PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

# PRMEGACE® OS

**(megestrol acetate)**

**Oral Suspension USP, 40 mg/mL**

**Antianorexic / Anticachectic**

Bristol-Myers Squibb Canada
Montreal, Canada
H4S 0A4

Date of Revision:
October 06, 2016



Submission Control No: 195954

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**MEGACE* OS**

(megestrol acetate)

## PART I: HEALTH PROFESSIONAL INFORMATION

### SUMMARY PRODUCT INFORMATION

| Route of Administration | Dosage Form / Strength | Clinically Relevant Nonmedicinal Ingredients |
|---|---|---|
| oral | Oral suspension, 40 mg/mL | For a complete listing see Dosage Forms, Composition and Packaging section. |

### INDICATIONS AND CLINICAL USE

MEGACE OS (megestrol acetate) is indicated for

- the treatment of anorexia, cachexia, or an unexplained significant weight loss in patients with a diagnosis of acquired immunodeficiency syndrome (AIDS).

#### Geriatrics (> 65 years of age)

Megestrol acetate is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see WARNINGS and PRECAUTIONS; Geriatric).

#### Pediatrics (< 18 years of age)

Safety and effectiveness in pediatric patients have not been established.

### CONTRAINDICATIONS

- Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see the Dosage Forms, Composition and Packaging section of the product monograph.
- MEGACE OS (megestrol acetate) should not be used as a diagnostic test for pregnancy.

### WARNINGS AND PRECAUTIONS

#### General

MEGACE OS (megestrol acetate) is not intended for prophylactic use to avoid weight loss.

Therapy with MEGACE OS for weight loss should only be instituted after treatable causes of weight loss are sought and addressed. These treatable causes include possible malignancies, systematic infections, gastrointestinal disorders affecting absorption, endocrine disease and renal or psychiatric disease.

**Carcinogenesis and Mutagenesis**

See TOXICOLOGY; Carcinogenesis.
No data on mutagenesis is currently available.

**Cardiovascular**

Use MEGACE/MEGACE OS with caution in patients with a history of thrombophlebitis.

**Endocrine and Metabolism**

The glucocorticoid activity of MEGACE OS has not been fully evaluated. Clinical cases of new onset diabetes mellitus, exacerbation of preexisting diabetes mellitus, and overt Cushing's syndrome have been reported in association with the chronic use of MEGACE OS. In addition, clinical cases of adrenal insufficiency have been observed in patients receiving or being withdrawn from chronic MEGACE OS therapy in the stressed and non-stressed state. Furthermore, adrenocorticotropin (ACTH) stimulation testing has revealed the frequent occurrence of asymptomatic pituitary-adrenal suppression in patients treated with chronic MEGACE OS therapy. Therefore, the possibility of adrenal insufficiency should be considered in any patient receiving or being withdrawn from chronic MEGACE OS therapy who presents with symptoms and/or signs suggestive of hypoadrenalism (e.g., hypotension, nausea, vomiting, dizziness, or weakness) in either the stressed or non-stressed state. Laboratory evaluation for adrenal insufficiency and consideration of replacement or stress doses of a rapidly acting glucocorticoid are strongly recommended in such patients. Failure to recognize inhibition of the hypothalamic-pituitary-adrenal axis may result in death. Finally, in patients who are receiving or being withdrawn from chronic MEGACE OS therapy, consideration should be given to the use of empiric therapy with stress doses of a rapidly acting glucocorticoid in conditions of stress or serious intercurrent illness (e.g., surgery, infection).

Long-term gonadal hormone modulations with MEGACE OS may lead **in some cases** to the development of osteoporosis/osteopenia or perturbation of bone mineral density (see ADVERSE REACTIONS).

**Immune**

Effects of MEGACE OS on HIV viral replication have not been determined.

***Special Populations***

**Pregnant Women**

THE USE OF PROGESTATIONAL AGENTS DURING THE FIRST FOUR MONTHS OF PREGNANCY IS NOT RECOMMENDED.

Progestational agents have been used beginning within the first trimester of pregnancy in an attempt to prevent habitual abortion or treat threatened abortion. There is no adequate evidence that such use is effective and there is evidence of potential harm to the foetus when such drugs are given during the first four months of pregnancy. Use of progestational agents, with their uterine-relaxant properties, in patients with fertilized defective ova may cause a delay in spontaneous abortion.

Several reports suggest an association between intrauterine exposure to progestational drugs in the first trimester of pregnancy and genital abnormalities in male and female fetuses. The risk of hypospadias, 5 to 8 per 1 000 male births in the general population, may be approximately doubled with exposure to these drugs. There are insufficient data to quantify the risk to exposed female fetuses, however some of these drugs induce mild virilization of the external genitalia of the female foetus.

If the patient is exposed to MEGACE OS during the first four months of pregnancy or if she becomes pregnant while taking this drug, she should be apprised of the potential risks to the foetus. Women of childbearing potential should be advised to avoid becoming pregnant.

### Nursing Women

Because many drugs are excreted in human breast milk and because of the potential for adverse reactions in nursing infants, nursing should be discontinued when receiving MEGACE OS therapy.

### Pediatrics (< 18 years of age)

Safety and effectiveness in pediatric patients have not been established.

### Geriatrics (> 65 years of age)

Insufficient data from clinical studies of megestrol acetate are available for patients 65 years of age and older to determine whether they respond differently than younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Megestrol acetate is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

## ADVERSE REACTIONS

### Adverse Drug Reaction Overview

Weight gain is a frequent side effect of megestrol acetate when it is used in patients with cancer of the breast or endometrium. This gain has been associated with increased appetite. It is this

effect which forms the basis for use of megestrol acetate in patients with anorexia, cachexia or weight loss. Weight gain is associated with an increase in fat and body cell mass.

Untoward reactions that have been reported to occur in patients receiving MEGACE OS (megestrol acetate) include nausea, vomiting, edema, and breakthrough uterine bleeding and occur in approximately 1% to 2% of patients. Gynecomastia and loss of hearing have also been reported. Dyspnea, pain, heart failure, hypertension, hot flashes, mood changes, cushingoid facies, tumor flare (with or without hypercalcemia), hyperglycemia, alopecia, carpal tunnel syndrome, diarrhea, lethargy and rash have also been reported.

Thromboembolic phenomenon including thrombophlebitis and pulmonary embolism (in some cases fatal) have also been reported.

Long-term gonadal hormone modulations with MEGACE OS may lead **in some cases** to the development of osteoporosis/osteopenia or perturbation of bone mineral density.

Pituitary adrenal axis abnormalities including glucose intolerance, new onset diabetes, and exacerbation of preexisting diabetes with decreased glucose tolerance and Cushing's syndrome have been reported with the use of megestrol acetate.

### Clinical Trial Adverse Drug Reactions

In clinical trials of megestrol acetate in patients with acquired immune deficiency syndrome, overall, there was no statistically significant difference between active and placebo treatment in patients reporting at least one adverse event. Events reported in $\geq 5\%$ of these study patients included diarrhea, impotence, rash, flatulence, asthenia and pain. Aside from impotence, all occurred more commonly in patients receiving placebo treatment.

Constipation and urinary frequency also have been reported in patients who received high doses of megestrol acetate in other clinical trials.

## DRUG INTERACTIONS

There are no alterations in pharmacokinetic parameters when megestrol acetate (oral suspension) is administered with zidovudine or rifabutin.

### Drug-Food Interactions

Interactions with food have not been established.

### Drug-Herb Interactions

Interactions with herbal products have not been established.

### Drug-Laboratory Interactions

Interactions with laboratory tests have not been established.

## DOSAGE AND ADMINISTRATION

For the following indications, at least two months of continuous treatment with MEGACE OS (megestrol acetate oral suspension) is recommended: **Anorexia, cachexia, or significant weight loss in patients with a diagnosis of acquired immunodeficiency syndrome (AIDS).**

Usual adult dose: 400 to 800 mg as a single daily dose (10 to 20 mL/day). A plastic dosage cup with 10 mL and 20 mL markings is provided for convenience. Half cup (10 mL) of oral suspension contains 400 mg and a full cup (20mL) contains 800 mg of megestrol acetate.

### Geriatric use:

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

### Missed Dose:

If the patient misses a dose, and remembers within a few hours of the missed dose, the patient should take MEGACE OS as soon as possible. If it is almost time for the next dose, the patient should be instructed to take their medication at the next regular time. The patient should not take double doses to make up for the missed dose.

## OVERDOSAGE

| For management of a suspected drug overdose, contact your regional Poison Control Centre. |
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Usual safety measures as with the overdose of any medication should be instituted. However, no serious unexpected side effects have resulted from studies involving MEGACE OS (megestrol acetate) administered in dosages as high as 1600 mg/day for 6 months or more. Megestrol acetate has not been tested for dialyzability; however, due to its low solubility, it is postulated that dialysis would not be an effective means of treating overdose.

Reports of overdose have also been received in the post-marketing setting. Signs and symptoms reported in the context of overdose included diarrhea, nausea, abdominal pain, shortness of breath, cough, unsteady gait, listlessness, and chest pain. There is no specific antidote for overdose with MEGACE OS. In case of overdose, appropriate supportive measures should be taken.

## ACTION AND CLINICAL PHARMACOLOGY

### Mechanism of Action

The precise mechanism of action by which megestrol acetate produces its antianorexic and anticachectic effects is unknown at present.

**Pharmacodynamics**

The gain in weight associated with megestrol acetate is associated with increased appetite, an increase in fat and body cell mass.

**Pharmacokinetics**

**Absorption:**

A single oral dose of radioactive megestrol acetate given to one male produced a maximum blood level in one to three hours and gradually fell over a 24-hour period.

In 24* healthy male volunteers (age 19-44 years) who received 160 mg of megestrol acetate given as a 40 mg qid regimen, the oral absorption of MEGACE OS (megestrol acetate) appeared to be variable. Peak drug levels for the first 40 mg dose ranged from 10 to 56 ng/mL (mean 27.6 ng/mL) and the times to peak concentrations ranged from 1.0 to 3.0 hours (mean 2.2 hours). The steady state plasma concentrations for a 40 mg qid regimen have not been established.

Plasma steady state pharmacokinetics of MEGACE OS were evaluated in 10 adult cachectic male patients (age 26-49 years) with acquired immunodeficiency syndrome (AIDS) and an involuntary weight loss greater than 10% of baseline. Patients received single oral dose of 800 mg/day of megestrol acetate for 21 days. Plasma concentration data obtained on day 21 were evaluated for up to 48 hours past the last dose. A high degree of interpatient variability in rate and extent of absorption was observed. Median peak plasma concentration ($C_{max}$) of megestrol acetate was 602 ng/mL (range 77 to 1670 ng/mL). Median area under the concentration versus time-curve (AUC) was 7547 ng·hr/mL (range 1550 to 27090 ng·hr/mL) and median $T_{max}$ value was 5.0 hr (range 1 to 8 hours).

Steady state plasma pharmacokinetics of MEGACE OS were evaluated in 24 asymptomatic HIV seropositive male patients (age 21-40 years). Patients received single oral dose of 750 mg of megestrol acetate for 14 days. The mean plasma concentration ($C_{max}$) of megestrol acetate was 490 ng/mL (range 156-1169 ng/mL). The mean area under the concentration vs time curve (AUC) was 6779 hr·ng/mL (range 1826 to 14094 hr·ng/mL) and median $T_{max}$ was 3.0 hours (range 0-8 hours).

Estimates of plasma levels of megestrol acetate are dependent on the measurement method used. Plasma levels depend on intestinal and hepatic inactivation of the drug, which may be affected by intestinal tract motility, intestinal bacteria, concomitant antibiotic administration, body weight, diet and hepatic function.

**Metabolism:**

The excretion occurred as three glucuronide conjugates with hydroxylation occurring at either the 2-α, or the 6-methyl position or at both positions. Other metabolites occur but only account for 5 - 8% of the dose.

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* Pharmacokinetic data from one patient excluded due to unusually high drug levels.

**Excretion:**

The major route of drug elimination in humans is urinary excretion and fecal excretion. Megestrol acetate when given orally to women exhibited an average excretion of 86.2% (range 83.1% to 94.7%), fecal excretion accounted for 19.8% (range 7.7% to 30.3%) and urinary excretion for 66.4% (range 56.5% to 78.4%). The biological half-life for doses of 60 - 90 mg was 3.5 days. The half-life of a 160 mg dose was 37.6 hours.

Respiratory excretion and fat storage may account for the fraction of an administered dose not found in urine or feces.

## STORAGE AND STABILITY

Store oral suspension at room temperature (15-30°C). Protect from temperatures above 30°C.

## SPECIAL HANDLING INSTRUCTIONS

Exposure at levels approaching recommended dosing levels or overdose could result in side effects described above (see WARNINGS and ADVERSE REACTIONS). Women at risk of pregnancy should avoid such exposure.

## DOSAGE FORMS, COMPOSITION AND PACKAGING

Bottles of 240 mL of MEGACE OS (megestrol acetate) is available as a lemon-lime flavored oral suspension containing 40 mg of micronized megestrol acetate per mL.

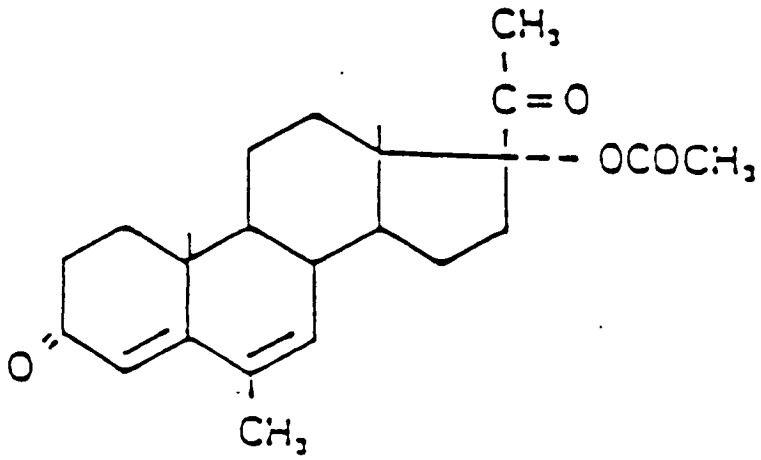
In addition to the active ingredient, megestrol acetate, each mL of oral suspension contains xantham gum, polysorbate 80, anhydrous citric acid, sucrose, sodium benzoate, sodium citrate dihydrate, polyethylene glycol 1450, purified water and natural and artificial lemon-lime flavor.

## PART II: SCIENTIFIC INFORMATION

## PHARMACEUTICAL INFORMATION

### Drug Substance

- Proper name: megestrol acetate
- Chemical name: 17-hydroxy-6-methylpregna-4, 6-diene-3, 20-dione acetate
- Molecular formula and molecular mass: $C_{24}H_{32}0_4$, 384.5
- Structural formula:




- Physicochemical properties: Megestrol acetate is a white to creamy-white, odourless, crystalline powder with a melting point of 213-219°C. It is insoluble in water; sparingly soluble in ethanol; and soluble in acetone and chloroform.

## DETAILED PHARMACOLOGY

### Animal Pharmacology

Besides its progestational effect, megestrol acetate also has antigonadotropic, antiuterotropic, and antiandrogenic/antimyotropic actions. It has a slight but definite glucocorticoid activity and a very slight mineralocorticoid action. It is inactive as an estrogen, androgen, or anabolic agent.

There were marginal or no significant effects in routine anticancer screening in mice and rats for mammary fibroadenoma or adenocarcinoma, methylcholanthrene carcinoma, acute leukemia and Dunning leukemia, and spontaneous uterine leiomyosarcoma. Malignant lymphoma in mice may have been stimulated.

## Human Pharmacology

Pharmacokinetics and Bioavailability

Megestrol acetate tablets, 750 mg (3 x 250 mg) and oral suspension 750 mg (40 mg/mL) was administered once daily to 24 asymptomatic, HIV seropositive male patients in a two-period bioequivalence study. Each treatment was administered for 14 days with no washout period between treatments. Steady-state plasma megestrol acetate concentrations were determined over a 24 hour period and pharmacokinetic parameters were determined non-compartmentally. When using the suspension as the reference dosage form, there was no significant difference in $T_{max}$ and $C_{max}$ plasma values for the tablet and suspension and the values fell within an 80 to 120% range; suggesting similar rates of bioavailability for the formulations. The mean AUC value for the tablet was 12% greater than for the suspension. Thus, it would appear that no clinically significant difference would be found between a dose of three 250 mg tablets and 750 mg of 40 mg/mL suspension, and they would be therapeutically interchangeable. Relative to the oral suspension, the 250 mg tablet had a mean bioavailability of 116%. The pharmacokinetic parameters are presented in Table 1.

**Table 1**

| Pharmacokinetic Parameter | 750 mg Tablet (3 x 250 mg) | 750 mg Oral Suspension (18.75 mL x 40 mg/mL) |
|---|---|---|
| $C_{max}$ (ng/mL) | 458.0 (183.0) | 490.0 (238.0) |
| $T_{max}$ (ng/mL) | 3.0 (1.0-6.0) | 3.0 (0.0-8.0)* |
| AUC (ng·hr/mL) | 7650.0 (3780.0) | 6779.0 (3048.0) |

* median value and range

In a pharmacokinetic study in patients with AIDS, ten, adult, male, cachectic patients (age 26-49 years) with an involuntary weight loss greater than 10% of baseline received daily oral doses of 800 mg of an oral suspension containing 40 mg/mL of micronized megestrol acetate for 21 days. Plasma samples were taken just prior to dosing on days 19, 20 and 21 and at intervals for 48 hours after dosing on day 21. All plasma samples were analyzed for intact megestrol acetate.

A high degree of intra patient variability in rate of absorption was observed. Table 2 provides a summary of the median pharmacokinetic parameters.

**Table 2**

| $AUC_{0-24}$ (ng·hr/L) | $C_{max}$ (ng/mL) | $T_{max}$ (ng/mL) |
|---|---|---|
| 7547.0 (1550.0-27090.0) | 602.0 (77.0-1670.0) | 5.0 (1.0-8.0) |

# TOXICOLOGY

## Acute Toxicity

A single dose of Megestrol acetate when given orally to mice is non-toxic at levels of 5 g/kg.

**Subacute and Chronic Toxicity**

Megestrol acetate given orally to rats for 3 months at doses of 1 mg/kg and 20 mg/kg had no effect on the growth of both males and females. Adrenal atrophy was seen in the females at the 20 mg/kg dose. Uterine sections showed endometrial hyperplasia, due to the progestational activity of megestrol acetate.

A trend toward increased frequency of respiratory infections, decreased lymphocyte counts and increased neutrophil counts was observed in a two-year chronic toxicity/carcinogenicity study of megestrol acetate conducted in rats.

Administration for up to 7 years of megestrol acetate to female dogs is associated with an increased incidence of both benign and malignant tumors of the breast. Comparable studies in monkeys for up to 10 years are not associated with an increased incidence of malignant tumours. The relationship of the dog tumors to humans is unknown but should be considered in assessing the benefit to risk ratio when prescribing megestrol acetate and in surveillance of patients on therapy.

Two long-term studies were performed on beagle dogs and monkeys. Groups of 20 female beagle dogs were given 0, 0.01, 0.10, or 0.25 mg/kg/day of megestrol acetate (0, 1, 10, or 25 times the anticipated human dose, on a mg/kg/basis) or 0.25 mg/kg/day of chlormadinone acetate. Groups of 20 female rhesus monkeys were given 0, 0.01, 0.10 or 0.50 mg/kg/day (0, 1, 10, or 50 times the anticipated human dose, on a mg/kg/basis) or 0.50 mg/kg/day of chlormadinone acetate. Up to the end of 7 years, 2 dogs at doses of 0.1 mg/kg/day and 5 dogs at 0.25 mg/kg/day exhibited mammary carcinoma with metastasis. Multiple mammary nodules were also seen in all dogs in these two dosage groups as well as one or two nodules in 3 of the 12 control animals. At the end of 5 years, one monkey at a dose of 0.01 mg/kg/day and one monkey at a dose of 0.10 mg/kg/day exhibited palpable nodules but were not malignant. Reduction in menses in the monkeys with near cessation of cyclic activity at 0.05 mg/kg/day, and a decreased evidence of estrus and mucoid vaginal discharges were noted in the beagle dogs.

At the end of the sixth year, elevations in erythrocyte sedimentation rate (ESR) were seen in dogs at the 0.1 and 0.25 mg/kg doses. Decreased hemoglobin (Hgb), hematocrit (Hct), and red blood cells (RBC) were seen in the latter group and scattered lowering of Hgb was observed in the former group. Serum cholesterol and blood sugar were elevated and serum calcium depressed in the 0.25 mg/kg/group. Serum cholesterol was elevated in the 0.1 mg/kg/group. Bilateral cataracts were observed in 1 of 6 dogs on the 0.25 mg/kg/dose. In addition to the changes in the breasts as previously described, necropsy findings in 3 of the 6 dogs at both doses included cachexia, discoloured lungs, enlarged livers, dark-green and viscous gallbladder contents, enlarged and discoloured kidneys, enlarged uteri and lymph nodes, and cystic ovaries.

In monkeys at the end of 5 years, physical, ophthalmoscopic examinations and clinical laboratory studies revealed no treatment-related effects. At the end of the 10 year study there were no compound related changes in mortality, physical appearance and behavior, body weight gain, ophthalmology, hematology, urinalysis, terminal body weights and gross tissue findings.

Minor related findings include a dose-dependent decrease in menstrual activity and in mean uterine weights, as well as a depressed estrogenic activity in the mid- and high-dose groups (0.1, 0.5 mg/kg/day). Histopathologic examination revealed inhibition of ovulation, increased numbers of hyalinized ovarian atretic follicules, increased cervical glandular dilatation, and increased cervical mucoid secretion in the mid and high dose groups. Cyclic endometrial changes were evident for all monkeys, but no mammary hyperplastic or neoplastic changes were found.

**Carcinogenesis**

Data on carcinogenesis were obtained from studies conducted in dogs, monkeys and rats treated with megestrol acetate. No males were used in the dog and monkey studies. In female beagle dogs, megestrol acetate (0.01, 0.1 or 0.25 mg/kg/day) administered for up to 7 years induced both benign and malignant tumors of the breast. In female monkeys, no tumors were found following 10 years of treatment with 0.01, 0.1 or 0.5 mg/kg/day megestrol acetate. Pituitary tumors were observed in female rats treated with 3.9 or 10 mg/kg/day of megestrol acetate for 2 years. The relationship of these tumors in rats and dogs to humans is unknown but should be considered in assessing the risk-to-benefit ratio when prescribing megestrol acetate and in surveillance of patients on therapy.

**Mutagenesis**

No data on mutagenesis is currently available.

**Impairment of Fertility**

Perinatal/postnatal (segment III) toxicity studies were performed in rats at doses of 0.05 to 12.5 mg/kg. In these low dose studies, the reproductive capability of male offspring of megestrol acetate-treated females was impaired. Similar results were obtained in dogs. Pregnant rats treated with megestrol acetate showed a reduction in fetal weight and number of live births, and feminization of male fetuses. No toxicity data are currently available on male reproduction (spermatogenesis).

**Teratology**

No adequate teratology information is available at clinically relevant doses.

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## READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

## PATIENT MEDICATION INFORMATION

## MEGACE OS

## Megestrol acetate Oral Suspension

Read this carefully before you start taking MEGACE OS and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about MEGACE OS.

### What is MEGACE OS used for?

MEGACE OS is used to treat patients with AIDS who have conditions characterized by weight loss.

### How does MEGACE OS work?

It is not known how MEGACE OS increases appetite. The weight gain is associated with an increase in fat and body cell mass.

### What are the ingredients in MEGACE OS?

Medicinal ingredient: **Megestrol acetate**

Non-medicinal ingredients: anhydrous citric acid, natural and artificial lemon-lime flavor, polyethylene glycol, polysorbate 80, purified water, sodium benzoate, sodium citrate dihydrate, sucrose and xantham gum.

### MEGACE OS comes in the following dosage forms:

Oral suspension of 40 mg/ml

### Do not use MEGACE OS if:

You are allergic to megestrol acetate or any of the ingredients in MEGACE OS.

MEGACE OS should not be used as a diagnostic test for pregnancy.

**To help avoid side effects and ensure proper use, talk to your healthcare professional before you take MEGACE OS. Talk about any health conditions or problems you may have, including if you:**

- Have diabetes. MEGACE OS may raise your blood sugar.
- Have a history of blood clots.
- Have or have had weak or brittle bones (**osteoporosis/ osteopenia**).

- Are you pregnant, planning to become pregnant or breast feeding.

**Other warnings you should know about:**

The use of MEGACE OS is not intended to prevent weight loss.

Use contraception while taking this medication if you are a woman capable of becoming pregnant. MEGACE OS may cause harm to an unborn baby. Tell your physician if you become pregnant while taking this medication.

**Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.**

Possible drug interactions of MEGACE OS with other medications are not known.

**How to take MEGACE OS:**

Take MEGACE OS:

- exactly as your doctor has told you
- for at least two months, to see if it is working
- until your doctor tells you to stop
- by mouth
- as a single dose
- with the attached measuring cup

Shake container well before use.

A cup is attached to the package. It is marked at 10 mL and 20 mL. Always use this cup to measure your dose.

- 10 mL contains 400 mg.
- 20 mL contains 800 mg.

**Usual adult dose:** 400 mg to 800 mg (10-20 mL) per day

If you are 65 or older, your doctor may start you on the lowest dose, and may watch your kidney function. Your doctor will decide on the correct dose for your condition. Always follow your doctor's instructions.

**Overdose:**

If you think you have taken too much MEGACE OS, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately even if there are no symptoms. Take the empty container and any remaining medicine with you.

**Missed Dose:**

If you miss a dose, do not worry. If you remember within a few hours of the missed dose take it as soon as possible, but if it is almost time for your next dose then skip the forgotten one and continue as before. DO NOT take double doses to make up for the one you missed.

**What are possible side effects from using MEGACE OS?**

These are not all the possible side effects you may feel when taking MEGACE OS. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:

- Weight gain
- Nausea, vomiting
- Constipation, diarrhea, flatulence
- Frequent urination
- Abnormal weakness or lack of energy
- Hot flashes, hair loss, mood change
- Rash
- Pain
- **Men** may get enlarged breasts, impotence

| **Serious side effects and what to do about them** | | | |
|---|---|---|---|
| Symptom / effect | Talk to your healthcare professional | | Stop taking drug and get immediate medical help |
| | Only if severe | In all cases | |
| **COMMON**<br>**Edema (caused by excess fluid):** swelling of arms or legs | | ✔ | |
| **VERY RARE**<br>**Adrenal insufficiency (adrenal glands do not make enough hormone):** craving salty food, abdominal pain, nausea, vomiting, dizziness, weakness, fatigue, low blood pressure and kidney failure. | | | ✔ |
| **Pulmonary embolism (blockage of a major artery in the lung):** sudden chest pain, shortness of breath, cough, fatigue, and heart | | | ✔ |

| Serious side effects and what to do about them | | | |
|---|---|---|---|
| Symptom / effect | Talk to your healthcare professional | | Stop taking drug and get immediate medical help |
| | Only if severe | In all cases | |
| palpitations | | | |
| **Tumor Flare:** temporary worsening of tumor symptoms, such as pain, redness, or tumor size | | ✔ | |
| **Vaginal bleeding:** breakthrough bleeding, spotting | ✔ | | |
| **UNKNOWN**<br>**Carpal tunnel syndrome:** numbness and tingling in the hand and arm | ✔ | | |
| **Cushing's syndrome:** round and red face, high blood pressure, abdomen obesity with thin arms and legs, red stretch marks, a fat lump between the shoulders, weak muscles, weak bones, acne, and fragile skin that heals poorly. Women may have more hair and irregular menstruation. | | ✔ | |
| **Dyspnea:** difficulty breathing, shortness of breath. | ✔ | | |
| **Heart failure:** shortness of breath, fatigue, swollen legs, rapid heartbeat | | | ✔ |
| **High blood pressure:** Headaches, vision disorders, nausea, and vomiting | | ✔ | |
| **Loss of hearing** | | ✔ | |
| **Osteoporosis/osteopenia (weak and brittle bones):** You break a bone in a situation where healthy people would not normally break a bone | | ✔ | |

| Serious side effects and what to do about them | | | |
|---|---|---|---|
| Symptom / effect | Talk to your healthcare professional | | Stop taking drug and get immediate medical help |
| | Only if severe | In all cases | |
| **New or worsening diabetes or hyperglycemia (high blood sugar):** unusual thirst, hunger, frequent urination, fatigue, or weight gain or loss | | ✔ | |
| **Thrombophlebitis (inflammation of veins):** Swelling, pain and redness in an arm or leg that can be warm to the touch | | ✔ | |

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

**Reporting Side Effects**

You can help improve the safe use of health products for Canadians by reporting serious and unexpected side effects to Health Canada. Your report may help to identify new side effects and change the product safety information.

**3 ways to report**:

- Online at MedEffect;
- By calling 1-866-234-2345 (toll-free);
- By completing a Consumer Side Effect Reporting Form and sending it by:
  - Fax to 1-866-678-6789 (toll-free), or
  - Mail to: Canada Vigilance Program
    Health Canada, Postal Locator 0701E
    Ottawa, ON
    K1A 0K9

  Postage paid labels and the Consumer Side Effect Reporting Form are available at MedEffect.

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

**Storage:**

Store MEGACE OS at room temperature (15-30°C). Keep out of reach and sight of children.

**If you want more information about MEGACE OS:**

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and

includes this Patient Medication Information by visiting the Health Canada website; the manufacturer's website http://www.bmscanada.ca, or by calling 1-866-463-6267.

This leaflet was prepared by Bristol-Myers Squibb Canada.

Last Revised: October 06, 2016