

Prescription hormonal drugs—including contraceptives, menopause hormone therapy (HT), androgens, selective estrogen-receptor modulators (SERMs; now termed estrogen agonists/antagonists by the US Food and Drug Administration)—and over-the-counter (OTC) hormone treatments are among the treatments considered for women during perimenopause and beyond. The majority are government approved for the indication(s) for which they are most commonly prescribed (see Box), whereas some are prescribed “off label” (ie, used for an indication other than the government-approved indication). OTC hormone treatments are classified as dietary supplements (“natural health products” in Canada) and are approved differently from prescription drugs. Hormonal drugs that are custom compounded from a prescription are not government approved, although some active ingredients meet the specifications of the United States *Pharmacopeia* (USP) (see page 218 for more about custom-compounded hormones).

What Does Government Approval Mean?

In the prescription drug approval process in the United States, a manufacturer sends study information on a particular product for a particular health indication to the US Food and Drug Administration (FDA). The FDA then considers the product’s effectiveness, dosage, side effects, and possible short-term and long-term risks. If FDA approval is given, the product may then be offered on the US market for the approved health indication(s), accompanied by the FDA-approved product labeling (ie, prescribing information or package insert). All advertising and education from the manufacturer must comply with the prescribing information. In Canada, a similar regulatory process exists with the Therapeutic Products Directorate of Health Canada.

Once a drug is on the market clinicians can legally prescribe it for “off-label” (unapproved) indications (eg, prescribing an oral contraceptive to treat hot flashes). This is a common medical practice that relies on additional research and clinical experience documenting safety, efficacy, and dose. Also, in certain US states with the patient’s permission, a pharmacist can substitute a generic equivalent drug, if available, for the one that was prescribed.

Clinicians can also legally write an individual prescription for a custom drug formulation that is mixed (compounded) by a pharmacist. Although the active ingredient(s) is government approved, the formulation is not.

OTC products are regulated differently from drugs, with the marketer not being required to prove efficacy, safety, and proper dose. These are regulated as “dietary supplements” (“natural health products” in Canada) even though they may not be used orally (see Section H, page 237, for more about how dietary supplements are regulated).

Contraceptives

Despite a decline in fertility during perimenopause, pregnancy is still possible until menopause is reached. Perimenopausal women who wish to guard against an unwanted pregnancy should be counseled regarding various birth control methods (see Section C, page 29, for more about fertility and nonhormonal options for birth control). Hormonal contraceptives—both with and without estrogen—offer a viable option for more perimenopausal women. Readers are referred to standard texts for listings of available hormonal contraceptives and their respective government-approved labeling (prescribing information).

Perimenopausal women should be aware that use of oral contraceptives (OCs) or any other hormonal or intrauterine contraceptive method does not reduce the risk of acquiring sexually transmitted infections (STIs). Accordingly, women at risk should protect themselves through use of “safer sex” practices (see Section C, page 156, for more about avoiding STIs).

Combination (estrogen-progestin) contraceptives. Many oral and nonoral options are available when prescribing a combination contraceptive (ie, containing estrogen and progestin).

Labeling for all estrogen-containing contraceptives in the United States and Canada contains a black box warning that cigarette smoking increases the risk of serious cardiovascular side effects from hormonal contraceptive use, and that this risk increases with age and with heavy smoking (≥ 15 cigarettes/d) and is quite marked in women over age 35. Women over age 35 who smoke should not use estrogen-containing contraceptives.

Labeling also lists other contraindications. These hormonal therapies increase the risk of venous thromboembolism (VTE). Although the incidence of VTE is very low in reproductive-age women, VTE risk increases with age and body mass index. Thus, an additional contraindication for perimenopausal women is obesity (see Table 1).

Combination estrogen-progestin contraceptives are a safe, effective birth control option for healthy, lean, nonsmoking, midlife women. Of these, combination OCs have been found to provide important noncontraceptive benefits, including regulation of irregular uterine bleeding, reduction of vasomotor symptoms, decreased risk for ovarian and endometrial cancer, and maintenance of bone density (with a potential for decreased risk for postmenopausal osteoporotic fractures). Use of low-dose OCs has not been found to increase the risk of myocardial infarction or stroke in these women, nor does long-term use appear to affect the risk of breast cancer. These benefits may apply for nonoral combination contraceptives as well. (Refer to labeling for details, including side effects, for each drug.)