Prescribing Information
Oestrogel (estradiol) Pump-Pack 750 micrograms/actuation Gel

For full prescribing information, including side effects, precautions and contraindications, please consult the Summary of Product Characteristics (SPC). **Presentation**: Transdermal gel. One gram of gel contains 0.6 mg of the active ingredient, Estradiol (0.06% w/w). Each pump actuation delivers 1.25 g of gel which contains 0.75 mg of Estradiol. This medicine contains 0.5 g alcohol (ethanol) in each dose of 1.25 g gel. **Indication:** 1. Hormone Replacement Therapy (HRT) for oestrogen deficiency symptoms in postmenopausal women. 2. Prevention of osteoporosis in postmenopausal women at high risk of future fractures who are intolerant of, or contraindicated for, other medicinal products approved for the prevention of osteoporosis. The experience treating women older than 65 years is limited. **Posology and method of administration:** *Menopausal and postmenopausal symptoms:* The usual starting dose is 2 pumps (2.5 g containing 1.5 mg estradiol) once daily. If effective relief is not obtained after one month's treatment, this may be increased to a maximum of four pumps (5 g containing 3.0 mg estradiol) daily. For initiation and continuation of treatment of postmenopausal symptoms, the lowest effective dose for the shortest duration should be used. *Postmenopausal osteoporosis:* The minimum effective dose is 2.5 g Oestrogel once daily for most patients. Oestrogel is an oestrogen-only product to be administered daily on a continuous basis for women without a uterus. In women with an intact uterus it is recommended to add a progestogen for at least 12 days of each month, in accordance with the manufacturers' recommendation. Unless there is a previous diagnosis of endometriosis, it is not recommended to add a progestogen in hysterectomised women. The pump pack will require priming before using a new pump pack for the first time. The first dose dispensed should be discarded. The gel should be applied to at least 750 cm^2 of clean, dry, intact areas of skin (e.g. arms, shoulders, inner thighs). It should not be applied on or near the breasts or on the vulval region. A frequent change in application sites is recommended. The patient should apply the gel herself and avoid skin contact with others, particularly a male partner, for at least 1 hour after application. Wash hands with soap and water after applying the gel. Patients should be informed that children should not come in contact with the area of the body where Oestrogel was applied on. **Contraindications:** Known, past or suspected breast cancer; known or suspected oestrogen-dependent malignant tumours (e.g. endometrial cancer); undiagnosed genital bleeding; untreated endometrial hyperplasia; previous or current venous thromboembolism (deep vein thrombosis, pulmonary embolism), known thrombophilic disorders, active or recent arterial thromboembolic disease (e.g. angina, myocardial infarction); acute liver disease or a history of liver disease as long as liver function tests have failed to return to normal; known hypersensitivity to the active substances or to any of the excipients; porphyria**. Warnings and Precautions for use:** For the treatment of postmenopausal symptoms: HRT should only be initiated for symptoms that adversely affect quality of life. The risks and benefits should be reviewed annually and HRT only continued as long as the benefit outweighs the risk. A personal and family medical history should be taken before initiating or reinstituting HRT. Periodic check-ups are recommended during treatment. Women should be advised what changes in their breasts should be reported to their doctor or nurse. Physical examination and investigations including appropriate imaging tools should be carried out according to the clinical needs of the patient. Patients should be closely supervised if any of the following conditions are present, have occurred previously and/or have been aggravated during pregnancy or previous hormone treatment since they may recur or be aggravated during treatment with Oestrogel: leiomyoma (uterine fibroids) or endometriosis; risk factors for thromboembolic disorders; risk factors for oestrogen-dependent tumours; hypertension; liver disorders; diabetes mellitus with or without vascular involvement; cholelithiasis; migraine or severe headache; systemic lupus erythematosus; history of endometrial hyperplasia; epilepsy; asthma and otosclerosis. Oestrogel should be discontinued if a contraindication is discovered or the following occur: jaundice or deterioration in liver function; significant increase in blood pressure; new onset of migraine-type headache; pregnancy. In women with an intact uterus the risk of endometrial hyperplasia and carcinoma is increased when oestrogens are administered alone for prolonged periods of time. The addition of a 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. Break through bleeding and spotting may occur during the first months of treatment but if they occur after some time on therapy or continue after treatment has been discontinued the reason should be investigated. Unopposed oestrogen stimulation may lead to premalignant or malignant transformation in the residual foci of endometriosis. Therefore, the addition of progestogens to oestrogen replacement therapy should be considered in women who have undergone hysterectomy because of endometriosis if they are known to have residual endometriosis. 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 taking HRT. HRT, especially oestrogen-progestogen combined treatment, increases the density of mammographic images which may adversely affect the radiological detection of breast cancer. Epidemiological evidence from a large meta-analysis suggests a slightly increased risk of ovarian cancer in women taking oestrogen-only or combined oestrogen-progestogen HRT which becomes apparent within 5 years of use and diminishes over time after stopping. HRT is associated with a 1.3 to 3-fold risk of developing venous thromboembolism. The occurrence of such an event is more likely in the first year of HRT than later. It is recommended to stop HRT 4 to 6 weeks prior to elective surgery if prolonged immobilisation is to follow. The benefit-risk of HRT should be considered in women already on chronic anticoagulant treatment. If venous thromboembolism occurs during treatment, HRT should be discontinued. Patients should contact their doctors immediately if they have potential thromboembolic symptoms. The relative risk of coronary artery disease (CAD) during use of combined oestrogen + progestogen HRT is slightly increased. As the baseline absolute risk of CAD is strongly dependent on age, the number of extra cases of CAD due to oestrogen + progestogen use is very low in healthy women close to menopause, but will rise with more advanced age. Combined oestrogen-progestogen and oestrogen-only therapy are associated with up to a 1.5-fold increase in risk of ischaemic stroke. The relative risk does not change with age or time since menopause. However, as the baseline risk of stroke is strongly age-dependent, the overall risk of stroke in women who use HRT will increase with age. Care should be taken with women with cardiac or renal dysfunction since oestrogens may cause fluid retention. Women with pre-existing hypertriglyceridaemia should be followed closely during oestrogen replacement or HRT since pancreatitis can result from rare cases of large increases in plasma triglycerides. Oestrogens increase thyroid binding globulin (TBG), leading to increased circulating total thyroid hormone. Other binding proteins may be elevated in serum, i.e. corticoid binding globulin (CBG), sex-hormone-binding globulin (SHBG) leading to increased circulating corticosteroids and sex steroids respectively. Other plasma proteins may be increased (angiotensinogen/renin substrate, alpha-I-antitrypsin, ceruloplasmin). HRT use does not improve cognitive function. There is some evidence of increased risk of probable dementia in women who start HRT after the age of 65. It may cause burning sensation on damaged skin. This product is flammable until dry. **Interactions:** Patients should avoid strong skin cleaners and detergents, skin products of high alcoholic content (e.g. astringents, sunscreens) and keratolytics which may alter the barrier structure or function of the skin. Use of any concomitant skin medication which alters skin production (e.g. cytotoxic drugs) should be avoided. 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 and nelfinavir exhibit inducing properties when used concomitantly with steroid hormones. Herbal preparations containing St John's wort (Hypericum perforatum) may induce the metabolism of oestrogens. Transdermally applied oestrogens may be less affected by enzyme inducers than oral hormones. Clinically, an increased metabolism of oestrogens and progestogens may lead to decreased effect and changes in the uterine bleeding profile. Hormone contraceptives containing oestrogens shown to significantly decrease plasma concentrations of lamotrigine when co-administered. This may reduce seizure control. **Pregnancy and lactation:** Oestrogel is not indicated in pregnancy. If pregnancy occurs during medication with Oestrogel, the treatment should be withdrawn immediately. The data relating to inadvertent foetal exposure to oestrogens indicate no teratogenic of foetotoxic effects. Oestrogel is not indicated during lactation. **Undesirable effects:** Based on post marketing experience, the following occur at a frequency not known (cannot be estimated from the available data) with Oestrogel: nausea, dizziness, headache, alopecia, pruritus. The following undesirable effects are observed with HRT products used in menopause at a common frequency (>1/100; <1/10); headache, nausea, abdominal pain, breast swelling/pain, breast enlargement, dysmenorrhoea, menorrhagia, metrorrhagia, leucorrhoea, endometrial hyperplasia, weight change (increase or decrease), water retention with peripheral oedema, uncommon frequency (≥1/1,000; <1/100) ; depression, mood swings, vertigo, migraine, venous thromboembolic disease, flatulence, vomiting, pruritus, benign breast neoplasm, increased volume of uterine, leiomyoma, vaginitis/vaginal candidiasis, asthenia, rare frequency, (≥1/10,000; <1/1,000) ; glucose intolerance, change in libido, aggravation of epilepsy, arterial hypertension, liver function tests abnormalities, skin decolouration, acne, galactorrhoea, anaphylactic reaction (in women with past history of allergic reaction). The following risks apply in relation to systemic oestrogen/progestogen treatment: breast cancer; endometrial cancer; ovarian cancer; venous thromboembolism; coronary artery disease; ischaemic stroke. For further information on side effects and risk estimates, please consult the SPC. **Overdose:** Overdosage is unlikely with transdermal applications. Overdoses of oestrogen may cause breast tenderness, nausea and withdrawal bleeding. These signs disappear when the treatment is stopped or when the dose is reduced. There are no specific antidotes and treatment should be symptomatic**. NHS Price:** 80g dispenser £6.17. **Legal category:** POM. **Marketing Authorisation number:** PL 28397/0002. **Marketing Authorisation Holder:** Besins Healthcare, Rue Washington 80, 1050 Ixelles, Belgium. **Date of preparation of Prescribing Information:** December 2023 OES/2023/046

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 Besins Healthcare (UK) Ltd, Drug Safety on 0203 862 0920
Email: pharmacovigilance@besins-healthcare.com