# Managing menopause

## Nonhormonal treatment options

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**When menopausal hormone therapy is not appropriate for or not desired by women who seek help with menopausal symptoms, a variety of nonhormonal pharmacotherapies and nonpharmacological treatments are available. Flexibility and shared decision making are key in finding effective, acceptable therapy for each woman.**

Menopause is a normal hormonal transition occurring around the time of a woman's last period. It may occur naturally, on average at around 50 years of age, or it may occur as a result of surgical removal of the ovaries or chemotherapy and radiotherapy treatment for some cancers. Given the prevalence of menopausal symptoms and their potential to have a significant impact on daily functioning, it is important for clinicians to be comfortable and confident in discussing menopausal symptoms, their impact on quality of life and the available treatment options.

Hormone therapy has been shown to be the most effective treatment for menopausal symptoms;[1,2] however, menopausal hormone therapy may not be appropriate for all women, including those receiving treatment for breast cancer, those with a history of venous thromboembolism or cardiovascular disease, or women seeking an alternative to menopausal hormone therapy. This article aims to equip clinicians to manage menopausal symptoms with nonhormonal treatments. Information for health professionals is also available on the Australasian Menopause Society website (https://www.menopause.org.au/hp/information-sheets), as well as fact sheets for consumers.

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### Clinical presentation

The most common presenting menopausal symptom is hot flushes, which may affect up to 80% of menopausal women.[3] Other symptoms and signs may include reduced libido, disturbed sleep, and vaginal dryness and irritation that may lead to painful intercourse. Mood disturbance is also common in the menopausal period and may affect up to 40% of menopausal women.[4] Although a combination of psychological and biological factors is likely to be at play, women with hot flushes are more likely to suffer mood disturbance, a risk which appears to be independent of previous depression.[5,6] Clinicians should be mindful of the range of menopausal symptoms and, more importantly, note how problematic they are to a woman's daily functioning, as this will help to guide treatment selection.

### Nonhormonal pharmacotherapies

Selective serotonin reuptake inhibitors (SSRIs), including escitalopram, paroxetine and sertraline, and serotonin-noradrenaline reuptake inhibitors (SNRIs), such as venlafaxine and desvenlafaxine, have been shown to be effective for reducing both the severity and frequency of hot flushes.[7,8] It is unclear whether one type of medication is more efficacious than any other as there is a lack of high-level head-to-head data directly comparing their performance. However, escitalopram, venlafaxine, desvenlafaxine and paroxetine have more consistently been shown to be effective in reducing hot flushes.[7-11]

The dosages of SSRIs and SNRIs used in the treatment of vasomotor symptoms are often less than that used for the treatment of depression, and this is an important point to discuss with patients, some of whom may be concerned about taking an antidepressant medication. Commonly used doses include, for example:

- venlafaxine, 37.5 mg daily increasing to 75 mg as needed
- desvenlafaxine, 100 mg daily
- escitalopram, 10 to 20 mg daily
- paroxetine, 10 to 20 mg daily.

The effect on vasomotor symptoms of these medications is more

rapid than their effect on mood symptoms, with an effect usually seen within the first few weeks of treatment. As with any new medication, the lowest possible dose that offers symptom improvement and minimises side effects should be used. Side effects may include nausea, dry mouth, somnolence and dizziness.

It is important to note that some SSRIs, including paroxetine, may impair the metabolism and efficacy of tamoxifen, a hormone receptor modulator often used in the treatment of breast cancer.[12] As a result, nonhormonal therapies, including SSRIs, should be carefully considered for women taking tamoxifen. Care should also be taken to avoid other drug interactions, particularly the effect of any complementary medicines, such as St. John's wort, which poses a risk of serotonin syndrome when taken with antidepressants.

Clonidine is an alpha-adrenergic agonist that has been shown to reduce the frequency of hot flushes. Compared with placebo, both the oral and transdermal formulations have been shown to reduce hot flush frequency and severity with eight to 12 weeks of treatment.[13-15] There are no studies directly comparing efficacy by route of administration. Several studies have compared clonidine to venlafaxine and have shown venlafaxine to have an earlier onset of action, but clonidine to be more efficacious over longer treatment courses of more than 12 weeks at a dose of 0.1 mg per day.[15-17]

Gabapentin is an anticonvulsant and neuropathic pain relief medication that has been found to be effective at reducing hot flushes. Several randomised controlled trials in women with and without breast cancer showed gabapentin reduced the frequency and severity of hot flushes by around 45% when given in doses of 900 mg.[18] Clinically, gabapentin is often given at a dose of 300 mg three times daily. Doses lower than this appear to offer minimal benefit.[18] It may be useful to start dosing in the evening if nighttime vasomotor symptoms and sleep disturbance are predominant symptoms. A starting dose of 300 mg at night may be uptitrated over several weeks, adding in daytime doses as tolerated by the patient. Side effects of gabapentin include somnolence and dizziness. A recent systematic review showed no clinical difference in efficacy between venlafaxine and gabapentin, but over two-thirds of patients preferred venlafaxine.[12]

Clonidine is the only nonhormonal pharmacotherapy discussed here that is approved by the TGA for use in treating menopausal symptoms (specifically, hot flushes). Use of SSRIs, SNRIs and gabapentin is off-label use.

Herbal remedies including black cohosh and Chinese herbal medicines have received attention for the potential treatment of vasomotor symptoms associated with menopause. However, their use is not recommended because there is insufficient evidence with regard to efficacy and safety.[19,20] Similarly, phytoestrogens, or isoflavones, are a group of phytochemicals with oestrogen-like activity, commonly found in soy-containing foods. Extensive research has not shown any superiority of phytoestrogens over placebo for reducing menopausal symptoms and their use is currently not recommended.[21]

Women may also seek treatment for vulvovaginal symptoms, including vaginal dryness and irritation or painful intercourse. Some women wanting to avoid systemic hormone therapy may find vaginal oestrogen acceptable, and this option should be explored. There is a wide range of over-the-counter vaginal moisturisers and lubricants available, yet high-level evidence does not show greater efficacy when they are compared with placebo.[22] The OVERcome study showed an improvement in quality of life and reduced dyspareunia with a combination of olive oil lubrication for intercourse, pelvic floor exercises and regular vaginal moisturisation in a cohort of breast cancer patients.[23] Further research is needed to evaluate how this translates to the general population. Vaginal symptoms and their impact on sexual function should be discussed with menopausal women, and multidisciplinary care including physiotherapy and sexual or psychological counselling should be considered.

## Nonpharmacological treatment

Several nonpharmacological interventions have been studied for evaluation of their impact on menopausal symptoms, including acupuncture, relaxation techniques and exercise. Currently, there is insufficient evidence to show their efficacy in treating menopausal symptoms, particularly hot flushes.[24] However, cognitive behavioural therapy has been shown to improve menopausal symptoms and is recommended in current menopause guidelines as a treatment to be considered.[21] Optimisation of health, including weight loss, dietary advice, smoking cessation and exercise, should be addressed during menopause as part of comprehensive, patient-focused care involving disease prevention in the ageing woman.

## Conclusion

Every woman will experience menopause differently, and this may be influenced by their age, cultural background and menopausal trigger. Not all women will be bothered by their symptoms, so not all will require treatment. Some women will seek nonhormonal treatment options, although for others hormonal treatments may be contraindicated. For these patients there is a range of nonhormonal treatments available. Clinicians should aim to make individualised treatment decisions through a process of shared decision making to find appropriate and effective treatment for each woman, ultimately aiming for the lowest dose that provides symptom relief. MT

## References

A list of references is included in the online version of this article (www.medicinetoday.com.au).

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