Ask an Expert: Menopause Management

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Menopause

- Definition = **last menstrual period**
- **Natural** versus **surgical** (removal of both ovaries)
- Average age = **51 years**
  - median 50-52 yrs.
- Basic physiology:
  - cessation of ovulation
  - loss of cyclical ovarian production of **oestrogen / progesterone**
- Premature menopause = menopause <40 yrs. of age
  - increased risks of osteoporosis and fracture, CVD, cognitive decline if not treated with some form of hormone until expected age of menopause

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Symptoms around menopause:

Vasomotor	Genito-urinary	Mood	Somatic	Other
Flushes	Vaginal dryness	Irritability	Formication / restless legs	Sleep disturbance
Sweats	Dyspareunia	Mood swings	Muscle / joint aches and pains	Insomnia
Sensation of generally feeling hot	Urinary frequency	Teariness	Weight gain	Lowered concentration
	Stress incontinence	Depression	Headaches / migraine	Fatigue / lowered energy
	Urinary urgency	Anxiety	Bloating	Word-finding difficulties

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Symptoms

- 20% of women have few or no symptoms
- 60% have 4 - 8 years of symptoms which can decrease quality of life
- 20% have severe symptoms
- Some women have symptoms that persist into the 60s and 70s

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Case study

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Case Study: Eva

- 52 years, single
- social worker, works full-time.

Symptoms:

- low mood, anxiety, lethargy, sleep disturbance
- feels hot generally
- night sweats – drenching, frequent flushes
- periods ceased a year ago, erratic for 12 months prior
- worried about her bone health - mother with osteoporosis and fracture.

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Management options

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Management

- Diagnosis
- Symptom control
- Disease prevention

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Management of symptoms

Treat symptoms when *bothersome*

1. Lifestyle measures
2. Hormone treatment
   (MHT [=HRT], vaginal oestrogen)
3. Non-hormonal options
   - medications
   - non-medical options

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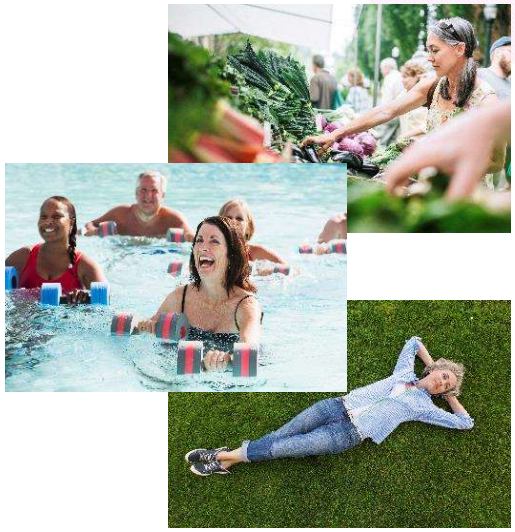
Lifestyle measures

- Avoid overheating
- Dress in breathable fabrics
- Avoid alcohol excess / spicy foods
- Healthy diet / regular exercise
- Stress management



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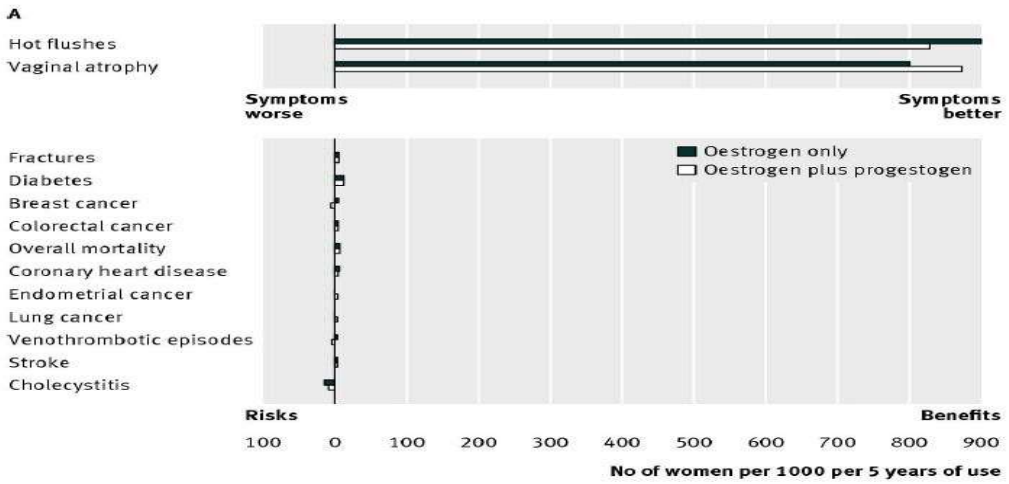
MHT: a 2020 approach to risks and benefits

- The benefits far outweigh the risks in healthy women around the time of perimenopause / menopause (consensus statements + guidelines)
- Increased risk of breast cancer after 5 years of use
- Multiple trials support the 'safe window' for prescribing
- Timing of initiation: <60 years or within 10 years of last menstrual period
- Younger women more likely to be symptomatic, have lower background risks for VTE and stroke, are more likely to derive cardiovascular benefit

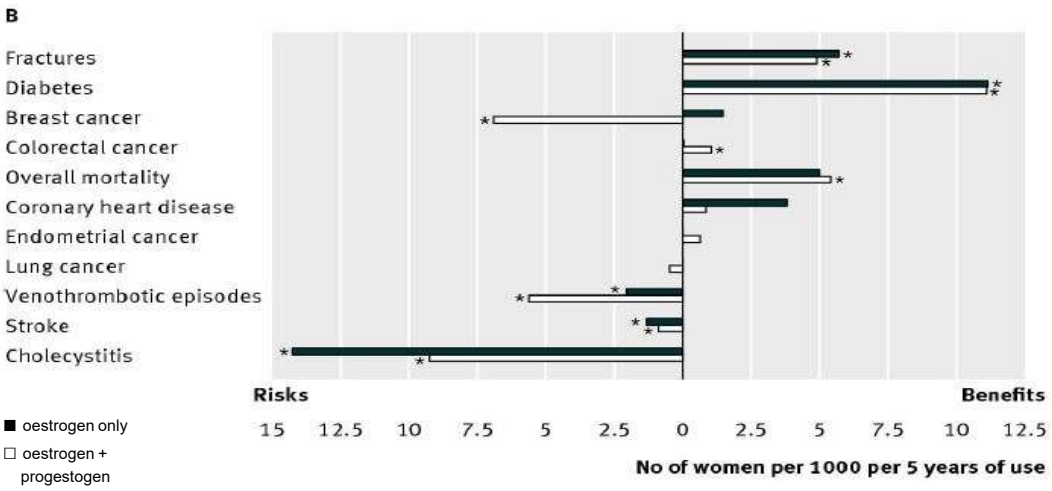
Risk and benefits of MHT between 50-59yrs or <10yr after menopause



Santen R J et al. JCEM 2010;95:s1-s66

The Journal of Clinical Endocrinology & Metabolism

Risk and benefits of MHT between 50-59yrs or <10yr after menopause



Santen R J et al. JCEM 2010;95:s1-s66

THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

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Before you prescribe

- Ensure there are no contraindications to 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

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Women and MHT :

Dose, delivery systems and regimens matter

Low dose therapy has:

- Less effect on thrombembolic risk
- Less effect on breast cancer risk

Transdermal therapy has:

- Less effect on thromboembolic risk
- Less effect on stroke risk

Oestrogen alone has:

- Less effect on cardiovascular risk
- Less effect on VTE risk
- Less effect on breast cancer risk and colorectal cancer risk reduction

Not all progestogens are created equal

- Micronised progesterone & dydrogesterone has less effect on breast cancer risk (vs MPA and NETA)

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Key considerations

1. Likelihood of bleeding (sequential vs. continuous)
2. Oestrogen only or oestrogen + progestogen or localised (PV oestrogen)
3. Risk factors
4. Presenting symptoms
5. Need for contraception (perimenopause)
6. Cost (PBS vs. non PBS)
7. Premature menopause (dose and duration)

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Bleeding

- High likelihood of bleeding on MHT if perimenopausal or recently postmenopausal
- Bleeding less likely if >1 yr after menopause
- Bleeding is common in the first 3 months of MHT
- Bleeding is more frequent when MHT dose is missed or delayed
- Levonorgestrel IUD can be used as the progestogen in MHT if bleeding is experienced or anticipated

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Continuous combined vs. sequential HRT/MHT

This is a decision based on the likelihood of bleeding

Continuous combined (=oestrogen and progestogen every day)

- 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 (=oestrogen every day; progestogen 12-14 days per month)

- 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)

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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
- Some women with a history of endometriosis may require a progestogen to inhibit potential recurrence

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Systemic MHT vs. vaginal oestrogen

Vaginal oestrogen

- appropriate if the woman has vaginal atrophy or urinary symptoms only
- safe for long term use

Systemic MHT for symptoms such as:

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

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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

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Types of MHT

- 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

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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 (most patches; 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
- Problems:
  - gel – messy
  - patch – local irritation (decreases absorption)

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Progestogens in MHT

A. Related to progesterone

– **Progesterone**

Micronised progesterone –oral / vaginal

– **Pregnane derivatives**

- Acetylated

Medroxy progesterone acetate - oral

Cyproterone acetate - oral

- Non-acetylated

Dydrogesterone - oral

B. Related to testosterone

– **19-nortestosterone derivatives**

Norethindrone /

Norethisterone acetate

- oral / transdermal

Levonorgestrel

- intrauterine system

– **Spironolactone derivatives**

Drospirenone

- oral

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Tibolone

- Appropriate if ≥1 year postmenopause
- Low-dose MHT
- Synthetic
- Oestrogenic / progestogenic / androgenic properties
- Does not increase breast density
- Less VTE risk vs. oral oestrogen + progestogen combination
- Consider if low libido a predominant symptom
- Slight increase in risk of stroke from 60s

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TSEC = Duavive

- Combination of conjugated oestrogen and SERM bazedoxifene
- Novel concept: beneficial effects of oestrogen systemically; oestrogen blocking effects at breast and endometrium)
- NO NEED for addition of progestogen
- Appropriate if ≥1 year postmenopause
- Not on PBS
- Low to mid-dose MHT
- May be a good option when progestogens have not been well tolerated previously

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Micronised progesterone = Prometrium

- "body-identical" progesterone
- Can be added to any oestrogen product
- Continuous combined dose = 100mg nocte; sequential = 200mg nocte for 12-14 days per month (not with food)
- Calming for mood, beneficial for sleep
- Not on PBS – cost considerations
- May be a good option when other progestogens have not been well tolerated previously
- Research – no increase in breast cancer risk up to 5 years use
  - E3N Study – French cohort of 80,000+ women
- Inconvenience of requiring 2 MHT products

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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, metabolic factors or VTE risk - **transdermal** approach
- Special scenarios: (see Jean Hailes HP Menopause tool)
  - scalp hair loss – oestradiol and drospirenone combination (Angeliq) 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 MHT previously
  - use the lowest dose
- In premature menopause (=menopause <40 yrs of age) a higher dose of oestrogen is recommended, until age 50 yrs (unless contraindicated)

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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 oestrogen /+/- progestogen (2-3 fold overall increase in risk)

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Breast cancer risk

- between **1 in 8 and 1 in 9** Australian women will develop breast cancer over their lifetime
- 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.

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Breast cancer risk cont..

- from the largest MHT study to date (WHI):
  - combined oestrogen and progestogen MHT increases breast cancer risk after 4-5 years use
  - oestrogen only MHT is associated with a decrease in risk to 7 yrs
- different progestogens have different effects on breast cancer risk
  - with dydrogesterone and micronised progesterone potentially having a lesser risk compared with medroxy-progesterone acetate
- discuss breast cancer risk and VTE risk specifically and document in their history.

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Review

- Ideally review at 3 months
- discuss negatives and positives and problem solve - e.g. bleeding / breast tenderness – consider using Menopause Score sheet
- 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)

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Ceasing HRT/MHT

- annual review of reasons for MHT
- trial a dose reduction to see if symptoms recur
- weaning rather than 'cold-turkey' cessation usually is better tolerated (although research studies suggest the same outcome)
- there is no 'ideal' duration of MHT use.

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Non-hormonal medications for symptom control SSRIs / SNRIs comparison – vasomotor symptoms

Agent	Dose	% reduction in flushes	Reference
Venlafaxine	75mg SR	60%	Loprinzi et al 2000
Desvenlafaxine	150mg	60%	Archer et al 2009
Paroxetine	12.5mg CR	56%	Steams et al 2005
Fluoxetine	20mg	50%	Loprinzi et al 2002

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Clonidine – vasomotor symptom control

= α-adrenergic agonist (blood pressure / migraine agent)

Dose:

1. 25 mcg twice daily
2. 50mcg twice daily after 2 weeks
3. 75mcg twice daily – maximal dose

Side effects:

- Dry mouth, visual disturbance, insomnia, drowsiness.

Goldberg et al J Clin Oncol 1994

Gabapentin – vasomotor symptom control

= GABA analogue; epilepsy agent

Effects:

- improvement in sleep disturbance, reduction in flushes (45% vs. 29% placebo)

Guttoso et al Obstet Gynecol 2003, Toulis et al Clin Ther 2009

Dose:

1. Start 100mg at bedtime – gradually increase to 100mg tds (increase dose every 3-5 days)
2. Maximal dose 300mg tds

Side effects:

- somnolence, drowsiness, dizziness.

‘Natural’ treatments for vasomotor symptoms

1. Remifemin / black cohosh
2. Phyto-oestrogens
3. Soy
4. Dong quai
5. Red clover
6. Vitamin E
7. Wild yam
8. Homeopathy

→ no benefit over placebo in clinical trials

Hirata et al 1997, Pockaj et al 2006, Barton et al 1998, Penotti et al 2003

Remifemin = black cohosh

- Relief of mild vasomotor symptoms

Side effects:

- potential liver toxicity
  - reports of abnormal liver function
  - fulminant hepatitis
  - liver failure requiring transplantation

Duration:

- 6 months

Levitsky et al 2005, Lynch et al 2006

Other options

1. Acupuncture
2. Breathing (paced respiration) / relaxation training / cognitive behavioural therapy
3. Hypnosis
4. Stellate ganglion block

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'Bio-identical' compounded hormones

- **Evidence lacking** for quality, safety, efficacy
- Risks of compounded hormones not well documented because formulations are not tested in clinical trials before being dispensed; no formal mechanism for reporting adverse events
- Australasian Menopause Society does not support their use
- FDA and North American Menopause Society (NAMS) have major warnings about their use
- Bio-identical progestogens may be ineffective at reducing endometrial thickening and protecting the endometrium
- If women want 'bio-identical' hormone therapy
  - consider 'body-identical' option

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Genitourinary Syndrome of the Menopause (GSM)
previously vulvovaginal atrophy

- Affects approx. 50% of women
- Vaginal dryness, dyspareunia and urinary symptoms; related to low oestrogen, changes in vaginal flora & pH
- Topical preparations 1st choice for symptoms confined locally
  - women using systemic MHT may require additional topical therapy
- Ovestin cream and ovules (1mg estriol/g); vagifem pessaries (10ug estradiol); daily for 2 weeks then 2 x weekly; progestogens not required with this regimen
- Use of vaginal estrogen for women with a hormone-dependent cancer is controversial
  - contraindicated in women taking aromatase inhibitors
- Non-hormonal vaginal moisturisers are available
- Vaginal laser therapy insufficient long-term data available

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Safety and efficacy of testosterone for women: a systematic review and meta-analysis of randomised controlled trial data.

36 RCT, 8480 , 20-77yrs

Testosterone vs. placebo / oestrogen +/- progestogen

Testosterone	Mean difference (95% CI)
Frequency of satisfying sexual events	⬆ 0.85 (0.52 to 1.18)
Sexual desire	⬆ 0.36 (0.22 to 0.50)
Pleasure	⬆ 6.86 (5.19 to 8.52)
Arousal	⬆ 0.28 (0.21 to 0.35)
Orgasm	⬆ 0.25 (0.18 to 0.32)
Responsiveness	⬆ 0.28 (0.21 to 0.35)
Self-image	⬆ 5.64 (4.03 to 7.26)
Sexual distress	⬇ 0.27 (-0.36 to -0.17)

All $P \leq 0.05$

Islam RM et al. Lancet Diabetes Endocrinol. 2019; Jul 25

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Safety and efficacy of testosterone for women: a systematic review and meta-analysis of randomised controlled trial data.

Adverse events

Testosterone	RR (95% CI)
Acne	⬆ 1.46 (1.11 to 1.92)
Hirsutism	⬆ 1.69 (1.33 to 2.14)
Weight	⬆ 0.36 (0.22 to 0.50)
Serious adverse events	⇔ 0.97 (0.65 to 1.44)

Other

Testosterone	
Virilisation	⇔
CVD / VTE events	⇔
Mammographic density	⇔
Breast cancer	⇔
Cognitive function	⇔
Well-being	⇔
BMD / body composition	⇔

Islam RM et al. Lancet Diabetes Endocrinol. 2019; Jul 25

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Global consensus position statement on the use of testosterone therapy in women

- HSDD = the only evidence-based indication in ♀
- Moderate therapeutic effect in PM ♀
- Meta-analyses – no severe adverse events with physiological use
- Safety of long-term use unknown
- HSDD diagnosis requires clinical assessment and identification and management of other contributors to sexual dysfunction
- Testosterone level not adequate to diagnose HSDD
- Rx – use only formulations that achieve blood levels that approximate premenopausal physiological levels
- No products for ♀ use approved; hence male formulations may be used in ♀ doses with regular monitoring of levels
- Compounded testosterone not recommended.

Davis SR et al. Climacteric, Menopause, JCEM, Maturitas, J Sexual Medicine. Sept 2019

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Case study: management

- Eva wished to pursue natural treatment
  - had a 3 month trial of black cohosh
  - bothersome symptoms persisted at 3 month review
- Trial of 'body-identical' MHT
  - oestradiol patch (twice weekly) and micronised progesterone (nocte)
- 3 month review
  - scant bleeding and breast tenderness – settled in first month
  - some patch site irritation
  - excellent symptom control
  - changed to daily oestradiol gel + micronised progesterone

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Questions

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Resources

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Health professional resources

Health professional tools:

Health professional education:

- e-learning courses:
  - Fertility, infertility and preconception care
  - Managing menopause: weighing up the evidence
  - Diagnosis and management of PCOS
- Webinars:
  - Premature menopause
  - Let's talk about sex: midlife sexual function
  - Menopause and mood

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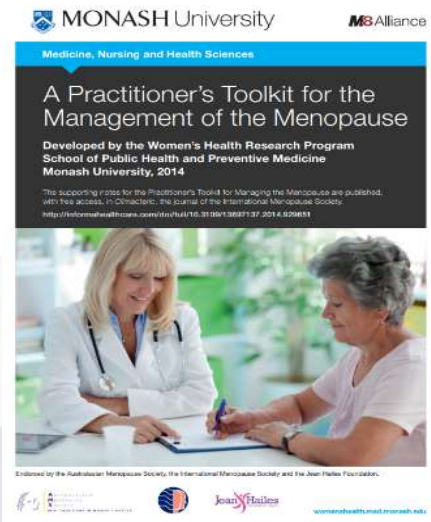

A practitioners toolkit for the management of the menopause
med.monash.edu.au/sphpm/womenshealth/info-4-health-practitioners/management-menopause-toolkit.pdf

AMS Guide to Equivalent MHT/HRT Doses

AUSTRALIA ONLY

This Information Sheet has been developed as a guideline only to approximately equivalent doses of the different TGA registered MHT/HRT products available in Australia in May 2020. Hormone Replacement Therapy (HRT) is now referred to as Menopausal Hormone Therapy (MHT). The intention of this sheet is to help physicians change their patients to higher or lower approximate doses of MHT if needing to tailor therapy, or remain within the same approximate dose if needing to change brands of MHT. Private/non-PBS script products are marked with an*

CYCLIC MENOPAUSAL HORMONE THERAPY (MHT)

Use continuous oestrogen and cyclic progestogen combinations at peri-menopause or if less than 12 months amenorrhoea

LOW DOSE		
PRODUCT	**PRESENTATION**	**COMPOSITION**
Femoston	tablet	1mg oestradiol/10mg dydrogesterone
Estrogel Pro*	Combination pack of oestradiol transdermal gel, with micronised progesterone capsules.	1 pump (0.75mg oestradiol) daily, and 2 capsules (200mg) micronised progesterone orally for 12 days out of a 28-day cycle
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)
Estrogel Pro*	Combination pack of oestradiol transdermal gel, with micronised progesterone capsules.	2 pumps (1.5mg oestradiol) daily, and 2 capsules (200mg) micronised progesterone orally for 12 days out of a 28-day cycle

CONTINUOUS COMBINED MENOPAUSAL HORMONE THERAPY (MHT)

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
Estrogel Pro*	Combination pack of oestradiol transdermal gel, with micronised progesterone capsules.	1 pump (0.75mg oestradiol) daily, and 1 capsule (100mg) micronised progesterone orally for 25 days out of a 28-day cycle^
OTHER LOW DOSE HORMONAL OPTIONS		
Livial*, Xyvion*	tablet	2.5mg tibolone
Duavive* (oestrogen/SERM combination)	tablet	0.45mg conjugated equine oestrogens / 20mg bazedoxifene
MEDIUM DOSE		
Kliogest*	tablet	2mg oestradiol/1mg norethistrone
Estalis continuous 50/140	transdermal patch	50mcg 17 B oestradiol/140mcg norethisterone acetate (twice weeklyapplication)
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)
Estrogel Pro*	Combination pack of oestradiol transdermal gel, with micronised progesterone capsules.	2 pumps (1.5mg oestradiol) daily, and 1 capsule (100mg) micronised progesterone orally for 25 days out of a 28-day cycle^

^Can be given daily if adherence is an issue

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EMPOWERING MENOPAUSAL WOMEN
www.menopause.org.au

https://www.menopause.org.au/hp/information-sheets/426-ams-guide-to-equivalent-mht-hrt-doses

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)
Estrogel*	gel	0.75mg oestradiol = 1 pump
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)
Estrogel*	gel	1.5mg oestradiol = 2 pumps
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)
Estrogel*	gel	2.25mg oestradiol = 3 pumps or 3.0mg oestradiol = 4 pumps

OESTROGEN ONLY VAGINAL THERAPY

If prescribing vaginal oestrogen rather than systemic hormone therapy, a progestogen is not required.

PRODUCT	PRESENTATION	COMPOSITION
Ovestin	cream	1mg/g oestriol
Ovestin	pessary	0.5mg 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
Prometrium*	capsule	100mg micronised progesterone orally for 25 days out of a 28-day cycle^ or 200mg orally daily for 12 days out of a 28-day cycle
Mirena*(PBS indication for contraception/menorrhagia)	device (5 years)	20mcg/24hrs levonorgestrel
MEDIUM DOSE for use with medium dose oestrogen		
PRODUCT	**PRESENTATION**	**COMPOSITION**
Primolut N (1/4 of 5mg tablet)	tablet	1.25 mg norethisterone
Provera, Ralovera	tablet	5mg medroxyprogesterone acetate
Prometrium*	capsule	100mg micronised progesterone orally for 25 days out of a 28-day cycle^ or 200mg orally for 12 days out of a 28-day cycle
Mirena*(PBS indication for contraception/menorrhagia)	device	20mcg/24hrs levonorgestrel (5 years)
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
Prometrium*	capsule	200mg orally daily for 12 days out of a 28-day cycle. Safe continuous dose unknown due to insufficient data

^Can be given daily if adherence is an issue

Low dose progestogen-only contraceptive pills (Microlut (30mcg levonorgestrel), and Noriday (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).

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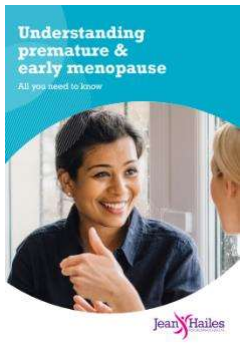
Consumer booklets and multilingual fact sheets



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