SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Utovlan 5 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5mg norethisterone .

Excipients with known effect
Each tablet contains lactose (as monohydrate)

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet
White, flat, circular, bevel-edged tablet inscribed 'SEARLE' on one side and 'U' on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

At low dose: Dysfunctional uterine bleeding, endometriosis, polymenorrhoea, menorrhagia, metropathia, haemorrhagia, postponement of menstruation and premenstrual syndrome.

At high dose: Disseminated carcinoma of the breast.

4.2 Posology and method of administration

Posology

Low dose

Dysfunctional uterine bleeding, polymenorrhoea, menorrhagia, dysmenorrhoea and metropathia haemorrhagia: 1 tablet three times daily for 10 days; bleeding usually stops within 48 hours. Withdrawal bleeding resembling true menstruation occurs a few days after the end of treatment. One tablet twice daily, from days 19 to 26 of the two subsequent cycles, should be given to prevent recurrence of the condition.

Endometriosis: 1 tablet three times daily for a minimum treatment period of six months. The dosage should be increased to 4 or 5 tablets a day if spotting occurs. The initial dosage should be resumed when bleeding or spotting stops.

Postponement of menstruation: 1 tablet three times daily, starting three days before the expected onset of menstruation. Menstruation usually follows within three days of finishing the treatment.

Pre-menstrual syndrome: 1 tablet daily from days 16 to 25 of the menstrual cycle.

High dose

For disseminated breast carcinoma the starting dose is 8 tablets (40mg) per day increasing to 12 tablets (60mg) if no regression is noted.

Method of administration

Oral Administration

4.3 Contraindications

Hypersensitivity to the active substance or any of the excipients listed in section 6.1

Pregnancy
Previous idiopathic or current venous thromboembolism (deep vein thrombosis, pulmonary embolism)
Active or recent arterial thromboembolic disease (e.g. angina, myocardial infarction)
Disturbance of liver function
History during pregnancy of idiopathic jaundice
Severe pruritus or pemphigoid gestationis
Undiagnosed irregular vaginal bleeding
Porphyria

4.4 Special warnings and precautions for use

If menstrual bleeding should fail to follow a course of Utovlan, the possibility of pregnancy must be excluded before a further course is given.

Therapy should be discontinued if the following occur:
- Jaundice or deterioration in liver function
- Significant increase in blood pressure
- New onset of migraine-type headache

Progestogens may cause fluid retention. Special care should be taken when prescribing norethisterone in patients with conditions which might be aggravated by this factor:
- Epilepsy
- Migraine
- Asthma
- Cardiac dysfunction
- Renal dysfunction

Risk of venous thromboembolism (VTE)

Long term use of low dose progestogens as part of combined oral contraception or combined hormone replacement therapy has been associated with an increased risk of venous thromboembolism, although the role of progestogens in this aetiology is uncertain. A patient who develops symptoms suggestive of thromboembolic complications should have her status and need for treatment carefully assessed before continuing therapy.

Any patient who develops an acute impairment of vision, proptosis, diplopia or migraine headache should be carefully evaluated ophthalmologically to exclude papilloedema or retinal vascular lesions before continuing medication.

Generally recognised risk factors for VTE include a personal history or family history, severe obesity (BMI >30 kg/m^2) and systemic lupus erythematosus (SLE). There is no consensus about the possible role of varicose veins in VTE.

Treatment with steroid hormones may add to these risk factors. Personal or strong family history of thromboembolism or recurrent spontaneous abortion should be investigated in order to exclude a thrombophillic predisposition. Until a thorough evaluation of thrombophillic factors has been made or anticoagulant treatment initiated, use of progestogens in these patients should be viewed as contraindicated. Where a patient is already taking anticoagulants, the risks and benefits of progestogen therapy should be carefully considered.

The risk of VTE may be temporarily increased with prolonged immobilisation, major trauma or major surgery. As in all post-operative patients, scrupulous attention should be given to prophylactic measures to prevent VTE. Where prolonged immobilisation is likely to follow elective surgery, particularly abdominal or orthopaedic surgery to the lower limbs, consideration should be given to stopping progestogen therapy 4-6 weeks pre-operatively. Treatment should not be restarted until the patient is fully remobilised.

If VTE develops after initiating therapy the drug should be withdrawn. Patients should be advised to contact their doctor immediately if they become aware of a potential thromboembolic symptom (e.g., painful swelling in the leg, sudden pain in the chest, dyspnoea).

Hepatic adenoma - In very rare cases, hepatic adenomas may be associated with progesterone-only pill (POP) use. In some cases the hepatic adenoma may decrease in size or become undetectable after discontinuation of norethisterone. Rupture of hepatic adenomas may cause death through intra-abdominal haemorrhage. In extremely rare cases, hepatocellular carcinoma may be associated with combined oral contraceptives use.

Depressed mood and depression are well-known undesirable effects of hormonal contraceptive use (see section 4.8). Depression can be serious and is a well-known risk factor for suicidal behaviour and suicide. Women should be advised to contact their physician in case of mood changes and depressive symptoms, including shortly after initiating the treatment.

Utovlan contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction with other medicines
The metabolism of progestogens may be increased by concomitant administration of compounds known to induce drug-metabolising enzymes, specifically cytochrome P450 enzymes. These compounds include anticonvulsants (e.g., phenobarbital, phenytoin, carbamazepine) and anti-infectives (e.g., rifampicin, rifabutin, nevirapine, efavirenz, tetracyclines, ampicillin, oxacillin and cotrimoxazole)

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. Progestogen levels may therefore be reduced.

Aminoglutethimide has been reported to decrease plasma levels of some progestogens.

Concurrent administration of cyclosporin and norethisterone has been reported to lead to increased plasma cyclosporin levels and/or decreased plasma norethisterone levels.

When used in combination with cytotoxic drugs, it is possible that progestogens may reduce the haematological toxicity of chemotherapy.

Special care should be taken when progestogens are administered with other drugs which also cause fluid retention, such as NSAIDs and vasodilators.

Other forms of interaction
Progestogens can influence certain laboratory tests (e.g., tests for hepatic function, thyroid function and coagulation).

4.6 Fertility, pregnancy and lactation

Contraindicated in pregnancy.

4.7 Effects on ability to drive and use machines

Utovlan has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Progestogens given alone at low doses have been associated with the following undesirable effects:

Genitourinary	breakthrough bleeding, spotting, amenorrhoea, abnormal uterine bleeding, (irregular, increase, decrease), alterations of cervical secretions, cervical erosions, prolonged anovulation
Reproductive system and breast disorders	galactorrhoea, mastodynia, tenderness
Central Nervous System	depression, headache, dizziness, fatigue, insomnia, nervousness, somnolence, confusion, euphoria, loss of concentration, vision disorders

Gastrointestinal/Hepatobiliary	nausea, vomiting, cholestatic icterus/jaundice, constipation, diarrhoea, dry mouth, disturbed liver function
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	hepatic adenoma
Metabolic & Nutritional	altered serum lipid and lipoprotein profiles, increased fasting glucose levels, increased fasting insulin levels, decreased glucose tolerance, adrenergic-like effects (e.g., fine hand tremors, sweating, cramps in calves at night), corticoid-like effects (e.g., Cushingoid syndrome), diabetic cataract, exacerbation of diabetes mellitus, glycosuria
Cardiovascular	thrombo-embolic disorders, cerebral and myocardial infarction, congestive heart failure, increased blood pressure, palpitations, pulmonary embolism, retinal thrombosis, tachycardia, thrombophlebitis
Skin & Mucous Membranes	acne, hirsutism, alopecia, pruritis, rash, urticaria
Allergy	hypersensitivity reactions (e.g., anaphylaxis & anaphylactoid reactions, angioedema)
Miscellaneous	oedema/fluid retention, bloating, weight gain, pyrexia, change in appetite, change in libido, hypercalcaemia, malaise

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 Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Overdosage may be manifested by nausea, vomiting, breast enlargement and later vaginal bleeding. There is no specific antidote and treatment should be symptomatic.

Gastric lavage may be employed if the overdosage is large and the patient is seen sufficiently early (within four hours).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmotherapeutic group (ATC code) L02A B.

Norethisterone given at intermediate doses (5-10mg) suppresses ovulation via its effect on the pituitary. The endogenous production of oestrogens and progesterones are also suppressed, and the ectopic endometrium is converted to a decidua resembling that of pregnancy. In carcinoma norethisterone may act by pituitary inhibition or by direct action on tumour deposits.

5.2 Pharmacokinetic properties

Norethisterone is rapidly and completely absorbed after oral administration, peak plasma concentration occurring in the majority of subjects between 1 and 3 hours. Due to first-pass metabolism, blood levels after oral administration are 60% of those after i.v. administration. The half life of elimination varies from 5 to 12 hours, with a mean of 7.6 hours. Norethisterone is metabolised mainly in the liver. Approximately 60% of the administered dose is excreted as metabolites in urine and faeces.

5.3 Preclinical safety data

The toxicity of norethisterone is very low. Reports of teratogenic effects in animals are uncommon. No carcinogenic effects have been found even in long-term studies.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

maize starch
polyvidone
magnesium stearate
lactose monohydrate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 25°C.
Store in the original package to protect from light and moisture.

6.5 Nature and contents of container

Pvc/foil blister packs of 30 and 90 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Pfizer Limited
Ramsgate Road
Sandwich
Kent CT13 9NJ
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 00057/1054

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15th July 2002
Date of latest renewal: 15th February 2003

10 DATE OF REVISION OF THE TEXT

16/06/2025