

## Medroxyprogesterone Tablets

### Background

All generic medroxyprogesterone (MPA) tablets are currently shorted. Due to increased demand for Provera™ tablets, the 10mg is also shorted and availability of the other strengths is sporadic.<sup>1</sup>

**Table 1: Canadian Suppliers of Medroxyprogesterone Tablets<sup>2</sup>**

Product	Strength	DIN	Manufacturer
Apo-Medroxy	2.5 mg	02244726	APX
	5 mg	02244727	
	10 mg	02277298	
	100 mg	02267640	
Provera™	2.5 mg	00708917	PFI
	5 mg	00030937	
	10 mg	00729973	
Teva-Medroxyprogesterone	2.5 mg	02221284	TEV
	5 mg	02221292	
	10 mg	02221306	

Health Canada approved indications of medroxyprogesterone tablets<sup>3</sup>:

- Hormonal replacement therapy, to oppose the effects of estrogen on the endometrium and significantly reduce the risk of hyperplasia and carcinoma;
- Functional menstrual disorders due to hormonal imbalance in non-pregnant women, in the absence of organic pathology;
- Adjunctive and/or palliative treatment of recurrent and/or metastatic endometrial carcinoma;
- Adjunctive and/or palliative treatment of hormonally-dependent, recurrent metastatic breast cancer in postmenopausal women.

This document will address alternative *hormonal* treatment options for the two most common MPA indications: hormonal replacement therapy and abnormal uterine bleeding.

### Management Options

- Please note: bulk medroxyprogesterone acetate is available for compounding from Medisca.<sup>4</sup>

Hormonal Replacement Therapy

Pharmacological Alternatives

**Progestogens:** Required to reduce the risk of endometrial hyperplasia in patients with an intact uterus who are on systemic estrogen.<sup>5,6</sup> Alternatives to MPA include:

### Micronized Progesterone

**Table 2: Canadian Suppliers of Micronized Progesterone Capsules<sup>2</sup>**

Product	Strength	DIN	Manufacturer
Auro-Progesterone	100 mg*	02493578	API
PMS-Progesterone	100 mg€	02476576	PMS
	200 mg*,^	02480247	
Progesterone	100 mg€	02516187	SAN
Prometrium®	100 mg€	02166704	ORG
Reddy-Progesterone	100 mg€	02463113	DLC
Teva-Progesterone	100 mg€	02439913	TEV

\* Not a benefit of the Saskatchewan Drug Plan (SDP) Formulary

^ Not a benefit of the Non-Insured Health Benefits (NIHB) Formulary

€ Open benefit of NIHB; requires EDS for SDP

- Usual dosage in combination with estrogen in patients with intact uterus:<sup>5,6</sup>
  - Cyclic regimen: 200 – 300 mg orally at bedtime for 10–14 days every month
  - Continuous: 100 – 200 mg orally at bedtime
- Common adverse effects:<sup>5,6</sup>
  - Drowsiness is common – bedtime dosing recommended.
- Adverse effects are similar to medroxyprogesterone, although less breakthrough bleeding is expected – particularly with the continuous regimen.
- Capsules may contain peanut oil, sunflower oil and/or soy lecithin – caution with allergies.<sup>5,6</sup>
- Medroxyprogesterone acetate is a synthetic progestogen, micronized progesterone is considered a “natural” progestogen.

### Levonorgestrel Intrauterine System (IUS) - Mirena® 52 mg<sup>6</sup>

- Mirena® is the only levonorgestrel IUS that has evidence for endometrial protection from unopposed estrogen over a period of 5 years.
- This indication is off label.
- The common side effects from progestogens: bloating, irritability, weight gain and mood swings, can occur with Mirena® use; however, to a lesser extent than with medroxyprogesterone.

### Estrogen/Progestogen Combination Products

**Table 3: Canadian Suppliers of Estrogen/Progestogen Combination Products for Hormonal Replacement<sup>2</sup>**

Product	Strength	DIN	Manufacturer
Activelle® Tablets*	Estradiol 1 mg/ Norethindrone 0.5 mg per tablet	02249405	NOO
Activelle® LD Tablets*	Estradiol 0.5 mg/ Norethindrone 0.1 mg per tablet	02309009	NOO

Angeliq® Tablets*	Estradiol 1 mg/ Drospirenone 1 mg per tablet	02268825	BAY
Estalis® Patch^	Estradiol 50 µg/ Norethindrone 140 µg/day	02241835	SDZ
	Estradiol 50 µg/ Norethindrone 250 µg/day	02241837	

\* Not a benefit of SDP or NIHB formularies

^ Open benefit of NIHB formulary; requires EDS for SDP formulary

- The above products do not contain medroxyprogesterone but do contain a progestogen – either norethindrone or drospirenone – in combination with estradiol. These may be attractive to those who like the convenience of a twice weekly patch or of having both hormonal components in 1 tablet to be taken once daily.
- Ensure patients discontinue their current single-ingredient estrogen if switched to a combination product.
- Continuous use decreases the chance of breakthrough bleeding.<sup>5,6</sup>

## Abnormal Uterine Bleeding (AUB)

### Pharmacological Alternatives

#### Oral Progestogens

- There is no clear consensus on dosing for this indication. Doses may vary with etiology. Examples of more commonly used dosing regimens:
  - Micronized progesterone (see Table 2 for availability)
    - 100-300 mg orally at bedtime from days 14-28<sup>7</sup>
    - 300 mg orally at bedtime for a minimum of 21 days/month<sup>8</sup>
  - Norethindrone (Norlutate®)
    - 5 -15 mg orally daily<sup>9</sup>
    - 2.5-15 mg orally daily on days 5-25 of cycle<sup>7,8,10,11</sup>

#### Levonorgestrel Intrauterine System (LNG-IUS)<sup>8-10,12</sup>

- Mirena® 52 mg q5yrs
- found to be more effective than other medications for AUB

#### Depot Medroxyprogesterone Acetate (DMPA)<sup>7-10,12</sup>

- 150 mg IM q3months
- Patients should be informed there may be a delay to fertility (up to 1 year after last injection).

#### Progestogen/Estrogen Combined Oral Contraceptives - Monophasic

- Products with ≥ 30 mcg ethinyl estradiol are preferred.<sup>7</sup>
- Triphasics are not suitable for this indication.<sup>7</sup>
- Suggested dosing:
  - 1 tablet orally 2 or 3 times daily until bleeding stops, then 1 tablet orally daily x 3 months, or

- 1 tablet orally daily for 21 days each month<sup>7</sup>

### *Progestogen/Estrogen Combined Contraceptive Patch and Vaginal Ring<sup>7-10,12</sup>*

- Nuvaring® and Evra®
  - Although not well-studied for this indication, both have been found to reduce menstrual blood flow in normally menstruating women.<sup>9</sup>
  - Either a continuous or a cyclic regimen may be used.

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