Dub-sterone

POM

Norethisterone Tablets BP

COMPOSITION:
Each uncoated tablet contains:

Norethisterone Acetate BP equivalent to Norethisterone	5 mg
Excipients	q.s

Contains : Lactose

PHARMACOLOGICAL ACTION
Pharmacodynamic properties
Complete transformation of the endometrium can be achieved with 80 to 150 mg norethisterone, spread over 8 to 10 days, in adequately estrogen-primed castrated women. This amount is sufficient to bring the endometrium up to the condition which it is normally in at the end of the luteal phase. The menstruation-like withdrawal bleeding begins almost invariably 2 to 4 days after discontinuation of the medication. Norethisterone has an inhibitory effect on the secretion of gonadotropins in the anterior lobe of the pituitary. Norethisterone increases the basal body temperature: 10 mg norethisterone daily increases it by about 0.5°C. In addition to the transformatory action norethisterone also has a styptic effect. A local influence on the endometrium leads to the cessation of dysfunctional bleeding.

Pharmacokinetic properties
Absorption: Orally administered norethisterone is absorbed over a wide dose range. Peak serum concentrations of about 16 ng/mL are reached within about 1.5 hours of administration of one 5 mg tablet Dub-sterone. Due to a marked first-pass effect, the bioavailability of norethisterone after an oral dose is about 64%.
Distribution: Norethisterone is bound to serum albumin and to sex hormone binding globulin (SHBG). Only about 3 to 4% of the total serum drug concentration is present as free steroid, about 35% and 61% is bound to SHBG and albumin, respectively. The apparent volume of distribution of norethisterone is 4.4 ± 1.3 L/kg. Following oral administration, the drug serum level-time course follows a biphasic pattern. Both phases are characterised by half-lives of 1 to 2 and about 5 to 13 hours respectively. Norethisterone is secreted into breast milk.
Metabolism: Norethisterone is mainly metabolised by saturation of the double bond in ring A and the reduction of the 3-keto group to a hydroxyl group, followed by conjugation to the corresponding sulphates and glucuronides. Some of these metabolites are eliminated slowly from plasma, with half-lives of about 67 hours. Therefore, during long-term treatment with daily oral administration of norethisterone, some of these metabolites accumulate in the plasma. Norethisterone is partly metabolised to ethinylestradiol.
Elimination: Norethisterone is not excreted unchanged to a significant extent. Predominantly hydroxylated metabolites, as well as their conjugates (glucuronides and sulphates), are excreted via urine and faeces at a ratio of about 7:3.
Steady-state conditions: During multiple-dose daily administration with norethisterone, an accumulation of the drug is unlikely because of the relatively short half-life of the drug. If, however, SHBG-inducing agents such as ethinylestradiol are co-administered, an increase in norethisterone serum levels can occur because of the binding of norethisterone to SHBG.

INDICATIONS
Dysfunctional uterine bleeding, Relief of primary and secondary amenorrhoea, Timing of menstruation, Endometriosis

CONTRA-INDICATIONS
Dub-sterone should not be used in the presence of any of these conditions:- Known or suspected pregnancy, Lactation, Active thromboembolic processes or a history thereof, Diabetes mellitus with vascular involvement, Presence or history of severe hepatic disease, as long as liver function values have not returned to normal, Presence or history of liver tumours (benign or malignant), Known or suspected sex hormone-dependent malignancies, Hypersensitivity to the active substance or to any of the Excipients. Should any of these conditions appear during the use of Dub-sterone, the use of the preparation must be discontinued immediately.

WARNINGS
If any of the conditions/risk factors mentioned below is present or deteriorates, an individual risk-benefit analysis should be done before Dub-sterone is started or continued.

Circulatory disorders
It has been concluded that the use of oral estrogen/progestogen containing ovulation inhibitors is attended by an increased incidence of arterial and venous thromboembolic diseases. Therefore one should keep the possibility of an increased thromboembolic risk in mind, particularly where there is a history of thromboembolic diseases.
Generally recognised risk factors for venous thromboembolism include a positive personal or family history (venous thromboembolism in a sibling or a parent at a relatively early age), age, obesity, prolonged immobilisation, major surgery or major trauma. The increased risk of thromboembolism in the puerperium must be considered. Treatment should be stopped at once there are symptoms of an arterial or venous thrombotic event or suspicion thereof.

Tumours
Benign liver tumours and malignant liver tumours. In isolated cases, these tumours have led to life-threatening intra-abdominal haemorrhages. A hepatic tumour should be considered in the differential diagnosis when severe upper abdominal pain, liver enlargement or signs of intra-abdominal haemorrhage occur in women taking Dub-sterone.

Reasons for immediate discontinuation of the tablets
Occurrence for the first time of migrainous headaches or more frequent occurrence of unusually severe headaches, sudden perceptual disorders (eg disturbances of vision or hearing), first signs of thrombophlebitis or thromboembolic symptoms (for example, unusual pains in or swelling of the legs, stabbing pains on breathing or coughing for no apparent reason), a feeling of pain and tightness in the chest, pending operations (six weeks beforehand), immobilisation (for instance, following accidents), onset of jaundice, onset of anicteric hepatitis, generalised pruritus, significant rise in blood pressure, pregnancy.

Other
Strict medical supervision is necessary if the patient suffers from diabetes.

DOSAGE AND DIRECTIONS FOR USE

Dysfunctional uterine bleeding
The administration of 1 tablet Dub-sterone 3 times daily over 10 days leads to the arrest of uterine bleeding not associated with organic lesions within 1 to 3 days. In individual cases, bleeding usually diminishes during the first few days after the commencement of tablet-taking and does not stop until about five days later. For the treatment to be successful, Dub-sterone administration should be continued regularly even after the arrest of bleeding (up to a total of 30 tablets). About 2 to 4 days after discontinuation of treatment a withdrawal bleeding will occur resembling a normal menstruation in intensity and duration. Occasionally, slight bleeding may occur after initial arrest of bleeding. In these cases tablet-taking must not be interrupted. If the bleeding does not stop in spite of regular tablet-taking, an organic cause must be considered. The attending physician must be informed immediately, because further measures are then mostly required. This also applies in cases where after initial arrest of haemorrhage, heavier bleedings still occur during tablet-taking.

Prevention of recurrence
To prevent the recurrence of dysfunctional bleeding, it is recommended to administer Dub-sterone prophylactically during the next three cycles, ie 1 tablet Dub-sterone 2 to 3 times daily from the 19th to the 26th day of the cycle (1st day of the cycle = 1st day of the last bleeding). The withdrawal bleeding occurs some days after administration of the last tablet. Only the physician can decide whether this measure is necessary

Relief of primary and secondary amenorrhoea
In the case of secondary amenorrhoea hormone treatment is to be given at the earliest 8 weeks after the last menstrual period. In order to induce a menstruation-like bleeding, an estrogen (eg estradiol valerate 10 mg) is to be given before the administration of Dub-sterone. However, before treatment is commenced, the presence of a prolactin-producing pituitary tumour should be excluded because the possibility cannot be ruled out that macroadenomas increase in size when exposed to higher doses of estrogen for prolonged periods of time.
Please note
During treatment pregnancy must not occur. Contraception should be practised with non-hormonal methods (with the exception of the rhythm and temperature methods). If withdrawal bleeding at regular intervals of about 28 days fails to occur under the therapeutic scheme, pregnancy must be considered despite the protective measures. The treatment must then be interrupted until the situation has been clarified by differential diagnosis.
Premenstrual syndrome, cyclical mastopathy
Premenstrual symptoms such as headaches, depressive moods, water retention, a feeling of tension in the breasts, may be relieved or palliated by 1 tablet Dub-sterone 2 to 3 times daily from the 19th to the 26th day of the cycle.
The remarks under "Please note" for the indication "Primary and secondary amenorrhoea" apply to this indication.

Timing of menstruation
The monthly bleeding can be brought forward or delayed if particular circumstances require this. However, Dub-sterone must be given only to those cases in which there is no possibility of early pregnancy in the cycle concerned.
Dosage: 1 tablet Dub-sterone 3 times daily, beginning about 3 days before the expected menstruation. Bleeding will occur 2 to 3 days after having stopped medication. If it does not, the doctor must be consulted.

Endometriosis
Treatment is commenced on the 5th day of the cycle with 1 tablet Dub-sterone twice daily, increasing to 2 tablets twice daily in the event of spotting. When the bleeding ceases, the initial dose can be resumed. Duration of treatment: at least 4 to 6 months. During treatment, ovulation and menstruation do not occur. After discontinuation of hormone treatment a withdrawal bleeding will occur.

SIDE EFFECTS AND SPECIAL PRECAUTIONS

Side effects
Undesirable effects are more common during the first months after start of intake of Dub-sterone, and subside with duration of treatment. In addition to the adverse effects listed under "Special precautions", the following undesirable effects have been reported in users of Dub-sterone, although a causal relationship could not always be confirmed.
In the indication of endometriosis, changes in bleeding pattern including irregular bleeding, scanty bleeding and amenorrhoea may occur.
Other side effects that have been reported in users of Dub-sterone but for which the association has been neither confirmed nor refuted are: Visual disturbances, Nausea Headache, oedema Migraine Dyspnoea Hypersensitivity reactions (eg rash, urticaria)

Special precautions
Diabetes mellitus must be actively excluded as this disease requires careful supervision. The requirements for oral antidiabetics or insulin may change.
Chloasma may occasionally occur, especially in women with a history of chloasma gravidarum. Women with a tendency to chloasma should avoid exposure to the sun or ultraviolet radiation when taking Dub-sterone.
Patients who have a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree.

Interaction with other medicines and other forms of interaction
Drug interactions which result in an increased clearance of sex hormones can lead to decreased therapeutic efficacy. This has been established with many hepatic enzyme-inducing drugs (including phenytoin, barbiturates, primidone, carbamazepine, and rifampicin); griseofulvin, oxcarbazepine, and rifabutin are also suspected.
Laboratory tests
The use of progestogens may influence the results of certain laboratory tests, including biochemical parameters of liver, thyroid, adrenal and renal function, plasma levels of (carrier) proteins, eg corticosteroid binding globulin and lipid/lipoprotein fractions, parameters of carbohydrate metabolism and parameters of coagulation and fibrinolysis. Changes generally remain within the normal laboratory range.
Pregnancy and lactation
The use of Dub-sterone during pregnancy is contra-indicated. Dub-sterone should not be used during lactation.

OVERDOSAGE AND ITS TREATMENT
Treatment is supportive and symptomatic.

STORAGE CONDITION: Store below 30 °C. Protect from light and moisture.
KEEP THE MEDICINE OUT OF REACH OF THE CHILDREN.

SHELF LIFE: 36 months

PRESENTATION: Blister pack of 3 x 10 tablets in a unit Carton.

Manufactured for & Distributed by:
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KEN-DAWA