MODUS® TABLETS

Medroxyprogesterone Tablets IP

QUALITATIVE AND QUANTITATIVE COMPOSITION

MODUS TABLET 2.5 mg
Each uncoated tablet contains:
Medroxyprogesterone acetate (MPA) IP 2.5 mg

MODUS TABLET 10 mg
Each uncoated tablet contains:
Medroxyprogesterone acetate (MPA) IP 10 mg

PHARMACEUTICAL FORM

Uncoated tablets

CLINICAL PARTICULARS

Therapeutic Indications

Progestogen. Indicated for dysfunctional (anovulatory) uterine bleeding, secondary amenorrhoea and for mild to moderate endometriosis.

Posology and Method of Administration

Oral.

Adults

Dysfunctional (anovulatory) uterine bleeding
2.5 - 10 mg daily for 5 - 10 days commencing on the assumed or calculated 16th - 21st day of the cycle. Treatment should be given for two consecutive cycles. When bleeding occurs from a poorly developed proliferative endometrium, conventional oestrogen therapy may be employed in conjunction with medroxyprogesterone acetate in doses of 5 - 10 mg for 10 days.
Secondary amenorrhoea
2.5 - 10 mg daily for 5 - 10 days beginning on the assumed or calculated 16th to 21st day of the cycle. Repeat the treatment for three consecutive cycles. In amenorrhoea associated with a poorly developed proliferative endometrium, conventional oestrogen therapy may be employed in conjunction with medroxyprogesterone acetate in doses of 5 - 10 mg for 10 days.

Mild to moderate endometriosis
Beginning on the first day of the menstrual cycle, 10 mg three times a day for 90 consecutive days.

10 mg dose only
Breakthrough bleeding, which is self-limiting, may occur. No additional hormonal therapy is recommended for the management of this bleeding.

Elderly
Not applicable

Children
Not applicable

Contraindications
Known, past or suspected breast cancer;
Previous idiopathic or current venous thromboembolism (deep venous thrombosis, pulmonary embolism);
Active or recent arterial thromboembolic disease (e.g angina, myocardial infarction);
Acute liver disease, or a history of liver disease as long as liver function tests have failed to return to normal;
Known hypersensitivity to the active substances or to any of the excipients;
Porphyria

Special Warnings and Special Precautions for Use

Medical Examination/Follow-Up
Before initiating or reinstituting therapy, a complete personal and family medical history should be taken. Physical (including pelvic) examination should be guided by this and by the contraindications (see Contraindications) and warnings for use. During treatment, periodic check-ups are recommended of a frequency and nature adapted to the individual woman, but
may include, if judged appropriate by the clinician, abdominal and pelvic examination. Women should be encouraged to undergo breast cancer screening (mammography) and cervical cancer screening (cervical cytology) as appropriate for their age.

The possibility of genital tract pathology should be considered before commencing treatment in women with abnormal uterine bleeding, especially in women over 45, who may require gynaecological investigation.

A negative pregnancy test should be demonstrated before starting therapy (see Pregnancy and Lactation).

Doses of up to 30 mg a day may not suppress ovulation and patients should be advised to take adequate contraceptive measures, where appropriate.

**Conditions which need Supervision**

If any of the following conditions are present, have occurred previously, and/or have been aggravated during pregnancy or previous hormone treatment, the patient should be closely supervised. It should be taken into account that these conditions may recur or be aggravated during treatment with MODUS, in particular:

- A history of, or risk factors for, thromboembolic disorders (see below)
- Risk factors for oestrogen dependent tumours, e.g. 1 degree heredity for breast cancer
- Hypertension
- Liver disorders (e.g. liver adenoma)
- Diabetes mellitus with or without vascular involvement
- Cholelithiasis
- Migraine or (severe) headache
- Systemic lupus erythematosus.
- Epilepsy
- Asthma
- Otosclerosis

Rare cases of thromboembolism have been reported with use of medroxyprogesterone acetate, especially at higher doses. Causality has not been established.

History or emergence of the following conditions require careful consideration and appropriate investigation: signs of a blood clot; migraine or unusually severe headaches or acute visual disturbances of any kind.

MODUS, especially in high doses, may cause weight gain and fluid retention. With this in mind, caution should be exercised in treating any patient with a pre-existing medical condition, such as
epilepsy, migraine, asthma, cardiac or renal dysfunction, that might be adversely affected by weight gain or fluid retention.

Some patients receiving MODUS may exhibit a decreased glucose tolerance. The mechanism for this is not known. This fact should be borne in mind when treating all patients and especially known diabetics.

This product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Patients with a history of treatment for mental depression should be carefully monitored while receiving MODUS therapy. Some patients may complain of premenstrual like depression while on MODUS therapy.

Reasons for Immediate Withdrawal of Therapy:
Therapy should be discontinued in case a contraindication is discovered and in the following situations:
- Jaundice or deterioration in liver function
- Significant increase in blood pressure
- New onset of migraine-type headache

Interaction with Other Medicaments and Other Forms of Interaction

Aminoglutethimide administered concurrently with MODUS may significantly depress the bioavailability of MODUS.

Interactions with other medicinal treatments (including oral anti-coagulants) have rarely been reported, but causality has not been determined. The possibility of interaction should be borne in mind in patients receiving concurrent treatment with other drugs.

The metabolism of progestogens may be increased by concomitant use of substances known to induce drug-metabolising enzymes, specifically cytochrome P450 enzymes, such as anticonvulsants (e.g. phenobarbital, phenytoin, carbamazepine) and anti-infectives (e.g. rifampicin, rifabutin, nevirapine, efavirenz).

Medroxyprogesterone acetate (MPA) is metabolized in-vitro primarily by hydroxylation via the CYP3A4. Specific drug-drug interaction studies evaluating the clinical effects with CYP3A4 inducers or inhibitors on MPA have not been conducted and therefore the clinical effects of CYP3A4 inducers or inhibitors are unknown.
Ritonavir and nelfinavir, although known as strong inhibitors, by contrast exhibit inducing properties when used concomitantly with steroid hormones. Herbal preparations containing St John's wort (Hypericum perforatum) may induce the metabolism of progestogens.

Clinically, an increased metabolism of progestogens may lead to decreased effect.

**Pregnancy and Lactation**

**Pregnancy**

*MODUS* is not indicated during pregnancy. If pregnancy occurs during medication with *MODUS*, treatment should be withdrawn immediately.

The results of most epidemiological studies to date relevant to inadvertent foetal exposure to progestogens indicate no teratogenic or foetotoxic effect.

**Lactation**

*MODUS* is not indicated during lactation.

Medroxyprogesterone acetate and its metabolites are secreted in breast milk, but there is no evidence to suggest that this presents any hazard to the child.

**Effects on Ability to Drive and Use Machines**

No adverse effect has been reported.

**Undesirable Effects**

The following medical events have been occasionally to rarely associated with the use of progestogens:

**Immune System disorders:** Hypersensitivity reactions (e.g., anaphylaxis & anaphylactoid reactions, angioedema)

**Metabolism and nutritional disorders:** Weight change, oedema/fluid retention

**Psychiatric disorders:** Depression, insomnia, nervousness

**Nervous system disorders:** Dizziness, headache, somnolence
Vascular disorders: Thromboembolic disorders

Gastrointestinal disorders: Nausea

Skin and subcutaneous tissue disorders: Acne, alopecia, hirsutism, pruritus, rash, urticaria

Reproductive system and breast disorders: Galactorrhoea, breast tenderness, breast pain.

General disorders and administration site conditions: Fatigue

Investigations: Decreased glucose tolerance

Overdose

In animals medroxyprogesterone acetate has been shown to be capable of exerting an adreno-corticoid effect, but this has not been reported in the human, following usual dosages. The oral administration of medroxyprogesterone acetate at a rate of 100 mg per day has been shown to have no effect on adrenal function.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Pharmacotherapeutic group: Progestogens – Pregnen (4) derivatives, ATC code: G03DA02

Medroxyprogesterone acetate has actions and uses similar to those of progesterone.

MPA has minimal androgenic activity compared to progesterone and virtually no oestrogenic activity.

Progestogens are used in the treatment of dysfunctional uterine bleeding, secondary amenorrhoea and endometriosis.

Pharmacokinetic Properties

MPA is rapidly absorbed from the GI tract with a single oral dose of 10-250 mg. The time taken to reach the peak serum concentration (T_{max}) was 2-6 hours and the average peak serum concentration (C_{max}) was 13-46.89 mg/ml.

Unmetabolised MPA is highly plasma protein bound. MPA is metabolised in the liver.
MPA is primarily metabolised by faecal excretion as glucuronide conjugated metabolite.

Metabolised MPA is excreted more rapidly and in a greater percentage following oral doses than after aqueous intramuscular injection

Preclinical Safety Data

None stated

PHARMACEUTICAL PARTICULARS

List of Excipients

Starch maize, lactose, polyvinyl pyrrolidone K-30, magnesium stearate, colloidal silicon dioxide

Incompatibilities

No known incompatibilities

Shelf Life

36 months

Expiry date is indicated on the packaging.

Special Precautions for Storage

Protect from light

Keep out of reach of children.

Nature and Specification of Container

10 Tablets per blister strip; 10 strips in a Carton

Instructions for Use / Handling

There are no special requirements for use or handling of the product.
For further information please contact:
GlaxoSmithKline Pharmaceuticals Limited.

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Dr. Annie Besant Road, Worli
Mumbai 400 030, India.

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Adapted from Provera Tablets 2.5 mg, & 10 mg. Summary of Product Characteristics last updated on the eMC: 11 Dec 2014 available at:
http://www.medicines.org.uk/EMC/medicine/20900/SPC/Provera+Tablets+2.5+mg%2c+Provera+Tablets+5+mg+Provera+Tablets+10+mg/