

## Megestrol acetate: Drug information

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(For additional information [see "Megestrol acetate: Patient drug information"](#) and [see "Megestrol acetate: Pediatric drug information"](#))

For abbreviations and symbols that may be used in Lexicomp ([show table](#))

**Brand Names: US** Megace ES; Megace Oral

**Brand Names: Canada** Megace OS; Megestrol

**Pharmacologic Category** Antineoplastic Agent, Hormone; Appetite Stimulant; Progestin

**Dosing: Adult** **Note:** Megace ES suspension is not equivalent to other formulations on a mg-per-mg basis.

**Anorexia or cachexia associated with AIDS:** Oral: Suspension:

*U.S. labeling:* Initial: 625 mg daily (of the 125 mg/mL suspension) or 800 mg daily (of the 40 mg/mL suspension); daily doses of 400 mg to 800 mg have been found to be effective

*Canadian labeling:* Usual dose: 400 to 800 mg once daily for at least 2 months

**Breast cancer, advanced:** Oral: Tablet:

*U.S. labeling:* 160 mg per day in divided doses of 40 mg 4 times daily for at least 2 months

*Canadian labeling:* 160 mg or 125 mg/m<sup>2</sup> daily (40 mg 4 times daily or 160 mg once daily) for at least 2 months

**Endometrial cancer, advanced:** Oral: Tablet:

*U.S. labeling:* 40 to 320 mg daily in divided doses for at least 2 months

*Canadian labeling:* 80 to 320 mg or 62.5 to 250 mg/m<sup>2</sup> daily in divided doses (40 to 80 mg 1 to 4 times daily or 160 to 320mg daily) for at least 2 months

**Cancer-related cachexia:** *Canadian labeling:* Oral: Tablet: 400 to 800 mg once daily for at least 2 months

**Cancer-related cachexia (off-label use/dosing in U.S.):** Oral: Doses ranging from 160 to 800 mg per day were effective in achieving weight gain, higher doses (>160 mg) were associated with more weight gain (Beller, 1997; Loprinzi, 1990; Loprinzi, 1993; Vadell, 1998); based on a meta-analysis, an optimal dose has not been determined (Ruiz Garcia, 2013)

**Dosing: Geriatric** Use with caution; refer to adult dosing.

**Dosing: Renal Impairment** There are no dosage adjustments provided in the manufacturer's labeling; however, the urinary excretion of megestrol acetate is substantial, use caution.

**Dosing: Hepatic Impairment** There are no dosage adjustments provided in the manufacturer's labeling.

**Dosage Forms** Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Suspension, Oral, as acetate:

Megace ES: 625 mg/5 mL (150 mL) [contains alcohol, usp, sodium benzoate; lemon-lime flavor]

Megace Oral: 40 mg/mL (240 mL) [lemon-lime flavor]

Generic: 40 mg/mL (10 mL, 240 mL, 480 mL); 400 mg/10 mL (10 mL); 625 mg/5 mL (150 mL)

Tablet, Oral, as acetate:

Generic: 20 mg, 40 mg

**Generic Equivalent Available (US)** Yes

**Dosage Forms: Canada** Information with regard to form, strength, and availability of products uniquely available in Canada but currently not available in the US. Refer also to Dosage forms.

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Tablet, Oral, as acetate: 160 mg

**Administration** Oral: Shake suspension well before use.

## Hazardous Drugs Handling Considerations

Hazardous agent (NIOSH 2016 [group 1]).

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage. NIOSH recommends single gloving for administration of intact tablets or capsules. NIOSH recommends double gloving, a protective gown, and (if there is a potential for vomit or spit up) eye/face protection for administration of an oral liquid/feeding tube administration (NIOSH 2016).

## Use

**Anorexia or cachexia:** *Suspension:* Treatment of anorexia, cachexia, or unexplained significant weight loss in patients with AIDS

Limitations of use: Treatment of AIDS-related weight loss should only be initiated after addressing the treatable causes (eg, malignancy, infection, malabsorption, endocrine disease, renal disease,

psychiatric disorder) for weight loss. Megestrol is not intended to prevent weight loss.

**Breast cancer:** *Tablet:* Treatment (palliative) of advanced breast cancer

**Endometrial cancer:** *Tablet:* Treatment (palliative) of advanced endometrial carcinoma

**Additional Canadian use (not an approved use in the U.S.):** *Tablet:* Treatment of anorexia, cachexia, or weight loss secondary to metastatic cancer

## Use: Off-Label

Treatment of cancer-related cachexia

## Medication Safety Issues

### Sound-alike/look-alike issues:

Megace may be confused with Reglan

Megestrol may be confused with mesalamine

### Geriatric Patients: High-Risk Medication:

Beers Criteria: Megestrol is identified in the Beers Criteria as a potentially inappropriate medication to be avoided in patients 65 years and older (independent of diagnosis or condition) due to an increased risk of thrombotic events and potentially death in older adults, with minimal effects on weight (Beers Criteria [AGS 2015]).

Pharmacy Quality Alliance (PQA): Megestrol is identified as a high-risk medication in patients 65 years and older on the PQA's Use of High-Risk Medications in the Elderly (HRM) performance measure, a safety measure used by the Centers for Medicare and Medicaid Services (CMS) for Medicare plans.

## Adverse Reactions

Frequency not always defined.

Cardiovascular: Hypertension (4% to 8%), cardiomyopathy (1% to 3%), chest pain (1% to 3%), edema (1% to 3%), palpitations (1% to 3%), peripheral edema (1% to 3%), cardiac failure

Central nervous system: Headache (3% to 10%), pain (4% to 6%, similar to placebo), insomnia (1% to 6%), abnormality in thinking (1% to 3%), confusion (1% to 3%), convulsions (1% to 3%), depression (1% to 3%), hypoesthesia (1% to 3%), neuropathy (1% to 3%), paresthesia (1% to 3%), carpal tunnel syndrome, lethargy, malaise, mood changes

Dermatologic: Skin rash (6% to 12%), alopecia (1% to 3%), dermatological disease (1% to 3%), diaphoresis (1% to 3%), pruritus (1% to 3%), vesicobullous dermatitis (1% to 3%)

Endocrine & metabolic: Hyperglycemia (6%), decreased libido (1% to 5%), albuminuria (1% to 3%), gynecomastia (1% to 3%), increased lactate dehydrogenase (1% to 3%), adrenocortical insufficiency,

amenorrhea, Cushing's syndrome, diabetes mellitus, hot flash, HPA-axis suppression, hypercalcemia, weight gain (not attributed to edema or fluid retention)

Gastrointestinal: Diarrhea (10%, similar to placebo), flatulence (6% to 10%), vomiting (4% to 6%), nausea (4% to 5%), dyspepsia (2% to 3%), abdominal pain (1% to 3%), constipation (1% to 3%), oral moniliasis (1% to 3%), sialorrhea (1% to 3%), xerostomia (1% to 3%)

Genitourinary: Impotence (4% to 14%), urinary incontinence (1% to 3%), urinary tract infection (1% to 3%), urinary frequency (1% to 2%), breakthrough bleeding

Hematologic & oncologic: Leukopenia (1% to 3%), sarcoma (1% to 3%), tumor flare

Hepatic: Hepatomegaly (1% to 3%)

Infection: Candidiasis (1% to 3%), herpes virus infection (1% to 3%), infection (1% to 3%)

Neuromuscular & skeletal: Weakness (5% to 6%)

Ophthalmic: Amblyopia (1% to 3%)

Respiratory: Cough (1% to 3%), dyspnea (1% to 3%), pharyngitis (1% to 3%), pulmonary disorder (1% to 3%), pneumonia (1%), hyperventilation

Miscellaneous: Fever (1% to 6%)

Postmarketing and/or case reports: Decreased glucose tolerance, thromboembolic phenomena (including deep vein thrombosis, pulmonary embolism, thrombophlebitis)

## Contraindications

Hypersensitivity to megestrol or any component of the formulation; known or suspected pregnancy (suspension).

Documentation of allergenic cross-reactivity for progestins is limited. However, because of similarities in chemical structure and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty.

## Warnings/Precautions

### ***Concerns related to adverse effects:***

- Adrenal suppression: May suppress hypothalamic-pituitary-adrenal (HPA) axis during chronic administration; consider the possibility of adrenal suppression in any patient receiving or being withdrawn from chronic therapy when signs/symptoms suggestive of hypoadrenalism are noted (during stress or in unstressed state). Laboratory evaluation and replacement/stress doses of rapid-acting glucocorticoid should be considered.
- Cushing syndrome: Has been reported with long-term use.

### ***Disease-related concerns:***

- AIDS-related cachexia: The effects on HIV viral replications are unknown.
- Diabetes: New-onset diabetes mellitus and exacerbation of pre-existing diabetes have been

reported with long-term use.

- Thromboembolism: Use with caution in patients with a history of thromboembolic disease.

### **Special populations:**

- Females: Vaginal bleeding or discharge may occur.

### **Concurrent drug therapy issues:**

- Drug-drug interactions: Potentially significant drug interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

### **Dosage form specific issues:**

- Benzyl alcohol and derivatives: Some dosage forms may contain sodium benzoate/benzoic acid; benzoic acid (benzoate) is a metabolite of benzyl alcohol; large amounts of benzyl alcohol ( $\geq 99$  mg/kg/day) have been associated with a potentially fatal toxicity (“gasping syndrome”) in neonates; the “gasping syndrome” consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction (including convulsions, intracranial hemorrhage), hypotension, and cardiovascular collapse (AAP [“Inactive” 1997]; CDC, 1982); some data suggests that benzoate displaces bilirubin from protein binding sites (Ahlfors, 2001); avoid or use dosage forms containing benzyl alcohol derivative with caution in neonates. See manufacturer’s labeling.
- Concentrated suspension: Megace ES suspension is not equivalent to other formulations on a mg-per-mg basis; Megace ES suspension 625 mg/5 mL is equivalent to megestrol acetate suspension 800 mg/20 mL.

**Metabolism/Transport Effects** None known.

## **Drug Interactions**

(For additional information: [Launch drug interactions program](#)) Lexicomp®

**Anticoagulants:** Progestins may diminish the therapeutic effect of Anticoagulants. More specifically, the potential prothrombotic effects of some progestins and progestin-estrogen combinations may counteract anticoagulant effects. Management: Carefully weigh the prospective benefits of progestins against the potential increased risk of procoagulant effects and thromboembolism. Use is considered contraindicated under some circumstances. Refer to related guidelines for specific recommendations. *Risk D: Consider therapy modification*

**Antidiabetic Agents:** Hyperglycemia-Associated Agents may diminish the therapeutic effect of Antidiabetic Agents. *Risk C: Monitor therapy*

**C1 inhibitors:** Progestins may enhance the thrombogenic effect of C1 inhibitors. *Risk C: Monitor therapy*

**Choline C 11:** Antiandrogens may diminish the therapeutic effect of Choline C 11. *Risk C: Monitor therapy*

**Dofetilide:** Megestrol may increase the serum concentration of Dofetilide. *Risk X: Avoid combination*

**Herbs (Progestogenic Properties) (eg, Bloodroot, Yucca):** May enhance the adverse/toxic effect of

Progestins. *Risk C: Monitor therapy*

Indium 111 Capromab Pendetide: Antiandrogens may diminish the diagnostic effect of Indium 111 Capromab Pendetide. *Risk X: Avoid combination*

Pomalidomide: Progestins may enhance the thrombogenic effect of Pomalidomide. Management: Canadian pomalidomide labeling recommends caution with use of hormone replacement therapy and states that hormonal contraceptives are not recommended. US pomalidomide labeling does not contain these specific recommendations. *Risk D: Consider therapy modification*

Ulipristal: May diminish the therapeutic effect of Progestins. Progestins may diminish the therapeutic effect of Ulipristal. Management: Ulipristal for uterine fibroids (Canadian indication): avoid progestins within 12 days of stopping ulipristal; as emergency contraceptive (U.S. indication): avoid progestins within 5 days of stopping ulipristal. *Risk X: Avoid combination*

**Pregnancy Risk Factor** D (tablet) / X (suspension) ([show table](#))

**Pregnancy Implications** Adverse events were demonstrated in animal reproduction studies. May cause fetal harm if administered to a pregnant woman. Use during pregnancy is contraindicated (suspension) and appropriate contraception is recommended in women who may become pregnant. In clinical studies, megestrol was shown to cause breakthrough vaginal bleeding in women.

**Breast-Feeding Considerations** Megestrol is excreted into breast milk. Information is available from five nursing women, ~8 weeks postpartum, who were administered megestrol 4 mg in combination with ethinyl estradiol 50 mcg daily for contraception. Maternal serum and milk samples were obtained over 5 days, beginning 10 days after therapy began. The highest concentrations of megestrol were found at the samples taken 3 hours after the maternal dose. Mean concentrations of megestrol were 6.5 ng/mL (maternal serum; range: 3.7 to 10.8 ng/mL), 4.6 ng/mL (foremilk; range: 1.1 to 12.7 ng/mL), and 5.6 ng/mL (hindmilk; range: 1.2 to 18.5 ng/mL) (Nilsson, 1977). Due to the potential for adverse reaction in the newborn, the manufacturer recommends discontinuing breast-feeding while receiving megestrol.

**Monitoring Parameters** Observe for signs of thromboembolic events; blood pressure, weight; serum glucose

**Mechanism of Action** A synthetic progestin with antiestrogenic properties which disrupt the estrogen receptor cycle. Megestrol interferes with the normal estrogen cycle and results in a lower LH titer. May also have a direct effect on the endometrium. Megestrol is an antineoplastic progestin thought to act through an antileutenizing effect mediated via the pituitary. May stimulate appetite by antagonizing the metabolic effects of catabolic cytokines.

## Pharmacodynamics/Kinetics

Onset of action: Antineoplastic: 2 months of continuous therapy; Weight gain: 2 to 4 weeks

Absorption: Well absorbed

Metabolism: Hepatic (to free steroids and glucuronide conjugates)

Half-life elimination: Suspension: 20 to 50 hours; Tablet: 13 to 105 hours

Time to peak, serum: Tablet: 2 to 3 hours; Suspension: 3 to 5 hours

Excretion: Urine (57% to 78%; 5% to 8% as metabolites); feces (8% to 30%) within 10 days

## Pricing: US

### Suspension (Megace ES Oral)

625 mg/5 mL (150 mL): \$1205.94

### Suspension (Megace Oral Oral)

40 mg/mL (240 mL): \$180.54

### Suspension (Megestrol Acetate Oral)

40 mg/mL (240 mL): \$143.95

625 mg/5 mL (150 mL): \$883.80

### Tablets (Megestrol Acetate Oral)

20 mg (100): \$69.20

40 mg (100): \$123.00

**Disclaimer:** The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

**International Brand Names** Apegestrol (BD); Apetrol (KR); Endace (IN); Maygace (ES); Megace (AR, AT, AU, BD, BE, BG, CL, CN, CO, CZ, DK, EE, EG, FR, GB, GR, HK, HN, HR, IE, IT, JO, JP, KR, KW, LB, LT, LU, MY, NL, NO, NZ, PK, PL, PT, QA, RU, SA, SG, SI, TH, TR, TW, UY, VN); Megaplex (ID, PH, RU, TH); Megase (VE); Megastrol (PY); Megatus (TW); Megejohn (TW); Megesia (KR); Megesin (HK, RO); Megestat (BR, DE); Megex-I (PE); Megostat (AU, HR); Mestrel (MX, TH); Mestrol (TW); Norea (ES); Onistrol (LK); Tracetate (ID)

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