Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Megace 40 mg/ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of suspension contains 40 mg micronized megestrol acetate.

Excipients with known effect:
Sucrose (50 mg/ml)
Sodium benzoate (2 mg/ml) (E211)
Sodium (<1 mmol/ml)
Ethanol (0.49 mg/ml), a component of the lemon-lime flavour.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral suspension
White to cream coloured, milky suspension.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Megace Oral Suspension is indicated in male and female patients for the treatment of anorexia or weight loss secondary to cancer or AIDS.

4.2 Posology and method of administration

Posology

Adults:

400-800 mg given as a single daily dose.

At least two months of continuous treatment is considered an adequate period for determining the efficacy of Megace Oral Suspension.

Paediatric population:

The Safety and efficacy of Megace Oral Suspension in children have not been established.

This medicine is not recommended for use in children.

Elderly:

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 (see section 4.4).

Renal impairment:

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.

Method of administration

For oral use only.

4.3 Contraindications

Megace is contraindicated in patients who have demonstrated hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Megace is also contraindicated in patients with thromboembolic disorders.

4.4 Special warnings and precautions for use

Megace should be used with caution in patients with a history of thrombophlebitis.

This product should be used under the supervision of a specialist and the patients kept under regular surveillance (see section 4.8 and 5.3).
This product can exert adrenocortical effects. This should be borne in mind in patient surveillance (see section 4.8).

Megace Oral Suspension contains 50 mg/ml of sucrose (0.5-1 g per dose) which may be harmful to the teeth. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Insufficient data from clinical studies of megesterol acetate are available for patients 65 years of age and older to determine whether they respond differently than younger patients. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general, dose selection for elderly patients should be cautious, 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 during treatment with megestrol acetate, and it may be useful to monitor renal function.

Megace Oral Suspension contains 40 mg sodium benzoate (E211) in each 20 ml dose which is equivalent to 2 mg/ml. Sodium benzoate may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

This medicine contains less than 1 mmol sodium (23 mg) per 20 ml, that is to say essentially 'sodium-free'.

This medicine contains 9.8 mg of alcohol (ethanol) in each 20ml dose, which is equivalent to 0.49 mg/ml. The amount of alcohol in a 20ml dose of this medicine is equivalent to less than 1 ml beer or 1 ml wine. The small amount of alcohol in this medicine will not have any noticeable effects.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed

4.6 Fertility, pregnancy and lactation

Pregnancy
Megace is not recommended for women who are pregnant or who are breast feeding.

Women of child bearing potential should be advised to avoid becoming pregnant.
Several reports suggest an association between intrauterine exposure to progestational drugs in the first trimester of pregnancy and genital abnormalities in male and female foetuses. The risk of hypospadias, 5 to 8 per 1,000 in male births in the general population may be approximately doubled with the exposure to progestational drugs.

If a patient is exposed to Megace during the first four months of pregnancy or if she becomes pregnant whilst taking Megace, she should be apprised of the potential risks to the foetus.

Breastfeeding
Because of the potential for adverse effects, nursing should be discontinued during treatment with Megace.

Fertility
There are insufficient data to quantify the risk to exposed female foetuses; however some progestational drugs may cause mild virilisation of the external genitalia of the female foetuses.

4.7 Effects on ability to drive and use machines

Megace Oral Suspension has no or negligible influence on the ability to drive or use machines.

4.8 Undesirable effects

Pituitary adrenal axis abnormalities including glucose intolerance, new onset diabetes, exacerbation of pre-existing diabetes with decreased glucose tolerance and Cushing's syndrome have been reported with the use of megestrol acetate. Clinically apparent adrenal insufficiency has been rarely reported in patients shortly after discontinuing megestrol acetate. The possibility of adrenal suppression should be considered in all patients taking or withdrawing from chronic megestrol acetate therapy. Replacement stress doses of glucocorticoids may be indicated.
Patients should be observed when Megace is abruptly withdrawn.

In clinical trials in patients with AIDS there was no significant difference between active and placebo treatment in patients reporting at least one adverse event. Events reported in ≥ 5% of these study patients included diarrhoea, impotence, rash. Other reported adverse events included flatulence, asthenia, and pain.

Similarly in patients with advanced non-endocrine sensitive cancer who received megestrol acetate for anorexia and weight loss, dyspnoea, nausea, oedema, pain, lethargy and diarrhoea were commonly observed.

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

A rarely encountered side effect of prolonged administration of megestrol acetate is urticaria, presumably an idiosyncratic reaction to the drug. The drug is devoid of the myelosuppressive activity characteristic of many cytotoxic drugs and it causes no significant changes in haematology, blood chemistry or urinalysis.

The list is presented by system organ class, MedDRA preferred term, and frequency using the following frequency categories: very common (≥1/10), common (≥1/100, < 1/10), uncommon (≥1/1000, <1/100), rare (≥1/10000, <1/1000), very rare (< 1/10000), and not known (cannot be estimated from the available data).

System Organ Class	Frequency	MedDRA Term
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	Common	Tumour flare [#]
Endocrine disorders	Very common	Adrenal insufficiency, cushingoid, Cushing's syndrome
Metabolism and nutrition disorders	Very common	Diabetes mellitus, glucose tolerance impaired, hyperglycaemia, increased appetite
Psychiatric disorders	Common	Mood altered
Nervous system disorders	Common	Carpal tunnel syndrome, lethargy
Cardiac disorders	Common	Cardiac failure
Vascular disorders	Very common	Thrombophlebitis, pulmonary embolism*, hypertension, hot flush
Respiratory, thoracic and mediastinal disorders	Very common	Dyspnoea
Gastrointestinal disorders	Common	Nausea, vomiting, diarrhoea, flatulence

	Very common	Constipation
Skin and subcutaneous tissue disorders	Common	Rash
	Common	Alopecia
Renal and urinary disorders	Common	Pollakiuria
Reproductive system and breast disorders	Common	Menrorrhagia, erectile dysfunction
General disorders and administration site condition	Common	Asthenia, pain, oedema
Investigations	Very common	Weight increased

[#]with or without hypercalcemia
* Pulmonary embolism (in some cases fatal)

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

HPRA Pharmacovigilance, Website: www.hpra.ie

4.9 Overdose

No acute toxicological effects have resulted from studies involving Megace (megestrol acetate) administered in dosages as high as 1600 mg/day for six months or more.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The major effect experienced by patients while taking megestrol acetate, particularly at high doses, is weight gain, which is usually not associated with water retention, but which is secondary to an increased appetite/food intake and an increase in fat and body cell mass. It is this effect which forms the basis for use of megestrol acetate in patients with anorexia or weight loss. The mechanism by which Megace produces its effects in anorexia and cachexia are unclear.

5.2 Pharmacokinetic properties

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.

Metabolites have accounted for only 5% to 8% of an administered dose of megestrol acetate. The major route of drug elimination in humans is urinary excretion averaging approximately 66% and faecal excretion averaging approximately 20% of the administered dose. Respiratory excretion and fat storage may account for the fraction of an administered dose not found in urine or faeces.

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

5.3 Preclinical safety data

The chronic administration of megestrol acetate to female dogs for up to 7 years was associated with an increased incidence of both benign and malignant tumours of the breast. Comparable studies in rats and studies in monkeys were not associated with

an increased incidence of tumours. The relationship of chronic megestrol acetate exposures and associated dog tumours to cancer induction in humans is unknown, but should be considered in assessing the benefit-to-risk ratio when prescribing Megace, and in surveillance of patients on therapy.

Fertility and reproduction studies with high doses of megestrol acetate have shown a reversible feminising effect on some male rat foetuses.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid anhydrous
Lemon-lime flavour
Polyethylene glycol
Polysorbate 80 (E433)
Sodium benzoate (E211)
Sodium citrate (E331)
Sucrose
Water
Xanthan gum (E415)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

High density polyethylene bottles with a child-resistant closure available in a 240 ml pack size.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Bausch Health Ireland Limited
3013 Lake Drive
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA22698/024/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10 December 1998

Date of last renewal: 10 December 2008

10 DATE OF REVISION OF THE TEXT

May 2023