Bijuve® (estradiol and progesterone) Abbreviated Prescribing Information

Please consult the Summary of Product Characteristics for other adverse reactions and full prescribing information before prescribing

Presentation: Bijuve 1 mg estradiol (as estradiol hemihydrate) and 100 mg progesterone soft capsules. Excipients with known effect: 0.042 mg Allura Red (E129). **Indication:** Continuous combined hormone replacement therapy (HRT) for estrogen deficiency symptoms in postmenopausal women with intact uterus and with at least 12 months since last menses. The experience in treating women older than 65 years is limited. **Dosage & administration**: The capsule should be taken every day without interruption. Take one capsule each evening with food. For initiation and continuation of treatment of postmenopausal symptoms, the lowest effective dose for the shortest duration should be used. Continuous combined treatment may be started with Bijuve depending on the time since menopause and severity of symptoms. Women experiencing a natural menopause should commence treatment with Bijuve 12 months after their last natural menstrual bleed. For surgically induced menopause, treatment may start immediately. Patients changing from a continuous sequential or cyclical preparation should complete the 28 day cycle and then change to Bijuve. ***Patients changing from another continuous combined preparation may start therapy at any time***. Missed dose: If a dose has been forgotten, it should be taken as soon as possible. If more than 12 hours have elapsed, treatment should be continued with the next capsule without taking the forgotten capsule. The likelihood of breakthrough bleeding or spotting may be increased. ***Paediatric population*:** Not indicated in children. **Method of Administration:** Oral. **Contraindications:** Known, past or suspected breast cancer. Known or suspected estrogen-dependent malignant tumours (e.g. endometrial cancer). Undiagnosed genital bleeding. Untreated endometrial hyperplasia. Previous or current venous thromboembolism (VTE) (deep vein thrombosis, pulmonary embolism). Known thrombophilic disorders (e.g. protein C, protein S, or antithrombin deficiency). 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. Porphyria. Known hypersensitivity to the active substances or to any of the excipients. **Special warnings and precautions for use**: HRT treatment should be initiated or re-instituted only for symptoms that adversely affect quality of life. In all cases, a careful appraisal of the risks and benefits should be undertaken at least annually, and HRT should only be continued as long as the benefit outweighs the risk. Evidence regarding the risks associated with HRT in the treatment of premature menopause is limited. Due to the low level of absolute risk in younger women, however, the balance of benefits and risks for these women may be more favourable than in older women. **Medical examination/follow up**: Before initiating or reinstituting HRT, a complete personal and family medical history should be taken. Physical (including pelvic and breast) examination should be guided by this and by the contraindications and warnings for use. During treatment, periodic check-ups are recommended of a frequency and nature adapted to the individual woman. Women should be advised what changes in their breasts should be reported to their doctor or nurse. Investgations, including appropriate imaging tools, e.g. mammography, should be carried out in accordance with currently accepted screening practices, modified to the clinical needs of the individual. ***Conditions which need supervision:*** If any of the following conditions are present, have occurred previously, and/or have been aggravated during pregnancy or previous hormone treatment, the patient should be closely supervised. It should be taken into account that these conditions may recur or be aggravated during treatment with Bijuve, in particular: Leiomyoma (uterine fibroids) or endometriosis, risk factors for thromboembolic disorders, risk factors for estrogen 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 erythematosus, a history of endometrial hyperplasia, epilepsy, asthma, otosclerosis. ***Therapy should be discontinued in cases where 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. Special warnings and precautions for use are also required in respect to**:** Endometrial hyperplasia and carcinoma, Breast cancer, Ovarian cancer, Venous thromboembolism, Coronary Artery disease, Ischaemic stroke, Other conditions - Please refer to the Summary of Product Characteristics (SmPC) for full details.

Interactions: No drug-drug interaction studies have been conducted with Bijuve. The drug-drug interactions of estradiol and progesterone have been extensively studied and are well established. Both estrogens and progesterone are metabolized via cytochrome P450. ***Effects of other medicinal products on Bijuve***: The metabolism of estrogens and progestogens may be increased by concomitant use of substances known to induce drug-metabolizing enzymes, specifically cytochrome P450 enzymes, such as anticonvulsants (e.g. phenobarbital, phenytoin, carbamazepine) and anti-infectives (e.g. rifampicin, rifabutin, nevirapine, efavirenz, and griseofulvin). Herbal preparations containing St John's Wort (Hypericum perforatum) may induce the metabolism of estrogens and progestogens. Ritonavir and nelfinavir, although known as strong inhibitors, by contrast exhibit inducing properties when used concomitantly with steroid hormones. Clinically, an increased metabolism of estrogens and progestogens may lead to decreased effect and changes in the uterine bleeding profile. Ketoconazole and other inhibitors of CYP450-3A4 may increase bioavailability of progesterone. Such interactions may increase the incidence of adverse effects such as nausea, breast tenderness, headaches associated with progesterone. ***Effects of Bijuve on other medicinal products***: Estrogen-containing HRT may lower lamotrigine plasma concentrations, potentially reducing seizure control. Although the potential interaction between HRT and lamotrigine has not been studied, it is expected that a similar interaction exists, which may lead to a reduction in seizure control among women taking both medicinal products together. Progesterone may raise the plasma concentration of ciclosporin. **Fertility**, **Pregnancy and lactation:** Bijuve is not indicated during pregnancy, lactation, or in women of childbearing potential. If pregnancy occurs, discontinue treatment immediately. **Effects on ability to drive and use machines:** Does not affect. **Side effects:** The most commonly reported related adverse drug reactions for Bijuve in clinical trials were breast tenderness (10.4%), headache (3.4%), nausea (2.2%), pelvic pain (3.1%), vaginal hemorrhage (3.4%), and vaginal discharge (3.4%). **Very Common ADRs (≥ 1/10)**: Breast tenderness. **Common ADRs (≥ 1/100, < 1/10):** Abdominal distension, abdominal pain, nausea, fatigue, weight increase, back pain, dizziness, headache, breast pain, pelvic pain, uterine pain/spasm, vaginal discharge, vaginal bleeding haemorrhage, acne, alopecia. **Uncommon ADRs (≥ 1/1,000, < 1/100) include**: anaemia, vertigo, hirsutism, visual impairment, abdominal discomfort, abdominal tenderness, constipation, diarrhea, dyspepsia, hyperphagia, dry mouth, oral discomfort, vomiting, dysgeusia, flatulence, pancreatitis acute, chills, hypersensitivity, gastroenteritis, furuncle, vaginal infection, vulvovaginal candidiasis, vulvovaginal mycotic infection, otitis media acute, weight decreased, prothrombin time prolonged, protein S increased, liver function test abnormal, blood pressure abnormal, blood fibrinogen increased, blood alkaline phosphatase increased, aspartate aminotransferase increased, alanine aminotransferase increased, activated partial thromboplastin time prolonged, fluid retention, hyperlipidemia, hyperphagia hyperuricemia, musculoskeletal pain, pain in extremity, arthralgia, muscle spasms, breast cancer, adnexa uteri cyst, disturbance in attention, memory impairment, migraine with aura, paresthesia, parosmia, somnolence, sleep disorder, abnormal dreams, agitation, anxiety, depression, insomnia, irritability, mood swings, libido increased, breast disorders (calcification, discharge, discomfort, enlargement swelling, fibrocystic disease, nipple pain, benign breast neoplasm) uterine/cervical disorders (dysplasia, polyp, cyst, uterine haemorrhage, leiomyoma, uterine polyp, bleeding), endometrial hypertrophy, abnormal biopsy, hot flush, metrorrhagia, post-menopausal haemorrhage, vulvovaginal pruritus, dry skin, pruritus, rash, telangiectasia, hypertension, superficial thrombophlebitis. Refer to SmPC for information on adverse effects of HRT, including breast and ovarian cancer, VTE, and cardiovascular risks. **Package Quantities & Cost:** 28 x capsules £8.14 **Marketing authorisation number:** PL 49876/0015. **Marketing authorisation holder:** Theramex Ireland Limited, 3rd Floor, Kilmore House, Park Lane, Spencer Dock, Dublin 1, D01 YE64, Ireland. **Legal classification:** POM. **Date of Preparation:** January 2025 Certification number:BIJUVA_HQ-UK_EN_21146_v1

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk or search for MHRA Yellowcard in the Google Play or Apple App store. Adverse events should also be reported to Theramex on medinfo.uk@theramex.com or Tel: +44 (0)333 0096795