COMPOSITION
Mestrol-40: Each film coated tablet contains Megestrol Acetate USP 40mg.
Mestrol-160: Each film coated tablet contains Megestrol Acetate USP 160mg.

DESCRIPTION
Megestrol Acetate is a synthetic, antineoplastic and progestational drug. Its molecular weight is 384.51. The molecular formula is $C_{24}H_{32}O_4$.

CLINICAL PHARMACOLOGY
Mechanism of Action:
The anti-tumour action of Megestrol Acetate on carcinoma of the breast is unclear. However, it is known to compete for progesterone, androgen and glucocorticoid receptors and effect pituitary functions.

Pharmacokinetics:
Absorption
Estimates of plasma levels of Megestrol Acetate are dependent on the measurement method used. Peak plasma concentrations occur 2 to 3 hours after a single oral dose 160mg tablets.

Distribution
Similar peak plasma concentrations (90-110ng/mL) occur after the administration of one 160mg tablet or four 40mg tablets given over 24 hours. The extent of absorption (AUC) was also not different between the two dosage forms. The plasma half-life was 33 to 38 hours.

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

Excretion
Approximately 66% of an administered dose is excreted in the urine and approximately 20% in the faeces. Respiratory excretion and fat storage may account for the fraction of an administered dose not found in urine or faeces.

INDICATIONS
Megestrol Acetate is indicated for the palliative treatment of advanced carcinoma of the breast or endometrium (i.e., recurrent, inoperable, or metastatic disease). It should not be used in lieu of currently accepted procedures such as surgery, radiation, or chemotherapy. It is also indicated for the treatment of anorexia, cachexia, or weight loss secondary to metastatic cancer.

DOSAGE AND ADMINISTRATION
Breast Cancer: 160mg/day (160mg taken once daily).
Endometrial Carcinoma: 40 to 320mg/day in divided doses (40-80mg one to four times daily or one to two 160mg tablets daily).
At least 2 months of continuous treatment is considered an adequate period for determining the efficacy of Megestrol Acetate.
Cachexia: 400 to 800mg/day.
Use in Children: Safety and effectiveness in pediatric patients have not been established.
Use in the Elderly: 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. Other reported clinical experience has not identified differences in responses between elderly and 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.

Maximum Tolerated Daily Dose:
Breast Cancer: 160mg/day.
Endometrial Carinoma: 320mg/day.
Cachexia: 800mg/day.

SIDE EFFECTS
Weight Gain: Weight gain is a frequent side effect of Megestrol. This gain has been associated with increased appetite and is not necessarily associated with fluid retention.
Thromboembolic Phenomena: Thromboembolic phenomena including thrombophlebitis and pulmonary embolism (in some cases fatal) have been reported.
Glucocorticoid Effects: Nausea and vomiting, edema, breakthrough menstrual bleeding, dyspnea, tumor flare (with or without hypercalcemia), hyperglycemia, glucose intolerance, alopecia, hypertension, carpal tunnel syndrome, mood changes, hot flashes, malaise, asthenia, lethargy, sweating and rash.

CONTRAINDICATIONS
It is contraindicated in patients with known hypersensitivity to Megestrol Acetate or any component of the formulation. It should not be used as a diagnostic test for pregnancy.

DRUG INTERACTIONS
There is no data available.

PRECAUTIONS
Close surveillance is indicated for any patient treated for recurrent or metastatic cancer. Megestrol Acetate should be used with caution in patients with a history of thromboembolic disease or diabetes.
Use in Pregnancy: Pregnancy Category D.
There are no adequate and well-controlled studies in pregnant women. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. Women of childbearing potential should be advised to avoid becoming pregnant.
Use in Lactation: 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 Megestrol Acetate therapy.

OVERDOSE
No serious unexpected side effects have resulted from studies involving Megestrol Acetate administered in dosages as high as 1600mg/day. Oral administration of large, single doses of Megestrol Acetate (5g/kg) did not produce toxic effects in mice.

PHARMACEUTICAL INFORMATION
Storage: Store below 25° C in a dry place. Protect from light. Keep out of the reach of children.
Packing: Mestrol-40: Each box contains 30 tablets in Alu-Alu blister pack. Mestrol-160: Each box contains 30 tablets in Alu-Alu blister pack.