Livial 2.5 mg tablets
tibolone

PRESCRIBING INFORMATION
Refer to Summary of Product Characteristics (SmPC) before prescribing

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to MSD, UK (tel: 01992 467272).

By clicking the above link you will leave the MSD website and be taken to the MHRA website.

PRESENTATION
Livial 2.5 mg tablets containing 2.5 mg of tibolone.

USES
Treatment of oestrogen deficiency symptoms in postmenopausal women, more than one year after menopause. Prevention of osteoporosis in postmenopausal women at high risk of future fractures, intolerant of, or contraindicated for, other osteoporosis prevention medications. Base decision to prescribe Livial on assessment of the individual's overall risks. In the over 60s, should include consideration of the risk of stroke.

DOSAGE AND ADMINISTRATION
One tablet per day. Elderly: No dose adjustment. Swallow tablets with water or other drink, preferably at the same time every day. For initiation and continuation of treatment of postmenopausal symptoms, use lowest effective dose for the shortest duration. Progestogen should not be added with Livial treatment.
Natural menopause: start treatment at least 12 months after last natural bleed.
Surgical menopause: start treatment immediately.
Women treated with gonadotrophin releasing hormone analogues may start treatment immediately. If changing from a sequential HRT preparation, treatment should start the day following completion of the prior regimen. If changing from a continuous-combined HRT preparation, start treatment at any time. Investigate irregular vaginal bleeding to exclude malignancy before starting Livial.

CONTRAINDICATIONS
Pregnancy and lactation, known past or suspected breast cancer, known or suspected oestrogen-dependent malignant tumours, undiagnosed genital bleeding, untreated endometrial hyperplasia, previous or current venous thromboembolism (DVT, PE), known thrombophilic disorders (e.g. protein C, protein S, or antithrombin deficiency) any history of arterial thromboembolic disease (e.g. angina, myocardial infarction (MI), stroke or TIA), acute liver disease, or a history of liver disease as long as liver function tests remain abnormal, known hypersensitivity to any ingredients, porphyria.

PRECAUTIONS
Only initiate treatment for postmenopausal symptoms if symptoms adversely affect quality of life. Carefully assess the risks of stroke, breast cancer and, in women with an intact uterus, endometrial cancer. Evidence regarding the risks associated with HRT or tibolone in the treatment of premature menopause is limited. Due to the low level of absolute risk in younger women, the balance of benefits and risks for these women may be more favourable than in older women.

Before initiating or reinstituting HRT or tibolone, take a complete personal and family medical history. Physical (including pelvic and breast) examination should be guided by this and by the contraindications / warnings for use. Periodic check-ups are recommended during treatment. Closely supervise the patient if they have experienced any of the following conditions: leiomyoma (uterine fibroids) or endometriosis, risk factors for thromboembolic disorders, risk factors for oestrogen dependent tumours, e.g. 1st 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 erythematosis, a history of endometrial hyperplasia, epilepsy, asthma, otosclerosis. Discontinue therapy if a contraindication is discovered and in situations of: jaundice or deterioration in liver function, significant increase in blood pressure or new onset of migraine-type headache. Observational studies show that women prescribed Livial in normal clinical practice are at an increased risk of having endometrial cancer diagnosed
which increases with duration of use. Tibolone increases endometrial wall thickness, as measured by transvaginal ultrasound. Break-through bleeding and spotting may occur during the first months of treatment. If it occurs after 6 months of treatment, or continues after treatment has been discontinued, advise patient to report to their doctor for gynaecological investigation to exclude endometrial malignancy. A meta-analysis of epidemiological studies showed a significant increase in the risk of breast cancer associated with use of a 2.5 mg dose of tibolone, which becomes apparent within 3 years of use, increasing with duration of intake. After stopping treatment, the excess risk decreases with time. The time needed to return to baseline depends on the duration of prior HRT use. When HRT was taken for more than 5 years, the risk may persist for 10 years or more. Any increased risk in users of oestrogen-only and tibolone therapy is lower than seen in users of oestrogen-progestogen combinations. Ovarian cancer is rarer than breast cancer. In one study, it was shown that the relative risk of ovarian cancer, with tibolone use, was similar to the risk associated with the use of other types of HRT. Oestrogen or oestrogen-progestogen HRT is associated with a 1.3-3 fold risk of developing venous thromboembolism (VTE), which is most likely in the first year of HRT. Patients with known thrombophilic states have an increased risk of VTE and HRT; tibolone may add to this risk. Recognised risk factors for VTE include oestrogen use, older age, major surgery, prolonged immobilization, obesity (BMI> 30 kg/m²), pregnancy/postpartum period, systemic lupus erythematosus (SLE) and cancer. Consider prophylactic measures to prevent VTE following surgery. Temporarily stop HRT or tibolone 4 to 6 weeks prior to elective surgery if prolonged immobilisation is expected. Do not restart treatment until the woman is completely mobilised. In women with no personal history of VTE but with a first degree relative with a history of thrombosis at young age, screening may be offered after careful counselling regarding its limitations. If a thrombophilic defect is identified which segregates with thrombosis in family members or if the defect is ‘severe’ (e.g. antithrombin, protein S, or protein C deficiencies or a combination of defects) tibolone is contraindicated. Consider the benefit-risk of women on anticoagulant treatment before treatment initiation. Discontinue treatment if VTE develops after initiating therapy. The risk of ischaemic stroke from the first year of treatment is increased, becoming greater with age. Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. Livial is not intended for contraceptive use. Carefully observe patients with cardiac or renal dysfunction, due to potential of fluid retention. Closely monitor women with pre-existing hypertriglyceridaemia. There is some evidence of increased risk of probable dementia in women who start using continuous combined or oestrogen-only HRT after the age of 65. The risk of coronary artery disease is slightly increased in users of combined estrogen-progestogen HRT over the age of 60. There is no evidence that the risk of MI with tibolone is different to that with other HRT.

Drug Interactions: Use caution during simultaneous use with anticoagulants, especially when starting or stopping concurrent Livial treatment. Adjust dose of warfarin if necessary. Livial may increase blood fibrinolytic activity, which may enhance the effect of anticoagulants. CYP3A4 inducing compounds such as barbiturates, carbamazepine, hydantoins and rifampicin may enhance the metabolism of tibolone and thus affect its therapeutic effect. Herbal preparations containing St.John’s wort (Hypericum Perforatum) may induce the metabolism of oestrogens and progestogens via CYP3A4. Clinically, an increased metabolism of oestrogens and progestogens may lead to decreased effect and changes in the uterine bleeding profile.

PREGNANCY AND LACTATION
Livial is contraindicated during pregnancy. If pregnancy occurs during medication with Livial, treatment should be withdrawn immediately. No clinical data on exposed pregnancies are available. Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown. Livial is contraindicated during breast-feeding.

SIDE EFFECTS
Refer to SPC for complete information on side effects.
Common: Lower abdominal pain, abnormal hair growth, vaginal discharge, endometrial wall thickening, postmenopausal haemorrhage, breast tenderness, genital pruritus, vaginal candidiasis, vaginal haemorrhage, pelvic pain, cervical
dysplasia, genital discharge, vulvovaginitis, weight increase and abnormal vaginal smear.

**PACKAGE QUANTITIES AND BASIC NHS COST:**
Cardboard boxes containing 1 or 3 push through packs of 28 white tablets.
3 x 28 tablets: £31.08
1 x 28 tablets: £10.36

**Marketing Authorisation Number:**
PL 00025/0599

**Marketing Authorisation Holder:**
Merck Sharp & Dohme Ltd
Hertford Road, Hoddesdon, Hertfordshire, EN11 9BU, UK.

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