrhagia)	device (5 years)	20mcg/24hrs levonorgestrel

Low dose progestogen-only contraceptive pills (Microlut (30mcg levonorgestrel) and Noriday (both 350mcg norethisterone) are used by some clinicians in various doses but there is limited data for dosages of these pills required for endometrial protection. 1 mg norethisterone was considered the minimum dose (cyclical or continuous) for adequate endometrial protection in the Cochrane Review (Cochrane Database Syst Rev. 2009 Apr 15;(2):CS000402).

Medium dose for use with medium dose estrogen		
Product	**Presentation**	**Dose**
Primolut N (1/4 of 5mg tablet)	tablet	1.25 mg norethisterone
Provera, Ralovera	tablet	5mg medroxyprogesterone acetate
Utrogestan (NZ only)	*capsule*	*100 mg micronized progesterone*
Mirena* (PBS indication for contraception/menorrhagia)	device (5 years)	20mcg/24hrs levonorgestrel
Higher dose (for use in cyclical therapy or continuous therapy with high dose oestrogen)		
Primolut N (1/2 5mg tablet)	tablet	2.5mg norethisterone
Provera, Ralovera	tablet	10mg medroxyprogesterone acetate
Utrogestan (NZ only)	*capsule*	*200 mg micronized progesterone*

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What type to choose?

Based on the woman's history and other factors

- if concerned about weight gain or breast tenderness - transdermal approach
- special scenarios:
  - scalp hair loss – oestradiol and drospirenone combination may be a good option
  - low libido - Tibolone may be a good option
- Start at the middle dose for the product and then can titrate up or down depending on response
- If the woman has had an adverse experience on HRT/MHT previously, use the lowest dose

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Potential side effects

- bleeding or breast tenderness is common in the first 3 months - reassure patient that it should settle
- if bleeding does not settle after 3 months and the woman is early postmenopausal, consider change to sequential regimen
- initial VTE risk increase on oral combined oestrogen and progestogen (2-3 fold overall increase in risk)

Breast cancer risk

- Between 1 in 8 and 1 in 9 Australian women will develop breast cancer over their lifetime
- HRT/MHT is associated with a similar risk of breast cancer as consuming 2 alcoholic drinks per day; the major risk factors for breast cancer are a family history of breast cancer and having dense breasts
- From the largest HRT/MHT study to date (WHI):
  - Combined oestrogen and progestogen HRT/MHT increases breast cancer risk after 4-5 years use
  - Oestrogen only HRT/MHT is associated with a decrease in risk
- Different progestogens have different effects on breast cancer risk, with dydrogesterone and micronised progesterone having a lesser risk compared with medroxy-progesterone acetate
- Discuss breast cancer risk and VTE risk specifically and document in their history

Review

- Ideally review at 3 months
- discuss negatives and positives and problem solve - e.g. bleeding / breast tenderness
- dose adjustment if required
- if change of product necessary then will need another review in 3 months otherwise 6 months (as most scripts will last this long)
- make sure screening is up to date (cervical screening / mammogram)

Ceasing HRT/MHT

- annual review of reasons for HRT/MHT
- trial a dose reduction to see if symptoms recur
- weaning rather than 'cold-turkey' cessation usually gets better results (although research studies suggest the same outcome)

Non-hormonal treatment options for vasomotor symptoms

Prescribed medications shown in RCTs to have evidence for efficacy and safety in the treatment of VMS

Note: 'off label use':

- SSRI/SNRI anti-depressant medications: effective in some women with added benefits on mood
  - See **menopause.org.au** for doses (link)
  - Caution in women on tamoxifen (paroxetine / sertaline / fluoxetine will inactivate tamoxifen and should not be used; venlafaxine, desvenlafaxine, citalopram and escitalopram appear to be safe options)
- Gabapentin: also useful for sleep; expensive and needs dosing 2-3 x daily
- Pregabalin (neuropathic pain)
- Clonidine – mixed trial results, effect modest (side effects dose related); this is the only PBS product available for VMS as a primary indication

Resources

jeanhailes.org.au

- Patient information & fact sheets
- GP menopause management tool (pictured)
- Green climacteric (symptom) scale
- Health professional webinar library

menopause.org.au (Australasian Menopause Society)

- A Practitioner's Toolkit for the Management of the Menopause
- Guide to HRT equivalent doses
- AMS symptom score sheet
- Patient information sheets

Jane

- 51 yr lady, last period 6 months ago, symptoms: flushes / drenching night sweats, irritability, vaginal dryness, joint aches and pains, sleep disturbance.
- Overweight, no other medical problems.

Maria

- 53 yr lady, amenorrhoea 2 yrs.
- Symptoms: insomnia, anxiety - impacting on general ability to function, urinary urgency, generally hot "like I'll combust".
- Hyperlipidemia, smoker, hypertension (stable - on meds)

Sophie

- 55yr lady, amenorrhoea 4 yrs.
- Symptoms: low libido, vaginal dryness.

Helen

- 52 yr lady, amenorrhoea 12 months. No symptoms.
- DXA - osteopaenia. Strong family history cardiovascular disease and osteoporosis with fracture. Maternal aunt had breast cancer in 40s.