SOGC

Hormone Therapy Products Available in Canada for the Treatment of

Menopausal Symptoms

Physician Desk Reference - 3rd Edition

A clinical resource provided to you by:
The Society of Obstetricians and Gynaecologists of Canada

PRESCRIBING HORMONE THERAPY

Physicians today have a wide selection of hormone therapies (HT) to choose from, if HT is deemed necessary for the management of troublesome menopausal symptoms. This guide aims to assist physicians with optimizing treatment decisions by summarizing some of the key information about all of the hormone therapies currently available in Canada. For complete information about the individual treatments reviewed in this guide, please consult the respective product monographs on Health Canada's drug product database.[3]

For more information about menopause, please consult the **2014 SOGC Clinical Practice Guideline, Managing Menopause**.

Clinical Guidance[1]

These are general recommendations that must be modified according to individual clinical situations and desires of the patient, after she has been fully assessed and informed of all the available treatment options.

BENEFITS AND RISKS OF HT	
BENEFITS	**RISKS**
Reduction of VMS	Thromboembolic events
Reduction of sleep problems	Stroke
Reduction of mood or anxiety problems	Breast cancer (after 4 to 5 years of EPT)
Reduction of CVD and all-cause mortality (when started younger than 60 years of age and within 10 years of menopause)	Coronary heart disease (for women older than 60 and those who are more than 10 years after menopause, E+P only)
Osteoporosis prevention and treatment	Endometrial hyperplasia and cancer (with estrogen-only regimens) in women with a uterus
Reversal of vulvar and vaginal atrophy (local ET if such atrophy is the only indication for therapy)	

CONTRAINDICATIONS TO HT	
CONTRAINDICATIONS TO ESTROGENS	**CONTRAINDICATIONS TO PROGESTOGENS**
Unexplained vaginal bleeding	Unexplained vaginal bleeding
Acute liver dysfunction	Breast cancer
Estrogen-dependent cancer (endometrial and breast cancer)	
Coronary heart disease	
Previous stroke	
Active thromboembolic disease	

Providers should check the full prescribing information for appropriate dosages for the indication and any updates or information that is not provided here, such as warnings and contraindications.

APPROXIMATE EQUIVALENTS OF ORAL AND TRANSDERMAL ESTROGENS[2]	
ORAL	**DOSE EQUIVALENT (MG)**
Conjugated equine estrogens	0.625
Conjugated estrogen sulphate	0.625
Estropipate (0.75)	0.625
17ß-estradiol	1.0
Ethinyl estradiol	5.0 µg
TRANSDERMAL	**DOSE EQUIVALENT**
17ß-estradiol	50 µg (patch)
17ß-estradiol	1.5 mg per 2 metered pumps (2.5 g of gel)

Estrogens – Vaginal

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S)
Estrone	**ESTRAGYN** Searchlight Pharma Inc.	**Cream** 0.1% 0.5-4 g	**Initial dose:** 0.5 g daily for two weeks **Maintenance dose:** 0.5-4 g daily adjusted to the lowest amount that controls symptoms	■ Symptoms of vulvovaginal atrophy due to estrogen deficiency
17ß-estradiol	**ESTRING** Pfizer Canada Inc.	**Silicone elastomer ring** 2 mg	Continuous use for 3 months	■ Postmenopausal urogenital complaints due to estrogen deficiency such as: – Atrophic vaginitis – Dyspareunia – Dysuria – Urinary urgency
Conjugated estrogens	**PREMARIN** Pfizer Canada Inc.	**Cream** 0.625 mg/g	Daily 0.5-2 g	■ Atrophic vaginitis ■ Dyspareunia ■ Kraurosis vulvae

Estrogens – Vaginal (continued)

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S)
Estradiol	**VAGIFEM 10** Novo Nordisk Canada Inc.	**Tablet** 10 µg	**Initial dose:** 1 tablet daily for two weeks **Maintenance dose:** 1 tablet twice weekly, with 3- or 4-d interval	■ Symptoms of vaginal atrophy due to estrogen deficiency

Prescribing tip: Low-dose vaginal estrogen may be prescribed without a progestin. Follow the product monograph indications for each specific product.

Estrogens – Oral

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S)
17ß-estradiol (micronized)	**ESTRACE** Acerus Pharmaceuticals Corporation	**Tablet** 0.5 mg 1 mg 2 mg	Daily	■ Symptomatic relief of menopausal symptoms ■ Prevention of osteoporosis
Conjugated estrogens	**PREMARIN** Pfizer Canada Inc.	**Tablet** 0.3 mg 0.625 mg 1.25 mg	Daily	■ Relief of menopausal and postmenopausal symptoms ■ Prevention of osteoporosis ■ Atrophic vaginitis ■ Vulvar atrophy ■ Hypoestrogenism due to hypogonadism

Prescribing tip: All systemic estrogens should be prescribed with an appropriate dosage of a progestin for women with an intact uterus in order to prevent endometrial hyperplasia/carcinoma. The exception is if it is a tissue-selective estrogen complex (TSEC) such as Duavive.

Estrogens – Transdermal

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S)
17ß-estradiol	**CLIMARA** Bayer Inc.	**Patch** 0.025 mg 0.05 mg 0.075 mg 0.1 mg	Once weekly	■ Relief of menopausal and postmenopausal symptoms ■ Prevention of osteoporosis (Climara 25 is not indicated for the prevention of osteoporosis)

Estrogens – Transdermal (continued)

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S)
17ß-estradiol	**DIVIGEL** Teva Canada Ltd.	**Gel** 0.1% 0.25 mg 0.5 mg 1 mg	Daily	■ Treatment of moderate to severe vasomotor symptoms associated with menopause
17ß-estradiol	**ESTRADOT** Novartis Pharmaceuticals Canada Inc.	**Patch** 0.025 mg 0.0375 mg 0.05 mg 0.075 mg 0.1 mg	Twice weekly	■ Relief of menopausal and postmenopausal symptoms ■ Prevention of osteoporosis
17ß-estradiol	**ESTROGEL** Merck Canada Inc.	**Gel** 0.06% 2 pumps (1.5 mg E_2)	Daily	■ Relief of menopausal and postmenopausal symptoms ■ Atrophic vaginitis
17ß-estradiol	**OESCLIM** Searchlight Pharma Inc.	**Patch** 0.025 mg 0.0375 mg 0.05 mg 0.075 mg 0.1 mg	Twice weekly	■ Relief of menopausal and postmenopausal symptoms

Prescribing tip: All systemic estrogens should be prescribed with an appropriate dosage of a progestin for women with an intact uterus in order to prevent endometrial hyperplasia/carcinoma. The exception is if it is a tissue-selective estrogen complex (TSEC) such as Duavive.

Estrogen and Selective Estrogen-Receptor Modulator (SERM)

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S)
Conjugated estrogens + bazedoxifene	**DUAVIVE** Pfizer Canada Inc.	**Tablet** 0.45 mg conjugated estrogens + 20 mg bazedoxifene	Daily	■ For women with a uterus: treatment of moderate to severe vasomotor symptoms

Prescribing tip: Patients receiving Duavive do not need to use a progestin, and should not be prescribed progestin or progesterone.

Progestogens – Oral

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S)
Norethindrone acetate	**NORLUTATE** Erfa Canada Inc.	**Tablet** 5 mg	Daily	■ Abnormal uterine bleeding due to hormonal imbalance in the absence of organic pathology, such as submucous fibroids or uterine cancer
Micronized progesterone	**PROMETRIUM** Merck Canada Inc.	**Tablet** 100 mg	Daily	■ For women with an intact uterus: adjunct to postmenopausal estrogen replacement therapy to significantly reduce the risk of endometrial hyperplasia and carcinoma
Medroxypro-gesterone acetate	**PROVERA** Pfizer Canada Inc.	**Tablet** 2.5 mg 5 mg 10 mg	Daily	■ For women with an intact uterus: hormonal replacement therapy, to oppose the effects of estrogen on the endometrium and significantly reduce the risk of hyperplasia and carcinoma

Progestogens – Intrauterine

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S)
Levonorgestrel	**MIRENA** Bayer Inc.	**Intrauterine** 52 mg	5 years	■ Treatment of idiopathic menorrhagia following appropriate diagnostic investigation in women accepting the contraceptive effect of MIRENA

Combined Estrogens and Progestogens – Oral*

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S)
17ß-estradiol (E_2) + norethindrone acetate (NETA)	**ACTIVELLE** Novo Nordisk Canada Inc.	**Tablet** 1 mg E_2 + 0.5 mg NETA	Daily	■ Treatment of moderate to severe vasomotor symptoms due to naturally or surgically induced estrogen deficiency states ■ Vulvar or vaginal atrophy
17ß-estradiol (E_2) + norethindrone acetate (NETA)	**ACTIVELLE LD** Novo Nordisk Canada Inc.	**Tablet** 0.5 mg E_2 + 0.1 mg NETA	Daily	■ Treatment of moderate to severe vasomotor symptoms due to naturally or surgically induced estrogen deficiency states
17ß-estradiol (E_2) + drospirenone (DRSP)	**ANGELIQ** Bayer Inc.	**Tablet** 1 mg E_2 + 1 mg DRSP	Daily	■ Relief of menopausal and postmenopausal symptoms, including symptoms of vulvar and vaginal dryness

* Recommended only in patients with an intact uterus since the regimen includes a progestogen whose role is to prevent endometrial hyperplasia.

Combined Estrogens and Progestogens – Transdermal*

ACTIVE INGREDIENT(S)	PRODUCT / MANUFACTURER	DOSAGE FORM / STRENGTH	SCHEDULE	CLINICAL INDICATION(S)
17ß-estradiol (E_2) + levonorgestrel (LNG)	**CLIMARA PRO** Bayer Inc.	**Matrix patch** 45 µg Estradiol + 15 µg LNG	Once weekly	■ Relief of menopausal and postmenopausal symptoms
17ß-estradiol (E_2) + norethindrone acetate (NETA)	**ESTALIS** Novartis Pharmaceuticals Canada Inc.	**Patch** 50 µg E_2 + 140 µg NETA 50 µg E_2 + 250 µg NETA	Twice weekly	■ Relief of menopausal and postmenopausal symptoms ■ Vulvar or vaginal atrophy

* Recommended only in patients with an intact uterus since the regimen includes a progestogen whose role is to prevent endometrial hyperplasia.

UNSUPPORTED HORMONE THERAPIES

The SOGC **DOES NOT** support the use of custom-compounded 'bioidenticals'.

Custom-compounded 'bioidenticals' hormone therapy **ARE NOT** regulated by Health Canada.

Custom-Compounded 'Bioidentical' Hormone Therapy

Estrogens, progesterone and testosterone are steroid hormones that, in nature, are only made in animals.

Compounded 'bioidentical' hormones are synthetic compounds that are manufactured to mimic natural hormones, and to interact with hormone receptors in the same way as natural, or conventional, prescription hormones. They have the risks listed below, in addition to the risks that they share with conventional, regulated hormonal therapy.

Example of custom-compounded 'bioidenticals': Bi-est cream, tri-est cream, estriol cream, progesterone cream and DHEA (dehydroepiandrosterone) tablets

The SOGC endorses the North American Menopause Society 2017 hormone therapy (HT) position statement which states:

- Compounded 'bioidentical' HT presents safety concerns, such as minimal government regulation and monitoring, overdosing or underdosing, presence of impurities or lack of sterility, lack of scientific efficacy and safety data, and lack of a label outlining risks.
- Salivary hormone testing to determine dosing is unreliable.
- Prescribers of compounded 'bioidentical' HT should document the medical indication for compounded HT over government-approved therapies, such as allergy, the need for dosing, or a formulation not available in approved products.

The Medical Letter Position (May 2010):

> There is no acceptable evidence that 'bioidentical' (custom-compounded) hormones are safe or effective. Patients should be discouraged from taking them.

References:

1. J Obstet Gynaecol Can 2014;36 (9 eSuppl A):S1-S80 (adapted from)

2. Ansbacher R. Bioequivalence of conjugated estrogen products. Clin Pharmacokinet 1993;24:271-4.

3. Health Canada Product Monographs.
   Available at: www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php