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Rethinking women's health.

Elleste Solo (estradiol), Elleste Duet (estradiol + estradiol/norethisterone acetate) and Elleste Duet Conti (estradiol/norethisterone acetate) tablets Prescribing Information. Please consult the Summary of Product Characteristics (SmPC) before prescribing

Product name and active ingredients: *Elleste Solo* 1 mg (white tablets) and 2 mg (orange tablets) film-coated tablets containing estradiol hemihydrate. *Elleste Duet* 1 mg film-coated tablets containing estradiol hemihydrate 1 mg (white tablets) and estradiol hemihydrate 1 mg plus norethisterone acetate 1 mg (pale green tablets). *Elleste Duet* 2 mg film-coated tablets containing estradiol hemihydrate 2 mg (orange tablets) and estradiol hemihydrate 2 mg plus norethisterone acetate 1 mg (grey tablets). *Elleste Duet Conti* film-coated tablets (grey tablets) containing 2 mg estradiol hemihydrate plus 1 mg norethisterone acetate. **Indications:** *Elleste Solo; Elleste Duet*; HRT for oestrogen deficiency symptoms in peri- and post-menopausal women. *Elleste Duet Conti*; HRT for oestrogen deficiency symptoms in women one-year since last menses. *Elleste Solo 2 mg; Elleste Duet 2 mg; Elleste Duet Conti*; Prevention of osteoporosis in post-menopausal women at high risk of future fractures who are intolerant of, or contraindicated for, other medicinal products approved for the prevention of osteoporosis. *Elleste Solo*; *Elleste Duet; Elleste Duet Conti;* The experience of treating women older than 65 years is limited. **Dosage and administration:** *Elleste Solo* is taken as one tablet (1 mg or 2 mg) daily continuously in hysterectomised women. In women with a uterus, it is recommended to add a progestogen for 12-14 days of each cycle. *Elleste Duet* is a continuous sequential HRT. One white (1 mg estradiol) tablet taken for 16 days followed by one pale green (1 mg estradiol/1 mg norethisterone) tablet for 12 days. Or for higher dose, one orange (2 mg estradiol) tablet taken for 16 days followed by one grey (2 mg estradiol/1 mg norethisterone) tablet for 12 days.). *Elleste Duet Conti* is a continuous combined HRT. One grey tablet (2 mg estradiol/1 mg norethisterone combined) is taken daily without interruption. Please consult the SmPC for further details. *Elderly:* No special dosage requirements for elderly patients. *Paediatric population:* Not to be used in children. **Contraindications:** Known, past or suspected breast cancer; known or suspected oestrogen-dependent malignant tumours; undiagnosed genital bleeding; untreated endometrial hyperplasia; previous idiopathic or current venous thromboembolism; known thrombophilic disorders; active or recent arterial thromboembolic disease; acute liver disease, or a history of liver disease as long as liver function tests have failed to return to normal; hypersensitivity to the active substances or to any of the excipients listed on the SmPC; porphyria. **Special warnings and precautions for use:** Before initiating/restarting HRT an appraisal of risks and benefits should be made and women should be reassessed at least annually. A complete personal and family medical history should be taken before starting/reinstituting HRT, and the patient should also be advised regarding what breast changes to report to their physician. If particular conditions are present, have occurred previously, and/or have been aggravated during pregnancy or previous hormone treatment, the patient should be closely supervised. These include leiomyoma (uterine fibroids) or endometriosis, risk factors for thromboembolic disorders; risk factors for oestrogen dependent tumours; hypertension; liver disorders; diabetes mellitus; cholelithiasis; migraine or (severe) headache; systemic lupus erythematosus (SLE); a history of endometrial hyperplasia; epilepsy; asthma; otosclerosis. Therapy should be discontinued if 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; pregnancy. *Endometrial hyperplasia and carcinoma*: In women with an intact uterus, the risk of endometrial hyperplasia and carcinoma is increased when oestrogens are administered alone for prolonged periods. For endometrial cancer risk among oestrogen-only users the risk is 2-to 12-fold greater than non-users, depending on the treatment duration and dose. After stopping treatment, risk may remain elevated for at least 10 years. Adding progestogen cyclically for at least 12 days per month/28-day cycle or continuous combined oestrogen-progestogen therapy in non-hysterectomised women prevents the excess risk associated with oestrogen-only HRT. Bleeding and spotting may occur during the first months of treatment, but if this continues further investigations may be required to exclude malignancy. *Breast cancer:* The overall evidence shows an increased risk of breast cancer in women taking combined oestrogen-progestogen or oestrogen-only HRT, that is dependent on the duration of HRT treatment. HRT, especially oestrogen-progestogen combined treatment, increases the density of mammographic images which may adversely affect the radiological detection of breast cancer. *Ovarian cancer:* Data from a large meta-analysis suggests a slightly increased risk in women taking oestrogen-only or combined oestrogen-progestogen HRT, which becomes apparent within 5 years of use and diminishes over time after stopping. *Venous thromboembolism:* HRT is associated with a 1.3-3 fold risk of developing venous thromboembolism (VTE). HRT is contraindicated in patients with known thrombophilic states or thrombophilic defects. Risk factors for VTE also include use of oestrogens, older age, major surgery, prolonged immobilisation, obesity (BMI>30 kg/m^2), pregnancy/postpartum period, SLE, cancer, patients in post-operative recovery, receiving anticoagulant treatment, having a first degree relative with history of VTE at early age. If VTE develops after initiating therapy, the drug should be discontinued. Patients should be told to contact their doctors immediately when they are aware of a potential thromboembolic symptom. *Coronary artery disease (CAD):* There is no evidence from randomised controlled trials of protection against myocardial infarction in women with or without existing CAD who received combined oestrogen-progestogen or oestrogen-only HRT. *Ischaemic stroke:* Combined oestrogen-progestogen and oestrogen-only therapy are associated with an up to 1.5-fold increase in risk of ischaemic stroke. The relative risk does not change with age or time since menopause. However, as risk of stroke is strongly age-dependent, the overall risk of stroke in women who use HRT will increase with age. *Hypothyroidism:* Patients receiving thyroid replacement therapy should have their thyroid function monitored regularly while receiving HRT. *Angioedema:* oestrogens may induce or exacerbate symptoms of this, particularly in those with hereditary angioedema. *Other conditions:* patients with cardiac or renal dysfunction should be carefully observed as oestrogens may cause fluid retention. Rare cases of large increases in plasma triglycerides (leading to pancreatitis) have been reported with oestrogen therapy in women with pre-existing hypertriglyceridaemia and close observation is advised. Oestrogens increase thyroid binding globulin and other binding proteins. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take these medicines. *Elleste Solo 2 mg and Elleste Duet 2 mg* contain sunset yellow (E110) which can cause allergic type reactions. These reactions are more common in those with allergy to aspirin. **Interactions:** The metabolism of oestrogens 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). Ritonavir, nelfinavir and St John's Wort should be used with caution. Hormone contraceptives containing oestrogens have been shown to significantly decrease plasma concentrations of lamotrigine. Caution with concomitant use of ombitasvir/paritaprevir /ritonavir with and without dasabuvir, and glecaprevir/ pibrentasvir. **Pregnancy and breastfeeding:** Not indicated in pregnancy or during lactation. If pregnancy occurs discontinue treatment immediately. **Undesirable effects:** *Elleste Solo*: *Common (> 1/100 to <1/10)*: weight increased, weight decreased, mood alterations including anxiety and depressed mood, libido disorder, metrorrhagia, breast tenderness, breast enlargement, uterine/vaginal bleeding including spotting, nausea, abdominal pain, headache, rash, pruritus, oedema; Other serious (not common): breast cancer, VTE. *Elleste Duet* and *Elleste Duet Conti: Very common (≥ 1/10):* headache, breast pain, breast tenderness, dysmenorrhoea, menstrual disorder; *Common (≥ 1/100 to <1/10):* depression, nervousness, affect lability, libido disorder, dizziness, insomnia, nausea, abdominal distension, diarrhoea, dyspepsia, abdominal pain, acne, rash, pruritus, dry skin, back pain, pain in extremity, breast enlargement, menorrhagia, genital discharge, irregular vaginal bleeding, uterine spasms, vaginal infection, endometrial hyperplasia, pain, asthenia, oedema peripheral, weight increased. Other serious (not common): breast cancer, VTE**. Please refer to SmPC for full details of side effects. Legal category:** POM**. Presentation and cost:** *Elleste Solo* (both strengths) – pack of 3x28 tablets £5.06 *Elleste Duet* (both strengths) – pack of 3x28 tablets £9.20; *Elleste Duet Conti* – pack of 3x28 tablets £17.02; **Marketing authorisation numbers:** *Elleste Solo* - PL 46302/0169 and PL 46302/0170 *Elleste Duet* – PL 46302/0164 and PL 46302/0165; *Elleste Duet Conti* – PL 46302/0166. Further information is available from Exeltis UK Limited, Two Snowhill, 7th Floor, Birmingham, B4 6GA. **Date of preparation of PI**: April 2024 **Job number**: EXE-E/INP-ELL-1379

Adverse events should be reported. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Exeltis UK Limited on 01494 411775 or by email to uk.medinfo@exeltis.com