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Summary of Product Characteristics last updated on the eMC: 24/04/2013

Utrogestan 100mg Capsules

1. Name of the medicinal product

UTROGESTAN 100MG CAPSULES

2. Qualitative and quantitative composition

Each capsule contains 100 mg micronised progesterone (INN). For excipients, see 6.1.

3. Pharmaceutical form

Capsules, soft

White

4. Clinical particulars

4.1 Therapeutic indications

Adjunctive use with estrogen in post-menopausal women with an intact uterus. (HRT)

4.2 Posology and method of administration

Posology

In women receiving estrogen replacement therapy there is an increased risk of endometrial cancer which can be countered by progesterone administration. The recommended dose is 200 mg daily at bedtime, for twelve days in the last half of each therapeutic cycle (beginning on day 15 of the cycle and ending on day 26). Withdrawal bleeding may occur in the following week. Alternatively 100 mg can be given at bedtime from day 1 to day 25 of each therapeutic cycle, withdrawal bleeding being less with this treatment schedule.

Children: Not applicable.

Elderly: As for adults

Method of Administration: Oral. Utrogestan 100mg Capsules should not be taken with food

4.3 Contraindications

Known allergy or hypersensitivity to progesterone or to any of the excipients. The capsules contain arachis oil (peanut oil) and should never be used by patients allergic to peanuts. Severe hepatic dysfunction. Undiagnosed vaginal bleeding. Mammary or genital tract carcinoma. Thrombophlebitis. Thromboembolic disorders. Cerebral haemorrhage. Porphyria.

4.4 Special warnings and precautions for use

Warnings:

Utrogestan 100mg Capsules are not a treatment for premature labour.

Prescription of progesterone beyond the first trimester of pregnancy may reveal gravidic cholestasis.

Utrogestan 100mg Capsules are not suitable for use as a contraceptive.

If unexplained, sudden or gradual, partial or complete loss of vision, proptosis or diplopia, papilloedema, retinal vascular lesions or migraine occur during therapy, the drug should be discontinued and appropriate diagnostic and therapeutic measures instituted.

Utrogestan 100mg Capsules are intended to be co-prescribed with an estrogen product as HRT. Epidemiological evidence suggests that the use of HRT is associated with an increased risk of developing deep vein thrombosis (DVT) or pulmonary embolism. The prescribing information for the co-prescribed estrogen product should be referred to for information about the risks of venous thromboembolism.

There is suggestive evidence of a small increased risk of breast cancer with estrogen replacement therapy. It is not known whether concurrent progesterone influences the risk of cancer in post-menopausal women taking hormone replacement therapy. The prescribing information for the co-prescribed estrogen product should be referred to for information about the risks of breast cancer.

Precautions

Prior to taking hormone replacement therapy (and at regular intervals thereafter) each woman should be assessed. A personal and family medical history should be taken and physical examination should be guided by this and by the contraindications and warnings for this product.

Utrogestan 100mg Capsules should not be taken with food and should be taken at bedtime. Concomitant food ingestion increases the bioavailability of Utrogestan 100mg Capsules.

Utrogestan 100mg Capsules should be used cautiously in patients with conditions that might be aggravated by fluid retention (e.g. hypertension, cardiac disease, renal disease, epilepsy, migraine, asthma); in patients with a history of depression, diabetes, mild to moderate hepatic dysfunction, migraine or photosensitivity and in breast-feeding mothers.

Clinical examination of the breasts and pelvic examination should be performed where clinically indicated rather than as a routine procedure. Women should be encouraged to participate in the national breast

cancer screening programme (mammography) and the national cervical cancer screening programme (cervical cytology) as appropriate for their age. Breast awareness should also be encouraged and women advised to report any changes in their breasts to their doctor or nurse.

4.5 Interaction with other medicinal products and other forms of interaction

Utrogestan 100mg Capsules may interfere with the effects of bromocriptine and may raise the plasma concentration of ciclosporin. Utrogestan 100mg Capsules may affect the results of laboratory tests of hepatic and/or endocrine functions.

Metabolism of Utrogestan 100mg Capsules is accelerated by rifamycin an antibacterial agent.

The metabolism of progesterone by human liver microsomes was inhibited by ketoconazole (IC_{50} <0.1 µM Ketoconazole is a known inhibitor of cytochrome P450 3A4. These data therefore suggest that ketoconazole may increase the bioavailability of progesterone. The clinical relevance of the in vitro findings is unknown.

4.6. Pregnancy and lactation

Pregnancy

Utrogestan 100mg Capsules are not indicated during pregnancy. If pregnancy occurs during medication, Utrogestan 100mg Capsules should be withdrawn immediately.

Lactation

Detectable amounts of progesterone enter the breast milk. There is no indication for prescribing HRT during lactation.

4.7 Effects on ability to drive and use machines

Utrogestan 100mg Capsules may cause drowsiness and/or dizziness in a minority of patients; therefore caution is advised in drivers and users of machines. Taking the capsules at bedtime should reduce these effects during the day.

4.8 Undesirable effects

Somnolence or transient dizziness may occur 1 to 3 hours after intake of the drug. Bedtime dosing and reduction of the dose may reduce these effects.

Shortening of the cycle or breakthrough bleeding may occur. If this occurs, the dose of Utrogestan 100mg Capsules can be reduced and taken at bedtime from day 1 to day 26 of each therapeutic cycle.

Acne, urticaria, rashes, fluid retention, weight changes, gastro-intestinal disturbances, changes in libido, breast discomfort, premenstrual symptoms, menstrual disturbances; also chloasma, depression, pyrexia, insomnia, alopecia, hirsutism; rarely jaundice.

Venous thromboembolism, i.e. deep leg or pelvic venous thrombosis and pulmonary embolism, is more frequent among hormone replacement therapy users than among non-users.

4.9 Overdose

Symptoms of overdosage may include somnolence, dizziness, euphoria or dysmenorrhoea. Treatment is observation and, if necessary, symptomatic and supportive measures should be provided.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group (ATC code: G03D)

Progesterone is a natural progestogen, the main hormone of the corpus luteum and the placenta. It acts on the endometrium by converting the proliferating phase to the secretory phase. Utrogestan 100mg Capsules have all the properties of endogenous progesterone with induction of a full secretory endometrium and in particular gestagenic, antiestrogenic, slightly anti-androgenic and antialdosterone effects.

5.2 Pharmacokinetic properties

Absorption

Micronised progesterone is absorbed by the digestive tract. Pharmacokinetic studies conducted in healthy volunteers have shown that after oral administration of 2 capsules (200mg), plasma progesterone levels increased to reach the Cmax of 13.8ng/ml +/- 2.9ng/ml in 2.2 +/- 1.4 hours. The elimination half-life observed was 16.8+/- 2.3 hours.

Although there were inter-individual variations, the individual pharmacokinetic characteristics were maintained over several months, indicating predictable responses to the drug.

Distribution

Progesterone is approximately 96%-99% bound to serum proteins, primarily to serum albumin (50%-54%) and transcortin (43%-48%).

Elimination

Urinary elimination is observed for 95% in the form of glycuroconjugated metabolites, mainly 3 α, 5 β–pregnanediol (pregnandiol).

Metabolism

Progesterone is metabolised primarily by the liver. The main plasma metabolites are 20 α hydroxy- Δ 4 α-prenolone and 5 α-dihydroprogesterone. Some progesterone metabolites are excreted in the bile and these may be deconjugated and further metabolised in the gut via reduction, dehydroxylation and epimerisation. The main plasma and urinary metabolites are similar to those found during the physiological secretion of the corpus luteum.

5.3 Preclinical safety data

Preclinical data revealed no special hazard for humans based on conventional studies of safety

pharmacology and toxicity.

6. Pharmaceutical particulars

6.1 List of excipients

Arachis oil

Soya lecithin

Gelatin

Glycerol

Titanium dioxide

6.2 Incompatibilities

None.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

No special precautions for storage.

6.5 Nature and contents of container

The product is supplied in PVC/Aluminium blisters contained in cartons.

Pack size: 30 capsules

6.6 Special precautions for disposal and other handling

Not applicable.

7. Marketing authorisation holder

Marlborough Pharmaceuticals Ltd

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8. Marketing authorisation number(s)

PL23138/0017

9. Date of first authorisation/renewal of the authorisation

16th April 2013

10. Date of revision of the text