

sexual interest, arousal, and orgasmic response independent from its role in treating menopause symptoms.¹⁰⁶⁻¹⁰⁸

If systemic hormone therapy is indicated in women with low libido, transdermal ET formulations may be preferred to oral, given increased sex hormone-binding globulin and reduced bioavailability of testosterone with oral ET.^{105,109,110}

Conjugated equine estrogens combined with BZA relieves dyspareunia and improves some aspects of sexual function in postmenopausal women.¹¹¹⁻¹¹⁴

Key points

Vasomotor symptoms

- Vasomotor symptoms may begin during perimenopause, and frequent VMS may persist on average 7.4 years or longer. They affect quality of life and may be associated with CV, bone, and brain health. (Level I/II)
- Hormone therapy remains the gold standard for relief of VMS.
 - Estrogen-alone therapy can be used for symptomatic women without a uterus. (Level I)
 - For symptomatic women with a uterus, EPT or a TSEC protects against endometrial neoplasia. (Level I)
- Shared decision-making should be used when considering formulation, route of administration, and dose of hormone therapy for menopause symptom management, with adjustment tailored to symptom relief, AEs, and patient preferences. (Level III)
- Periodic assessment of the need for ongoing use of hormone therapy should be individualized on the basis of a woman's menopause symptoms, general health and underlying medical conditions, risks, treatment goals, and personal preferences. (Level III)
- Micronized progesterone 300 mg nightly significantly decreases VMS (hot flashes and night sweats) compared with placebo and improves sleep. Synthetic progestins have also shown benefit for VMS in some studies. No long-term study results are available, and use of progestogens without estrogen for either indication is off-label. (Level II)

Sleep disturbances

- During the menopause transition, women with VMS are more likely to report disrupted sleep. (Level I)
- Hormone therapy improves sleep in women with bothersome nighttime VMS by reducing nighttime awakenings. Estrogen may have some effect on sleep, independent of VMS. (Level II)

Genitourinary symptoms

- Low-dose vaginal ET preparations are effective and generally safe for the treatment of GSM, with minimal systemic absorption, and are preferred over systemic therapies when ET is used only for genitourinary symptoms. (Level I)
- For women with breast cancer, low-dose vaginal ET should be prescribed in consultation with their oncologists. (Level III)
- Progestogen therapy is not required with low-dose vaginal estrogen, but RCT data are lacking beyond 1 year. (Level II)
- Nonestrogen prescription FDA-approved therapies that improve VVA in postmenopausal women include ospemifene and intravaginal DHEA. (Level I)

- Vaginal bleeding in a postmenopausal woman requires thorough evaluation. (Level I)

Urinary tract symptoms (including pelvic floor disorders)

- Systemic hormone therapy does not improve urinary incontinence and may increase the incidence of stress urinary incontinence. (Level I)
- Low-dose vaginal ET may provide benefit for urinary symptoms, including prevention of recurrent UTIs, overactive bladder, and urge incontinence. (Level II)
- Hormone therapy does not have FDA approval for any urinary health indication. (Level I)

Sexual function

- Both systemic hormone therapy and low-dose vaginal ET increase lubrication, blood flow, and sensation of vaginal tissues. (Level I)
- Systemic hormone therapy generally does not improve sexual function, sexual interest, arousal, or orgasmic response independent of its effect on GSM. (Level I)
- If sexual function or libido are concerns in women with menopause symptoms, transdermal ET may be preferable over oral ET because of minimal effect on sex hormone-binding globulin and free testosterone levels. (Level II)
- Low-dose vaginal ET improves sexual function in postmenopausal women with GSM. (Level I)
- Nonestrogen alternatives FDA approved for dyspareunia include ospemifene and intravaginal DHEA. (Level I)

PRIMARY OVARIAN INSUFFICIENCY

Women with loss of ovarian function at a young age experience an extended period without ovarian hormones compared with women experiencing menopause at the typical age. Premature menopause is defined as menopause before age 40 years, and early menopause is defined as menopause that occurs between the ages of 40 and 45 years. Whereas menopause implies the permanent cessation of menses, POI describes the loss of ovarian function before age 40 years but with the potential for intermittent, transient return of hormone production and menstrual cycles. Women with early or premature loss of ovarian function at any age are at increased risk for AEs related to ovarian hormone deficiency. Causes of early or premature loss of ovarian function may be genetic, autoimmune, toxic, metabolic, and iatrogenic, including chemotherapy, radiation, and surgery.

Health risks of POI and premature menopause are well documented.^{40,41} The strongest evidence from meta-analyses and systematic reviews links early loss of ovarian function to decreased quality of life and increased risk of fracture, CVD, heart failure, diabetes mellitus (DM), and overall mortality.¹¹⁵⁻¹²¹ Other significant issues may include persistent VMS, loss of fertility, bone loss, genitourinary symptoms, sexual dysfunction, cognitive and mood changes, and increased risk of dementia, ophthalmic conditions, and depression.^{40,41,122-124} Although these risks are generally because of estrogen deficiency, some of these risks may be reflective of premature aging, as evidenced in some studies by shortened telomere length.¹²⁵