Drug Monograph

Drug Name | Mechanism of Action and Pharmacokinetics | Indications and Status | Adverse Effects | Dosing | Administration Guidelines | Special Precautions | Interactions | Recommended Clinical Monitoring | Supplementary Public Funding | References | Disclaimer

A - Drug Name

megestrol

SYNONYM(S): BDH 1298; MEG; megestrol acetate

COMMON TRADE NAME(S): Megace® (Bristol-Myers Squibb)

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B - Mechanism of Action and Pharmacokinetics

Megestrol was initially developed as a contraceptive and was first evaluated in breast cancer treatment in 1967. It is a synthetic progestin and has the same physiologic effects as natural progesterone. Megestrol has direct cytotoxic effects on breast cancer cells in tissue culture and suppresses luteinizing hormone release from the pituitary. The precise mechanism of megestrol's antianorexic and anticachetic effects is unknown.

Absorption	Bioavailability	Oral: Variable, but well absorbed
Distribution	Found in breast milk.	
	Cross blood brain barrier?	No information found
	Volume of distribution	No information found
Metabolism	Mainly in liver to free steroids and glucuronide conjugates.	
	Active metabolites	no
	Inactive metabolites	yes
Elimination	Predominantly excreted by kidneys, 19.8% within 10 days in feces.	
	Urine	66.4% within 10 days
	Half-life	34 hours

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C - Indications and Status

Health Canada Approvals:

- Anorexia, cachexia or weight loss secondary to metastatic cancer
- Adjunctive or palliative treatment of recurrent, inoperable or advanced breast and endometrial cancer.
- Palliative treatment of hormone responsive advanced (stage D2) carcinoma of the prostate

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D - Adverse Effects

Emetogenic potential: Not applicable

Extravasation Potential: Not applicable

ORGAN SITE	SIDE EFFECT* (%)	ONSET**		
Auditory	Hearing impaired (less common)	E	D	
Cardiovascular	Hypertension (unusual)	E		
	Venous thromboembolism		D	
Dermatological	Alopecia (mild, rare)		D	
	Hirsutism	E		
	Rash (unusual)	I	E	
	Skin discolouration (chloasma)		E	
Gastrointestinal	Appetite improved		E	
	Constipation		E	
	Diarrhea (unusual)		E	
	Nausea, vomiting (2%)	I		
	Weight gain		E	
General	Edema (mild fluid retention)		E	
	Fatigue		E	
	Tumour flare		E	
Hepatobiliary	↑ LFTs (rare)	E	D	
	Cholecystitis (rare)		D	
Metabolic / Endocrine	Adrenal insufficiency (adrenocortical suppression - rare)			L
	Cushingoid		D	

	Hyperglycemia	E	
Musculoskeletal	Other (carpal tunnel syndrome - rare)	E	
Nervous System	Insomnia (less common)	E	D
	Memory impairment	E	
	Mood changes (unusual)		D
Reproductive and breast disorders	Erectile dysfunction	E	
	Gynecomastia	E	
	Vaginal bleeding (2%)		D
Respiratory	Dyspnea	E	
Urinary	Urinary frequency	E	
Vascular	Hot flashes (rare)	E	

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.
"*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.
Dose-limiting side effects are underlined.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
D = *delayed* (weeks to months) L = *late* (months to years)

Weight gain has been reported in one third of patients on megestrol 160mg daily. Weight gain is associated with an increase in fat and body cell mass. This effect has been used therapeutically in the treatment of cachexia.

Spotting may occur during treatment with megestrol. **Vaginal bleeding** is not uncommon following withdrawal of megestrol. May cause tumour flare with increased pain and hypercalcemia. There is a theoretical risk of adrenal insufficiency after prolonged treatment.

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E - Dosing

Refer to protocol by which patient is being treated. Exclude treatable causes of weight loss prior to starting treatment with megestrol for anorexia and weight loss.

Adults:

Breast Cancer: 160mg or 125mg/m^2 PO daily as a single or divided daily dose(s)

Endometrial Cancer: 80-320 mg or 125mg/m^2 daily in divided doses

Prostate Cancer: 120 mg (93.8 mg/m^2) daily as a single daily dose

(Continued on next page)

Anorexia, cachexia, or significant weight loss in patients with cancer: 400-800 mg daily as a single daily dose

Dosage with Toxicity:

Dosage in myelosuppression: No adjustment required

Dosage with Hepatic Impairment:

No information found

Dosage with Renal Impairment:

No information found

Children:

Safety and efficacy have not been established.

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F - Administration Guidelines

- Oral self-administration; drug available by outpatient prescription.

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G - Special Precautions

Other:

Megestrol is **contraindicated** in patients who are sensitive to megestrol or any ingredients in the dosage forms. It should be used with caution in patients with arterial or venous thromboembolic disorders. Tablets contain lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.

The **mutagenic** potential of megestrol is not known. An increased incidence of breast (benign and malignant) and pituitary tumours have been observed in animals after prolonged megestrol use. Megestrol is **fetotoxic**. **Contraindicated in pregnancy**. Detectable amounts excreted in breast milk; therefore, **breast feeding** is not recommended. Fertility may be affected in females.

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H - Interactions

AGENT	EFFECT	MECHANISM	MANAGEMENT
Dofetilide	↑ dofetilide effect	Megestrol ↓ renal secretion	Avoid combination

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I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- Clinical toxicity assessment for venous thromboembolism, edema and GI effects.
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Liver function tests; baseline and regular

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J - Supplementary Public Funding

ODB - General Benefit (ODB Formulary)

- oral tablets

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K - References

Canetta R, Florentine S, Hunter H, et al. Megestrol Acetate, Cancer Treat Rev 1983;10(3):141-57.

Foitl DR, Hyman G, Lefkowitch JH. Jaundice and intrahepatic cholestasis following high dose megestrol acetate for breast cancer. Cancer 1989;63:438-9.

Megestrol: The Merck Manual [Internet]; 2011 [cited 2012 April 3]. Available from: http://www.merckmanuals.com/professional/lexicomp/megestrol.html

Product Monograph: Megestrol. AA Pharma Inc., May 28, 2010.

Product Monograph: Megestrol. Aspen Pharma Pty Ltd (Australia), April 2011.

Prescribing information: Megace® OS, Bristol-Myers Squibb (US)., March 2011.

March 2013: Added public funding info; revised April 2012

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L - Disclaimer

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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