

Management of vasomotor and genitourinary symptoms of menopause

Quick Reference Guide

This quick reference guide (QRG) is informed by the RANZCOG Management of vasomotor and genitourinary symptoms of menopause guideline. It provides evidence-based guidance for health care professionals to support women experiencing vasomotor and genitourinary symptoms associated with menopause.

How is menopause diagnosed and what tests are needed?

The time of menopause is most typically defined in retrospect after 12 months of amenorrhoea. The mean age for menopause is 51 years in Australia (with a range of 45 to 55 years). Perimenopause (the transition phase prior to menopause) is based on a combination of factors, including age, irregular or absent menstrual periods and the presence of menopausal symptoms, and was out of scope for the guideline.

Diagnostic investigations, including imaging and hormone levels, are not routinely recommended for determining menopause stage in women over 45 years of age. If the diagnosis is unclear, blood tests or scans may rule out other medical conditions. Women with GUS should be offered a genital exam to assess for other possible causes or contributors to their symptoms. Women who start MHT should be encouraged to participate in breast screening according to local protocols.

What are the symptoms of menopause?

Vasomotor symptoms (VMS)

Hot flushes and night sweats affect up to 75% of women at the time of menopause. These symptoms are associated with a decrease in estrogen levels. Hot flushes can vary from a transient feeling of warmth to a sudden heat that spreads over the upper body and face, causing reddening of the skin and marked sweating. They can last from a few seconds to a few minutes and can happen during the day or night with varying frequency. During sleep severe sweating may occur making it difficult to get back to sleep.

Genitourinary symptoms (GUS)

Dryness of the vagina and vulva are the most common GUS. These symptoms are related to a decrease in estrogen involving changes to the labia majora and minora, clitoris, vestibule, introitus, vagina, urethra and bladder. Symptoms may include genital symptoms of dryness, burning, and irritation of the vulva and vagina; sexual symptoms of lack of lubrication, discomfort or sexual pain, and impaired function; or urinary symptoms of urgency, dysuria and recurrent urinary tract infections.

Other symptoms

RANZCOG acknowledges the increasing number of reported symptoms and signs associated with menopause transition such as depression and anxiety, stiff or painful joints, migraine, change in sexual desire (libido), mood change, cognitive function or quality of life. These topics were out of scope for this guideline and not covered in this QRG. Women with current, past or a high inherited risk (BRCA1 and/or BRCA2) of breast cancer and menopause symptoms are also not covered in this quick reference guide, but are in the full guideline.

<https://ranzco.org.au/wp-content/uploads/Managing-Menopausal-Symptoms.pdf>

How can vasomotor or genitourinary symptoms of menopause be managed?

Not all women with symptoms require a pharmacological intervention, whereas others may experience symptoms that make it hard to perform daily activities. There are various options of pharmacological treatments listed in the tables below. Be aware that some medications may not be available or subsidised.

For troublesome hot flushes and night sweats (vasomotor symptoms):

Menopausal hormone therapy (MHT)

Previously known as HRT (hormone replacement therapy), MHT is recommended as a first line pharmacological treatment for people seeking treatment for vasomotor symptoms (see tables below for more details).

- MHT can help with vasomotor symptoms associated with menopause where there are no contraindications
- MHT (estrogen component) can be used orally (pills), or transdermally (skin patches, gels, and sprays)
- MHT (progestogen component) can be used orally (pills), transdermally (skin patch) or as an IUD
- Transdermal estrogen is likely to have fewer risks of adverse events (VTE or gallbladder disease) than oral estrogen
- There is little difference in the effectiveness between the different preparations of MHT
- Ideally start with the lowest dose and increase according to individual requirements
- Women using MHT should be reviewed annually, and the benefits and risks of continuing or stopping treatment should be discussed
- Women who want to stop taking MHT should be advised that they can stop at any time, but that symptoms may occur

- Women aged > 60 years old who are considering starting MHT should be advised of the small increased risk of cardiovascular events (including stroke), venous thrombosis and dementia with oral MHT. Transdermal preparations are not associated with an increased VTE risk, however evidence is limited in this age group
- MHT is not recommended for the treatment of VMS for women with current or past breast cancer
- Women without a uterus do not need progestogen
- Commonly reported side effects include unscheduled bleeding, breast tenderness, headaches and bloating.

Contraindications for menopausal hormone therapy (oral and transdermal)

This list was developed using information from Australian and Aotearoa New Zealand regulatory body websites and oral and transdermal MHT websites.

- Known or suspected hormone-dependent malignancy (including breast and endometrial cancer)
- Active or history* of coronary heart disease, stroke, myocardial infarction or thromboembolism
- Unexplained vaginal bleeding
- Untreated endometrial hyperplasia
- Active or chronic liver disease
- Inherited high risk of thromboembolic disease*
- Severe uncontrolled hypertension
- Porphyria
- Severe hypertriglyceridemia (contraindicated for oral MHT, not transdermal MHT)

Additional considerations

- For women with a uterus, estrogen-only therapy is contraindicated, as they require progestogen for endometrial protection
- There are no contraindications to MHT for women with epilepsy, migraine, malabsorption, gallbladder disease, or receiving thyroid therapy. Transdermal preparations are preferable

** requires a case by case discussion.*

Non-hormonal pharmacological treatments:

- Oxybutynin: decreases symptoms but has side effects that may include dry mouth (50%), gastrointestinal symptoms, urinary tract infections
- Other treatments: neurokinin 3 receptor antagonists (like fezolinetant), antidepressants and gabapentin reported small improvements for VMS.

Non-pharmacological treatments:

- Some women might prefer non-pharmacological interventions such as hypnosis, acupuncture, and cognitive behavioural therapy (CBT), although the evidence varies for VMS improvement. Hypnosis may slightly decrease vasomotor symptoms and improve sleep, but the evidence is uncertain for CBT and acupuncture.
- The guideline did not consider the following complementary and alternative medicines (CAM), including vitamins, minerals, meditation, herbal medicines, aromatherapy, and traditional Chinese medicine. There is limited evidence about their effectiveness and safety.

Lifestyle interventions

- There is a lack of evidence that exercise has direct benefit for VMS frequency and severity. Improvement in mental health, cognitive function, sleep, muscle mass and bone density, are well established.
- Low quality studies report that women with increased body mass index (BMI) experience more VMS than women with normal BMI. The effectiveness of weight loss for VMS is uncertain.

For troublesome genitourinary symptoms:

Local therapy consists of treatments that are delivered into the vagina to target localised symptoms. They have minimal absorption into the body. They can be delivered as vaginal cream, pessary, tablet or ring (depending on local product availability). Local therapy can be used alongside systemic hormone therapy.

- Vaginal estrogens are likely to improve vulvovaginal dryness and pain with sex. They can be used as a cream, pessary, tablet or ring according to availability and individual preferences. They can be used in combination with vaginal moisturisers or lubricants.
- Vaginal DHEA (if available) could be considered as an alternative to vaginal estrogen as it is likely to be helpful for vulvovaginal dryness and pain with sex.
- CO₂ lasers are not recommended for the treatment of genitourinary symptoms, as evidence suggests it does not improve genitourinary symptoms.
- It is uncertain if vaginal oxytocin gel, vaginal testosterone and laser (Er:YAG) help or not due to limited evidence.

How long should women use MHT and other pharmacological treatment for?

- There are no time limits for therapy.
- Women can stop at any time (either gradually or completely); however, symptoms may occur.
- The decision to continue or stop treatment may differ depending on age, severity of symptoms, other medical conditions and individual risk factors and preferences.

Relevant resources:

Osteoporosis

This topic was out of scope for this guideline. RANZCOG suggests further information about osteoporosis can be found:

- RACGP - Osteoporosis management and fracture prevention in post-menopausal women and men > 50 years of age
<https://www.racgp.org.au/getattachment/487c5b92-7bd0-4b1c-86f5-2d86c649f92f/Osteoporosis-management-and-fracture-prevention-in-post-menopausal-women-and-men-50-years-of-age.aspx>
- Breaking a Bone and Bone Health - Healthy Bones Australia
<https://healthybonesaustralia.org.au/resource-hub/fact-sheets/breaking-bone/>

Breast Cancer

RANZCOG suggests further information about breast cancer risk can be found:

- Breast Cancer Risk Calculator For Women Aged 25-54 Years
<https://www.breastnet.nz/topic/risk-calculator>
- Cancer Australia: Check Your Cancer Risk online tool
<https://cancer-risk-calculator.org/>
- PeterMac. iPrevent tool
<https://www.petermac.org/patients-and-carers/health-services-for-cancer-patients/cancer-prevention/iprevent>

Premature Ovarian Insufficiency (POI)

RANZCOG suggests further information about POI can be found:

- Guideline on premature ovarian insufficiency
<https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Premature-ovarian-insufficiency>

Medications

Table 1. Continuous combined (estrogen and progestogen) MHT

Should be used if 12 months since last menstrual period, or after 12 months of receiving cyclical (sequential) MHT. Unscheduled bleeding after three months of therapy should be reviewed.

Hormone (delivery)	Trade name	Low dose	Moderate dose	High dose	Registered	
					NZ	AUS
Estradiol + norethisterone acetate (oral)	Kliovance®/ Kliogest®	Kliovance® 1 mg estradiol/0.5mg norethisterone acetate (daily)	Kliogest® 2 mg estradiol/1mg norethisterone acetate (daily)	n/a	yes	yes
Estradiol + micronised progesterone (oral)	Bijuva®	1mg estradiol/ 100mg micronised progesterone (daily)	n/a	n/a	no	yes
Estradiol + dydrogesterone (oral)	Femoston®	Femoston® 1/10: 1mg estradiol/5mg dydrogesterone (daily)	Femoston® 2/10: 2mg estradiol, 10mg dydrogesterone (daily)	n/a	no	yes
Estrogen + SERM combination (oral)	Duavive®	0.45 mg conjugated equine estrogens/20 mg bazedoxifene acetate (daily)	n/a	n/a	no	yes
Estradiol + drospirenone (oral)	Angeliq®	1mg estradiol/2 mg drospirenone (daily)	n/a	n/a	no	yes
Estradiol + norethindrone (transdermal)	Estalis®	16 cm ² patch (applied twice weekly = 50µg estradiol and 250µg norethindrone acetate per day). Option for continuous or cyclical use.	n/a	n/a	no	yes
Estradiol gel (transdermal) + micronised progesterone (oral)	EstroGel Pro®	1 pump gel (0.75 mg of estradiol) + 100mg micronised progesterone	2 pumps gel + 100mg micronised progesterone	3 pumps gel + 100mg micronised progesterone ¹	yes	yes
Other continuous treatment						
Tibolone (oral)	Livial®, Xyvion®	2.5 mg tibolone	n/a	n/a	yes	yes

1. There are limited data for the dose of micronised progesterone with high-dose estrogen. The above regimen is currently recommended; however, if bleeding is an issue and investigations are normal, then micronised progesterone may need to be increased to 200mg daily for continuous combined MHT.

Table 2. Cyclical (sequential) combined (estrogen and progestogen) MHT

Should be used if within 12 months since last menstrual period.

Hormone	Trade name	Low dose	Moderate dose	High dose	Registered	
					NZ	AUS
Estradiol norethisterone acetate combination (oral)	Trisequens®	n/a	Twelve 2mg estradiol tablets, ten 1mg estradiol with 1mg norethisterone acetate, six 1mg estradiol tablets	n/a	yes	yes
Continuous estrogen + 12-14 days of progesterone	See Table 3a and 3b for options for estrogen and progestogens	n/a	n/a	n/a	yes	yes
Estradiol gel (transdermal) + micronised progesterone (oral)	EstroGel Pro®	1 pump (daily) + 200mg for 12 to 14/ 28 days	2 pumps (daily) + 200mg for 12 to 14/ 28 days	3 pumps (daily) + 200mg for 12 to 14/ 28 days ²	no	yes

2. There are limited data for the dose of micronised progesterone with high-dose estrogen. The above regimen is currently recommended; however, if bleeding is an issue and investigations are normal, then micronised progesterone may need to be increased to 300-400mg for 12-14 days for cyclical MHT

Table 3a. Estrogen and progestogen hormones (either estrogen alone or in combination)

Combinations should start with low-dose estradiol and low-dose progestogen.

Estrogen - Prescribe estrogen only if the patient has had hysterectomy or has a Mirena <5 years						
Hormone product	Trade name	Low dose	Moderate dose	High dose	Registered	
					NZ	AUS
Estradiol hemihydrate (oral)	Estrofem®	1mg estradiol hemihydrate	2mg estradiol hemihydrate	n/a	yes	yes
Estradiol valerate (oral)	Progynova®	1mg estradiol valerate	2mg estradiol valerate	n/a	no	yes
Estradiol patch (transdermal)	Estradot®	25mcg/ day estradiol (twice weekly)	50mcg/ day estradiol (twice weekly)	75 or 100 mcg/day estradiol (twice weekly)	no	yes
	Mylan®	0.025mg/ day (twice-weekly)	0.05mg/ 24 hrs estradiol (twice weekly)	0.075-1.0mcg/ day (twice weekly)	yes	yes
Estradiol patch (transdermal)	Estradot®	25mcg/ day estradiol (twice weekly)	50mcg/ day estradiol (twice weekly)	75 or 100 mcg/day estradiol (twice weekly)	yes	yes
	Sandrena®	1 sachet daily	2 sachet daily	3 sachet daily	no	yes
Estradiol spray (transdermal)	Lenzetto®	Estradiol 1.53 mg = 1 spray	2 sprays per day	3 sprays per day	no	yes
Conjugated equine estrogen (oral)	Premarin®	0.3mg conjugated equine estrogen	0.625mg conjugated equine estrogen	n/a	yes	yes

Table 3b. Estrogen and progestogen hormones (either estrogen alone or in combination)

Combinations should start with low-dose estradiol and low-dose progestogen.

Progestogen - May be given sequentially (cyclically) – daily dose for 12-14 days a month or as a daily dose in continuous combined (CC) regimens for endometrial protection. Progestogen is unnecessary if the patient has had a hysterectomy or a Mirena<5 years						
Hormone product	Trade name	Low dose	Moderate dose	High dose	Registered	
					NZ	AUS
Medroxyprogesterone acetate (oral)	Provera®	2.5mg (1/2 of 5mg)	5mg	10mg	yes	yes
Norethisterone acetate (oral)	Primulot N®	1.25mg (1/4 of 5mg)	2.5mg (1/2 of 5mg)	5mg	yes	yes
Micronised Progesterone (oral)	Utrogestan®	100mg daily for CC	100mg daily for CC	100mg daily for CC	yes	yes
	Prometrium®	OR 200mg for 14/28 days for cyclical	OR 200mg for 14/28 days for cyclical	OR 200mg for 12-14 /28 days for cyclical ³	no	yes
52mg of levonorgestrel (IUD) (transdermal)	Mirena®	n/a	n/a	n/a	yes	yes

3. There are limited data for the dose of micronised progesterone with high-dose estrogen. The above regimen is currently recommended; however, if bleeding is an issue and investigations are normal, then micronised progesterone may need to be increased to 300-400mg for 12-14 days for cyclical MHT

Table 4. Estrogen only vaginal therapy

Product	Presentation	Composition	Regimen	Registered	
				NZ	AUS
Estriol (Ovestin®)	Vaginal cream Vaginal pessary	0.5 mg estriol per cream applicator or pessary	One dose daily for 2–3 weeks, then reduce to twice weekly maintenance	yes	yes
Conjugated equine estrogen cream (Premarin®)(oral)	Vaginal cream	0.625mg/g	0.5–2 g daily initially, then maintenance dosing	no	yes
Estradiol vaginal tablet (Vagifem Low®) Progesterone (oral)	Vaginal tablet	10mcg estradiol	One tablet daily for 2 weeks, then one tablet twice weekly	no	yes
Prasterone (DHEA) (Intrarosa®)(IUD) (transdermal)	Vaginal pessary	6.5mg	DHEA inserted nightly	no	yes

Table 5. Non-hormonal treatments for vasomotor symptoms

Class of drug	Drug name	Starting dose	Available	
			NZ	AUS
SSRI low dose	Escitalopram	5mg	yes	yes
	Paroxetine	10mg	yes	yes
SNRI low dose	Venlafaxine	37.5mg	yes	yes
	Desvenlafaxine	50mg	no	yes
Neurokinase 3 antagonist	Fezolinetant	45 mg daily	no	yes
Anticholinergic	Oxybutynin	2.5–5 mg bd	yes	yes
Gabapentinoid	Gabapentin	100 mg nocte	yes	yes

Summary of management of vasomotor and genitourinary symptoms associated with menopause

Vasomotor or genitourinary symptoms associated with menopause in women >40yrs

Comprehensive assessment including for common and troublesome symptoms of menopause

- Frequency and severity of hot flushes
- Night sweats
- Vaginal dryness/soreness
- Bladder/urinary symptoms

Share information about common and troublesome symptoms of menopause

- Discuss other possible contributors to symptoms for the person (environment and lifestyle).
- Provide support to maintain general health and have other evidence- and risk-based health checks including breast screening.
- Enquire about symptoms associated with menopause among First Nations, Māori and Pacific women and other people who may experience significant barriers to treatment, including cost of medication, rural access, language or cultural differences.

Vasomotor symptoms

Hormonal treatment

Discuss benefits and risks of MHT treatment (contraindications, side effects, and availability).

Menopausal Hormone Therapy

Systemic MHT (transdermal, oral, or tibolone) improves vasomotor symptoms

- Women with a uterus should have progestogen in combination with estrogen therapy to protect the endometrium
- No difference between preparations of estrogen and progesterone
- Start with the lowest dose and increase if symptoms persist
- Review annually and discuss continuing or stopping treatment
- Treatment can stop at any time (either gradually or completely)
- Women > 60 yo have small increased risk with oral MHT for cardiovascular events, venous thrombosis and dementia
- Not recommended for women with current or past breast cancer.

Non-hormonal and non-pharmacological treatment

Non-pharmacological treatment can be used separately or at the same time as MHT.

Offer:

- Oxybutynin: improves symptoms.

Consider (small benefit):

- Neurokinin 3 receptor antagonists (NK3R) (e.g. fezolinetant) May be associated with dry mouth, nausea, GI symptoms, or fatigue. Uncommon or rare serious adverse events include liver injury. LFTs are recommended, see the full guideline for details.
- SSRIs/ SNRIs* Women taking tamoxifen for breast cancer should not be prescribed paroxetine or fluoxetine. May be associated with dry mouth, nausea, GI symptoms, or insomnia.
- Gabapentin May be associated with nausea, dizziness or somnolence.

Discuss:

- Hypnosis: may improve VMS and sleep
- Exercise such as aerobic exercise, resistance training, and yoga: may improve VMS, quality of life, mental health, cognitive function, sleep, muscle mass and bone density.
- Cognitive behavioural therapy (CBT): not recommended as first-line treatment.

Not recommended:

Clonidine, stellate ganglion block, acupuncture.

*SSRI: Selective serotonin reuptake inhibitors; SNRI: serotonin–norepinephrine reuptake inhibitors.

Genitourinary symptoms

Offer a genital exam to women with GUS to assess for other possible causes or contributors to their symptoms.

Treatment options

All options can be used with systemic MHT.

Vaginal estrogen improves vulvovaginal dryness and pain with sex.

- Can be used with, vaginal moisturisers or lubricants
- May weaken latex condoms (up to 72 hours after use).

Vaginal DHEA improves vulvovaginal dryness and pain with sex.

Vaginal oxytocin gel, the addition of oral raloxifene to oral estrogen, vaginal testosterone and laser Er YAG. There is limited evidence for these treatments. There are no recommendations for their use.

Contraindications for menopausal hormone therapy (oral and transdermal)

- Known or suspected hormone-dependent malignancy (including breast and endometrial cancer)
- Active or history* of coronary heart disease, stroke, myocardial infarction or thromboembolism
- Unexplained vaginal bleeding
- Untreated endometrial hyperplasia
- Active or chronic liver disease
- Inherited high risk of thromboembolic disease*
- Severe uncontrolled hypertension
- Porphyria
- Severe hypertriglyceridemia (contraindicated for oral MHT, not transdermal MHT)

There are no contraindications to MHT for women with epilepsy, migraine, malabsorption gallbladder disease or receiving thyroid therapy. Transdermal preparations are preferable.

*requires a case by case discussion.



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