



Hormone Replacement Therapy Shortage

For the current status of drug shortages and discontinuations, refer to Drug Shortages Canada at www.drugshortagescanada.ca.

TABLE 1: Selected estrogen products marketed in Canada¹

| Product | Active Ingredient, Formulation | Strength | DIN | Manufacturer |
|-----------------|--|----------|----------------------------------|---------------------------------|
| Climara | 17-beta estradiol, patch | 25 mg | 02247499 | Bayer Incorporated |
| | | 50 mg | 02231509 | |
| | | 75 mg | 02247500 | |
| Lupin-Estradiol | 17-beta estradiol, tablet | 0.5 mg | 02449048 | Lupin Pharma Canada Limited |
| | | 1 mg | 02449056 | |
| | | 2 mg | 02449064 | |
| Estrogel | 17-beta estradiol, gel | 0.06% | 02238704 | Organon Canada Incorporated |
| Premarin | conjugated estrogens, sustained-release tablet | 0.3 mg | 02414678 | Pfizer Canada |
| | | 0.625 mg | 02414686 | |
| | | 1.25 mg | 02414694 | |
| Estradiol Derm | 17-beta estradiol, patch | 50 mcg | 02246969 | Sandoz Canada Incorporated |
| | | 75 mcg | 02246967 | |
| | | 100 mcg | 02246968 | |
| Estradot | 17-beta estradiol, patch | 25 mcg | 02245676 | Sandoz Canada Incorporated |
| | | 37.5 mcg | 02243999 | |
| | | 50 mcg | 02231509 | |
| | | 75 mcg | 02247500 | |
| | | 100 mcg | 02244002 | |
| Divigel | 17-beta estradiol, gel | 0.1% | 02424835 02424843 02424924 | Searchlight Pharma Incorporated |
| Oesclim | 17-beta estradiol, patch | 25 mcg | 02243722 | Searchlight Pharma Incorporated |
| | | 50 mcg | 02243724 | |

TABLE 2: Selected estrogen/progestin combination products marketed in Canada¹

| Product | Active Ingredient, Formulation | Strength | DIN | Manufacturer |
|-------------------------|---|---------------|----------|----------------------------------|
| Angeliq | 17-beta estradiol/drospirenone, tablet | 1 mg/1 mg | 02268825 | Bayer Incorporated |
| Bijuva | estradiol hemihydrate/ micronized progesterone, capsule | 1 mg/100 mg | 02505223 | Knight Therapeutics Incorporated |
| Activelle LD, Activelle | estradiol hemihydrate/ norethindrone acetate, tablet | 0.5 mg/0.5 mg | 02309009 | Novo Nordisk |
| | | 1 mg/0.5 mg | 02249405 | |
| Estalis | 17-beta estradiol/norethindrone acetate, patch | 140/50 mcg | 02241835 | Sandoz Canada Incorporated |
| | | 250/50 mcg | 02241837 | |

Health Canada–approved indications for estrogen and estrogen/progestin hormone therapy:²

- The relief of menopausal and postmenopausal symptoms occurring in naturally or surgically induced estrogen-deficiency states

Common off-label uses of estrogen and estrogen/progestin hormone therapy:

- Transdermal estradiol can be used in transgender and gender-diverse patients who may benefit from feminizing hormone therapy as part of their gender-affirming care³
- Add-back hormone therapy to mitigate perimenopausal symptoms and bone loss in patients receiving gonadotropin-releasing hormone (GnRH) agonists (e.g., endometriosis, heavy menstrual bleeding)⁴

Management options:⁵

Hormone replacement therapy (HRT) is the most effective treatment for vasomotor symptoms of menopause (VMS) in patients who are <60 years of age or <10 years postmenopause.

Transdermal estrogen products have some advantages over oral products, including a potentially lower risk of venous thromboembolism, and may be considered over oral estrogen in certain patient groups (e.g., patients with migraines, hypertension). There are 2 transdermal formulations of estrogen available in Canada: topical gel (e.g., EstroGel) and topical patches (e.g., Estradot).

Multiple factors can influence the selection of an alternative hormonal therapy agent, including cost, adherence and patient preference. A list of alternative hormonal therapy products is shown in Table 3. Clinicians should monitor for efficacy and safety when switching between HRT products and titrate doses accordingly. For individuals with intact uteri switching from a combination systemic estrogen/progestogen product to a systemic estrogen product alone, a progestogen agent should be added to lower the risk of endometrial hyperplasia.

Nonhormonal medications can also be considered for the treatment of VMS in patients for whom HRT is undesirable or contraindicated. A list of nonhormonal medications used in the management of VMS is listed in Table 4.

The information presented here is generalized, and patients should be assessed on an individual basis. Patient assessment requires professional knowledge and judgment beyond the scope of this document. Consult CPS Full Access or other references if required.

TABLE 3: **Alternative hormonal products**⁵

| Drug | Dosage | Adverse Effects |
|----------------------------------|-----------------------------------|---|
| Conjugated estrogen/bazedoxifene | 1 tablet (0.45 mg/20 mg) daily PO | Breakthrough bleeding/spotting, nausea, bloating/water retention, chloasma. |
| Tibolone | 2.5 mg daily PO | Breakthrough bleeding/spotting, nausea, gastrointestinal upset, fatigue, breast tenderness, bloating/water retention, increased appetite. |



TABLE 4: Alternative nonhormonal products used in the management of menopausal symptoms⁵

| Drug | Dosage | Adverse Effects |
|---|---------------------|---|
| Alpha₂-adrenergic Agonists | | |
| Clonidine | 0.05 mg BID PO | Dizziness, dry mouth, drowsiness, constipation. |
| Anticholinergic Agents | | |
| Oxybutynin | 2.5-5 mg BID PO | Dry mouth, constipation, tachycardia. |
| Oxybutynin, extended release | 15 mg daily PO | Dry mouth, constipation, tachycardia. |
| Gamma-aminobutyric Acid Derivatives | | |
| Gabapentin | 300 mg TID PO | Somnolence, dizziness. |
| Pregabalin | 150-300 mg daily PO | Somnolence, dizziness. |
| Selective Serotonin Reuptake Inhibitors | | |
| Citalopram | 10-20 mg daily PO | Gastrointestinal upset, sexual dysfunction, weight gain. |
| Escitalopram | 10-20 mg daily PO | Gastrointestinal upset, sexual dysfunction, weight gain. |
| Paroxetine | 10-20 mg daily PO | Gastrointestinal upset, sexual dysfunction, weight gain. |
| Serotonin-Norepinephrine Reuptake Inhibitors | | |
| Desvenlafaxine | 50-100 mg daily PO | Gastrointestinal upset, dry mouth, drowsiness, nervousness, sexual dysfunction. |
| Venlafaxine | 37.5-75 mg daily PO | Gastrointestinal upset, dry mouth, drowsiness, nervousness, sexual dysfunction. |

References

1. Health Canada. *Drug product database online query* [internet]. Available from: <https://health-products.canada.ca/dpd-bdpp/index-eng.jsp>. Accessed April 17, 2024.
2. Health Canada. Drug Product Database. *Climara* (Bayer Inc.) [product monograph]. 2016. Available from: www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html.
3. Coleman E, Radix AE, Bouman WP et al. Standards of care for the health of transgender and gender diverse people, version 8. *Int J Transgend Health* 2022;23(Suppl 1):S1-S259.
4. Gilliland GB. *Endometriosis* [internet]. April 19, 2021. Available from: <https://cps.pharmacists.ca>. Subscription required. Accessed April 18, 2024.
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