EVOREL® 25,50,75,100 (estradiol/patch) Abbreviated Prescribing Information

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

Presentation: Evorel 25: 1.6mg estradiol patch; Evorel 50: 3.2mg estradiol patch; Evorel 75: 4.8mg estradiol patch; Evorel 100: 6.4mg estradiol patch. **Indication:** Hormone Replacement Therapy (HRT) for oestrogen deficiency symptoms in peri- and post-menopausal women. Evorel 50, 75 and 100 only: 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. **Dosage & administration:** ***Adults:*** Evorel is an oestrogen-only HRT patch applied to the skin twice weekly. For initiation and continuation of treatment of menopausal symptoms, the lowest effective dose for the shortest duration should be used. For women with an intact uterus progestogen should normally be added to Evorel for the prevention of adverse endometrial effects, e.g. hyperplasia and cancer. The regimen may be either cyclic or continuous sequential. Only progestogens approved for addition to oestrogen treatment may be prescribed (e.g. oral norethisterone, 1mg/day or medroxyprogesterone acetate, 2.5mg/day) and should be added for at least 12-14 days every month/28-day cycle. Unless there is a previous diagnosis of endometriosis, it is not recommended to add a progestogen in hysterectomised women. ***Treatment of oestrogen deficiency symptoms:*** Therapy should be started with one Evorel 50 patch (delivering 50 µg of estradiol/24 hours) and the dose adjusted after the first month if necessary, depending on efficacy and signs of over-oestrogenisation. For maintenance therapy the lowest effective dose should be used; a maximum dose of 100 µg of estradiol/24 hours should not be exceeded. ***Evorel 50, 75, 100: Prevention of post-menopausal osteoporosis:*** Therapy should be started with Evorel 50. The dose may be adjusted depending on efficacy and signs of over-oestrogenisation. The efficacy of Evorel 25 for the prevention of post- menopausal osteoporosis has not been demonstrated. For maintenance therapy, the lowest effective dose should be used. A dose of 100 µg of estradiol/24 hours should not be exceeded. ***Guidance on how to start therapy:*** Post-menopausal women currently not on HRT may start Evorel at any time. Peri-menopausal women who are still having regular menstrual cycles and are not currently on HRT should start Evorel within 5 days of the start of bleeding. Peri-menopausal women with irregular menstrual cycles, for whom pregnancy has been excluded, can start Evorel at any time. ***Switching from other HRT:*** The switch from another oestrogen-only therapy in post-menopausal women to Evorel may occur at any time. Women on a continuous combined regimen wishing to switch from another oestrogen to Evorel may do so at any time. Women on a cyclic or continuous sequential regimen wishing to switch from a sequential combined HRT preparation to Evorel may do so at the end of a cycle of the current therapy or after a 7-day hormone free interval. ***Method of Administration:*** Evorel should be applied to the skin as soon as it is removed from the wrapper and should remain in place during bathing and showering. Recommended application sites are on clean, dry, healthy, intact skin and each application should be made to a slightly different area of skin on the trunk below waistline. Evorel Should not be applied on or near the breasts. ***Missed Dose*****:** If the patient forgets to change their patch, they should change it as soon as possible and apply the next one at the normal time. However, if it is almost time for the next patch, the patient should skip the missed one and go back to their regular schedule. Only one patch should be applied at a time. There is an increased likelihood of break-through bleeding and spotting when a patch is not replaced at the normal time. ***Children*****:** Not indicated. ***Elderly:*** Data are insufficient in the elderly (>65 years old). ***Route of administration:*** Transdermal use. **Contraindications:** Known, current or past or suspected breast cancer. Known or suspected oestrogen-dependent malignant tumours. Undiagnosed genital bleeding. Untreated endometrial hyperplasia. Previous or current venous thrombo-embolism (VTE). Known thrombophilic disorders. Active or recent past arterial thrombo-embolic (ATE) disease. Acute liver disease, or a history of liver disease if liver function tests have failed to return to normal. Known hypersensitivity to the active substances or to any of the excipients. Porphyria. **Special warnings and precautions for use:** For the treatment of menopausal symptoms, HRT should only be initiated for symptoms that adversely affect quality of life. Before initiating or re-instituting 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. ***Conditions which need supervision:*** If any of the following conditions are present, occurred previously, have been aggravated during pregnancy or previous hormone treatment, supervise patient closely. Conditions may recur or be aggravated during treatment, in particular: Leiomyoma or endometriosis, risk factors for thrombo-embolic 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, otosclerosis, hereditary angioedema and mastopathy. ***Conditions which require monitoring while on oestrogen therapy:*** Oestrogens may cause fluid retention. Cardiac or renal dysfunction should be carefully observed. Disturbances or mild impairment of liver function. History of cholestatic jaundice. Pre-existing hypertriglyceridaemia. Rare cases of large increases of plasma triglycerides leading to pancreatitis have been reported with oestrogen therapy in this condition. ***Therapy should be discontinued if a contraindication is discovered and in the following situations:*** jaundice/deterioration in liver function, significant increase in blood pressure, new onset of migraine-type headache, pregnancy. For Evorel 75 and 100 the endometrial safety of added progestogens has not been studied. ***Special warnings and precautions for use are also required in respect to:*** Endometrial hyperplasia and carcinoma, Breast cancer, Ovarian cancer, Venous thrombo-embolism, Coronary Artery disease, Ischaemic stroke – please refer to the SmPC for full details. **Interactions:** The metabolism of oestrogens (and progestogens) may be increased by concomitant use of substances known to induce drug-metabolising enzymes, specifically cytochrome P450 enzymes, such as anticonvulsants, anti-infectives and bosentan. Ritonavir, nelfinavir and herbal preparations containing St. John's Wort may induce the metabolism of oestrogens and progestogens. Clinically, an increased metabolism of oestrogens and progestogens may lead to decreased effect and changes in the uterine bleeding profile. Oestrogen-containing oral contraceptives have been shown to significantly decrease plasma concentrations of lamotrigine when co-administered due to induction of lamotrigine glucuronidation. This may reduce seizure control. Therefore, dose adjustment of lamotrigine may be necessary. **Pregnancy and lactation:** Not indicated. **Side effects:** Adverse reactions observed in clinical trials: **Very common** (≥1/10)**:** Application site pruritus, Application site rash. **Common** (≥1/100 to <1/10)**:** Depressed mood, Migraine, Dizziness, Headache, Abdominal pain, Diarrhoea, Nausea, Pruritus, Rash, Arthralgia, Breast pain, Metrorrhagia, Pain, Application site erythema, Application site oedema, Application site reaction, Weight change. **Uncommon** (≥1/1,000 to <1/100)**:** Genital candidiasis, Hypersensitivity, Palpitations, Flatulence, Myalgia, Dysmenorrhoea, Breast enlargement, Oedema Generalised Oedema. **Rare** (≥1/10,000 to <1/1,000)**:** Breast cancer, Epilepsy, Thrombosis, Abdominal distension, Cholelithiasis, **Frequency not known** (cannot be estimated from the available clinical trial data)**:** Endometrial cancer**,** Cerebrovascular accident, Myocardial infarction, Deep vein thrombosis, Pulmonary embolism, Angioedema. **Overdose:** Effects can if necessary be reversed by removal of the patch. **Package Quantities & Cost:** Each Evorel patch size is presented in a sealed protective pouch. The pouches are packed in a cardboard carton. Cost: 25 (1x8) £4.07; 50 (1x8) £4.62; 50 (1x24) £13.87; 75 (1x8) £4.90; 100 (1x8) £5.09. **Marketing authorisation number:** Evorel 25 PL 49105/0005; Evorel 50 PL 49105/0006; Evorel 75 PL 49105/0007; Evorel 100 PL 49105/0008. **Marketing authorisation holder:** Theramex HQ UK Limited, 50 Broadway, 5th Floor, London, SW1H 0BL, UK.

Legal classification: POM. **Date of Preparation:** October 2024. EVOR_UK_EN_20241_v1(V1.3)

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Adverse events should also be reported to Theramex on medinfo.uk@theramex.com or Tel: 0333 0096795

EVOREL® Conti (estradiol hemihydrate norethisterone acetate) Abbreviated Prescribing Information

Please consult the Summary of Product Characteristics (SmPC) for other adverse reactions and full prescribing information

Presentation: Evorel Conti 3.2 mg of estradiol hemihydrate, 11.2 mg of norethisterone acetate transdermal patch. **Indication:** Hormone Replacement Therapy (HRT) for oestrogen deficiency symptoms in postmenopausal women more than 6 months post-menopause (or 18 months since last period). 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. **Dosage & administration:** ***Adults:*** Evorel Conti is a continuous combined HRT preparation. Patches are applied to the skin twice weekly. One Evorel Conti patch should be worn at all times, without interruptions. For initiation and continuation of treatment of menopausal symptoms, the lowest effective dose for the shortest duration should be used. ***Guidance on how to start therapy:*** Post-menopausal women currently not on HRT may start Evorel Conti at any time. ***Switching from other HRT:*** Women on a continuous combined regimen wishing to switch from another oestrogen to Evorel Conti may do so at any time. Women on a cyclic or continuous sequential regimen wishing to switch from a sequential combined HRT preparation to Evorel Conti may do so at the end of a cycle of the current therapy or after a 7-day hormone free interval. Unless there is a previous diagnosis of endometriosis, it is not recommended to add a progestogen in hysterectomised women. **Method of Administration:** The sachet containing one Evorel Conti patch should be opened and one part of the protective foil removed at the S- shaped incision. The patch should be applied to clean, dry, healthy, intact skin as soon as it is removed from the sachet. The patient should avoid contact between fingers and the adhesive part of the patch during application. Each application should be made to a different area of the skin, on the trunk below the waist. The patch should not be applied on or near the breasts and should remain in place during bathing and showering. Should a patch fall off, it should be replaced immediately with a new patch, however the usual day of changing Evorel Conti patches should be maintained. **Missed Dose**: If the patient forgets to change their patch, they should change it as soon as possible and apply the next one at the normal time. However, if it is almost time for the next patch, the patient should skip the missed one and go back to their regular schedule. Only one patch should be applied at a time. Wearing a patch for > 4 days by mistake or any period without a patch may increase the likelihood of breakthrough bleeding or spotting. ***Children*****:** Not indicated. ***Elderly:*** Data are insufficient in the elderly (>65 years old). ***Route of administration:*** Transdermal use. **Contraindications:** Known, past or suspected breast cancer. Known or suspected oestrogen-dependent malignant tumours or pre-malignant tumours. Undiagnosed genital bleeding. Untreated endometrial hyperplasia. Previous idiopathic or current venous thrombo-embolism (VTE). Active or recent past arterial thrombo-embolic (ATE) disease. Known thrombophilic conditions. Acute liver disease, or a history of liver disease if liver function tests have failed to return to normal. Known hypersensitivity to the active substances or to any of the excipients. Porphyria. **Special warnings and precautions for use:** For the treatment of menopausal symptoms, HRT should only be initiated for symptoms that adversely affect quality of life with careful appraisal of the risks and benefits at least annually. Evidence regarding the risks associated with HRT in the treatment of premature menopause is limited. Before initiating or re-instituting HRT, a complete personal and family medical history should be taken and together with contra-indications and warnings for use, should guide physical (including pelvic and breast) examination. ***Conditions which need supervision:*** If any of the following conditions are present, occurred previously, have been aggravated during pregnancy or previous hormone treatment, supervise patient closely. Conditions may recur or be aggravated during treatment, in particular: Leiomyoma or endometriosis, a history of, or risk factors for thrombo-embolic 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, otosclerosis and mastopathy. ***Conditions which require monitoring while on oestrogen therapy:*** Oestrogens may cause fluid retention. Cardiac or renal dysfunction should be carefully observed. Disturbances or mild impairment of liver function. History of cholestatic jaundice. Pre-existing hypertriglyceridaemia. Rare cases of large increases of plasma triglycerides leading to pancreatitis have been reported with oestrogen therapy in this condition. ***Therapy should be discontinued if a contraindication is discovered and in the following situations:*** jaundice/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 thrombo-embolism, Coronary Artery disease, Ischaemic stroke, Hypothyroidism, Angioedema – please refer to the SmPC for full details. **Interactions:** The metabolism of oestrogens and progestogens may be increased by concomitant use of substances known to induce drug-metabolising enzymes, specifically cytochrome P450 enzymes, such as anticonvulsants, anti-infectives and bosentan. Ritonavir, telaprevir, nelfinavir and herbal preparations containing St. John's Wort may induce the metabolism of oestrogens and progestogens. Clinically, an increased metabolism of oestrogens and progestogens may lead to decreased effect and changes in the uterine bleeding profile. Oestrogen-containing oral contraceptives have been shown to significantly decrease plasma concentrations of lamotrigine when co-administered due to induction of lamotrigine glucuronidation. This may reduce seizure control. Therefore, dose adjustment of lamotrigine may be necessary. **Fertility**, **Pregnancy and lactation:** Not indicated, treatment should be withdrawn immediately. Data on a limited number of exposed pregnancies indicate adverse effects of norethisterone on the foetus. At doses higher than normally used in oral contraceptives and HRT formulations, masculinisation of female foetuses was observed. **Side effects:** Adverse reactions observed in clinical trials: **Very common** (≥1/10)**:** Application site erythema, Application site pruritus, Application site rash, Application site reaction, breast tenderness. **Common** (≥1/100 to <1/10)**:** Hypersensitivity**,** Depression, Insomnia, Anxiety, Nervousness, Paraesthesia, Headache, Palpitations, Hypertension, Varicose veins, Vasodilation, Abdominal pain, Diarrhoea, Nausea, Rash erythematous, Arthralgia, Back pain, Breast pain, Cervical polyp, Endometrial hyperplasia, Genital discharge, Dysmenorrhoea, Menorrhagia, Menstrual disorder, Metrorrhagia, Pain, Oedema, Application site oedema, Fatigue, Weight increased, Affect lability, Dyspepsia, Acne, Dry skin, Pain in extremity, Uterine spasms, Vaginal infection. **Uncommon** (≥1/1,000 to <1/100) **include:** Candidiasis, Migraine, Myalgia, Generalised Oedema, Oedema peripheral, Transaminases increase. **Rare** (≥1/10,000 to <1/1,000)**:** Epilepsy, Thrombosis, Gallbladder disorder, Myasthenia, Uterine leiomyoma, fallopian tube cysts. **Very rare** (<1/10,000): cholestatic jaundice **Frequency not known include** (cannot be estimated from the available clinical trial data)**:** Breast neoplasms, Endometrial cancer**,** Cerebrovascular accident, Deep vein thrombosis, Pulmonary embolism, Abdominal distension, Cholelithiasis, Stevens-Johnson syndrome. **Package Quantities & Cost:** Each carton box has 8 or 24 Transdermal Delivery Systems in individual foil-lined sachets. Cost – 1x8 £15.47; 1x24 £44.28. **Marketing authorisation number:** PL 49105/0009 **Marketing authorisation holder:** Theramex HQ UK Limited, 50 Broadway, 5th Floor, London, SW1H 0BL, UK. **Legal classification:** POM. **Date of Preparation:** October 2024: EVOR_UK_EN_20239_v1(v1.3).

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EVOREL® Sequi (estradiol hemihydrate norethisterone acetate) Abbreviated Prescribing Information

Please consult the Summary of Product Characteristics (SmPC) for other adverse reactions and full prescribing

Presentation: Evorel Sequi is a transdermal therapy comprising a) 4 Evorel 50 Transdermal Delivery Systems (TDSs), each containing: 3.2 mg of estradiol hemihydrate. b) 4 Evorel Conti TDSs, each containing: 3.2 mg of estradiol hemihydrate, 11.2 mg of norethisterone acetate. **Indication:** Hormone Replacement Therapy (HRT) for oestrogen deficiency symptoms in peri- and post-menopausal women. 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. **Dosage & administration:** ***Adults:*** Evorel Sequi is a continuous sequential HRT preparation. Patches are applied to the skin twice weekly. One Evorel Sequi patch should be worn at all times, without interruptions. For initiation and continuation of treatment of menopausal symptoms, the lowest effective dose for the shortest duration should be used. ***Guidance on how to start therapy:*** Any previous therapy with HRT must be stopped prior to starting Evorel Sequi. Post-menopausal women currently not on HRT may start Evorel Sequi at any time. Peri-menopausal women who are still having regular menstrual cycles and are not currently on HRT should start Evorel Sequi within 5 days of the start of bleeding. Peri-menopausal women with irregular menstrual cycles, for whom pregnancy has been excluded, can start Evorel Sequi at any time. ***Switching from other HRT:*** Women on a continuous combined regimen wishing to switch from another oestrogen to Evorel Sequi may do so at any time. Women on a cyclic or continuous sequential regimen wishing to switch from a sequential combined HRT preparation to Evorel Sequi may do so at the end of a cycle of the current therapy or after a 7-day hormone free interval. Unless there is a previous diagnosis of endometriosis, it is not recommended to add a progestogen in hysterectomised women. ***Method of Administration:*** A treatment cycle with Evorel Sequi is 28 days. During the first 14 days, one estradiol-only (Evorel 50) patch should be worn at all times without interruption. During days 15-28, one estradiol + norethisterone (Evorel Conti) patch should be worn and should remain in place during bathing and showering. A subsequent treatment cycle should follow immediately, without a treatment free interval. Patches should be applied to the trunk, below the waist. Patches should be changed twice a week, i.e. every three to four days. Application of a new patch should be to a site different from the previous application site. The patch should not be applied on or near the breasts. ***Missed dose:*** Change as soon as possible and apply the next one at normal time unless it is almost time for the next patch, then the patient should skip the missed one and return to regular schedule. Only one patch should be applied at a time. Wearing a patch for >4 days or any period without a patch may increase the likelihood of breakthrough bleeding or spotting. ***Children*****:** Not indicated. ***Elderly:*** Data are insufficient in the elderly (>65 years old). ***Route of administration:*** Transdermal use. **Contraindications:** Known, past or suspected breast cancer. Known or suspected oestrogen-dependent malignant tumours or pre-malignant tumours. Undiagnosed genital bleeding. Untreated endometrial hyperplasia, Previous idiopathic or current venous thrombo-embolism (VTE). Active or recent past arterial thrombo-embolic (ATE) disease. Acute liver disease, or a history of liver disease if liver function tests have failed to return to normal. Known thrombophilic conditions. Known hypersensitivity to the active substances or to any of the excipients. Porphyria. **Special warnings and precautions for use:** For the treatment of menopausal symptoms, HRT should only be initiated for symptoms that adversely affect quality of life with careful appraisal of the risks and benefits at least annually. Evidence regarding the risks associated with HRT in the treatment of premature menopause is limited. Before initiating or re-instituting HRT, a complete personal and family medical history should be taken and together with contra-indications and warnings for use, should guide physical (including pelvic and breast) examination. ***Conditions which need supervision:*** If any of the following conditions are present, occurred previously, have been aggravated during pregnancy or previous hormone treatment, supervise patient closely. Conditions may recur or be aggravated during treatment, in particular: Leiomyoma or endometriosis, a history of, or risk factors for, thrombo-embolic disorders or oestrogen dependent tumours, hypertension, liver disorders, diabetes mellitus, cholelithiasis, migraine or (severe) headache, systemic lupus erythematosus, history of endometrial hyperplasia, epilepsy, asthma, otosclerosis, hereditary angioedema and mastopathy. ***Conditions which require monitoring while on oestrogen therapy:*** Oestrogens may cause fluid retention. Cardiac or renal dysfunction should be carefully observed. Disturbances or mild impairment of liver function. History of cholestatic jaundice. Pre-existing hypertriglyceridaemia. Rare cases of large increases of plasma triglycerides leading to pancreatitis have been reported with oestrogen therapy in this condition. ***Therapy should be discontinued if a contraindication is discovered and in the following situations:*** jaundice/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 thrombo-embolism, Coronary Artery disease, Ischaemic stroke, Hypothyroidism, Angioedema – please refer to the SmPC for full details. **Interactions:** The metabolism of oestrogens and progestogens may be increased by concomitant use of substances known to induce drug-metabolising enzymes, specifically cytochrome P450 enzymes, such as anticonvulsants, anti-infectives and bosentan. Ritonavir, telaprevir, nelfinavir and herbal preparations containing St. John's Wort may induce the metabolism of oestrogens and progestogens. Clinically, an increased metabolism of oestrogens and progestogens may lead to decreased effect and changes in the uterine bleeding profile. Oestrogen-containing oral contraceptives have been shown to significantly decrease plasma concentrations of lamotrigine when co-administered due to induction of lamotrigine glucuronidation. This may reduce seizure control. Therefore, dose adjustment of lamotrigine may be necessary. **Fertility**, **Pregnancy and lactation:** Not indicated, treatment should be withdrawn immediately. Data on a limited number of exposed pregnancies indicate adverse effects of norethisterone on the foetus. At doses higher than normally used in oral contraceptives and HRT formulations, masculinisation of female foetuses was observed. **Side effects:** Adverse reactions observed in clinical trials: **Very common** (≥1/10)**:** Application site erythema, Application site pruritus, Application site rash, Application site reaction. Breast tenderness. **Common** (≥1/100 to <1/10)**:** Depression, Insomnia, Affect lability, Nervousness, Migraine, Headache, Hypertension, Abdominal pain, Gastrointestinal disorder, Diarrhoea, Flatulence, Nausea, Pruritus, Rash erythematous, Arthralgia, Back pain, Myalgia, Breast pain, Dysmenorrhoea, Menorrhagia, Menstrual disorder, Pain, Oedema, Malaise, Weight increased. Dyspepsia, Acne, Dry skin, Pain in extremity, Genital discharge, Uterine spasms, Vaginal infection. **Uncommon** (≥1/1,000 to <1/100) **include:** Candidiasis, Breast neoplasms, Fibroadenoma of breast, Hypersensitivity, Paraesthesia, Palpitations, Endometrial hyperplasia, Metrorrhagia, Generalised oedema, Transaminases increase. **Rare** (≥1/10,000 to <1/1,000) **include:** Gallbladder disorder, Myasthenia, **Very rare** (<1/10,000): Cholestatic jaundice **Frequency not known include:** Endometrial cancer**,** Cerebrovascular accident, Epilepsy, Deep Vein Thrombosis, Thrombosis, Pulmonary Embolism, Abdominal distension, Cholelithiasis, Rash, Stevens-Johnson syndrome, Oedema peripheral, Application site oedema. **Package Quantities & Cost:** Each carton box has 8 TDSs in individual foil-lined sachets. One Evorel Sequi box contains 4 Evorel 50 TDS and 4 Evorel Conti TDSs. Cost: £13.20. **Marketing authorisation number:** PL 49105/0010. **Marketing authorisation holder:** Theramex HQ UK Limited, 50 Broadway, 5th Floor, London, SW1H 0BL, UK. **Legal classification:** POM. **Date of Preparation:** October 2024: EVOR_UK_EN_20240_v1(v1.4).

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FemSeven® 50, 75, 100 micrograms/24 hours transdermal patch. Abbreviated Prescribing Information

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

Presentation: FemSeven 50: 1.5 mg estradiol hemihydrate patch; FemSeven 75: 2.25 mg estradiol hemihydrate patch; FemSeven 100: 3 mg estradiol hemihydrate patch. Releases estradiol at 50, 75, or 100 micrograms per 24 hours, respectively. **Indication:** Hormone Replacement Therapy (HRT) for estrogen deficiency symptoms in postmenopausal women. 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. Experience of treating women older than 65 years is limited. **Dosage & administration:** FemSeven is an estrogen-only patch that should be applied to the skin once weekly on a continuous basis, i.e. each patch is replaced with a new one after 7 days. In women with an intact uterus, the addition of a progestogen for at least 12 to 14 days every month/28-day cycle is essential to help prevent any endometrial hyperplasia induced by the estrogen. Unless there is a previous diagnosis of endometriosis, it is not recommended to add a progestogen in hysterectomised women. For initiation and continuation of treatment of postmenopausal symptoms, the lowest effective dose for the shortest duration should be used (50 mcg of estradiol in 24 hours); a maximum dose of 100 mcg estradiol per day should not be exceeded. If there are persistent signs of overdose, such as breast tenderness, the dose should be reduced accordingly. Hysterectomised and non-hysterectomised women not taking HRT or transferring from another HRT product may start treatment with FemSeven on any convenient day. In non-hysterectomised women switching from sequential HRT regimens, treatment with FemSeven should start after the previous treatment regimen has ended. Consecutive new patches should be applied to different sites. It is recommended that sites are chosen below the waist where little wrinkling of the skin occurs e.g., buttocks, hip or abdomen. FemSeven must not be applied on or near the breasts. The patch should be applied to clean, dry, healthy and intact skin. The patch should be applied to the skin as soon as it is removed from its wrapping. Should part or all of a patch detach prematurely (before 7 days) it should be removed, and a new patch applied. Forgetting a patch may increase the likelihood of break-through bleeding or spotting. **Contraindications:** Known, past or suspected breast cancer. Known or suspected estrogen-dependent malignant tumours. Undiagnosed genital bleeding. Untreated endometrial hyperplasia. Active or past venous thromboembolism (VTE, e.g., 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. Known hypersensitivity to the active substance or to any of the excipients. Porphyria. **Special warnings and precautions for use:** Before initiating or reinstituting HRT, a complete personal and family medical history should be taken. Women should be advised what changes in their breasts should be reported to their doctor or nurse. ***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. Conditions may recur or be aggravated during treatment, in particular: Leiomyoma or endometriosis, risk factors for thromboembolic disorders or estrogen 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. ***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. The WHI trial found no increase in the risk of breast cancer in hysterectomised women using estrogen-only HRT. Randomised controlled data found no increased risk of Coronary artery disease (CAD) in hysterectomised women using estrogen-only therapy. 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:** The metabolism of estrogens may be increased by concomitant use of substances known to induce drug-metabolising enzymes, specifically cytochrome P450 enzymes, such as anticonvulsants and anti-infectives. Ritonavir, nelfinavir and herbal preparations containing St. John's Wort may induce the metabolism of estrogens. At transdermal administration, the first-pass effect in the liver is avoided and, thus, transdermally applied estrogens HRT might be less affected than oral hormones by enzyme inducers. Clinically, an increased metabolism of estrogens may lead to decreased effect and changes in the uterine bleeding profile. 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. **Pregnancy and lactation:** 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 frequently reported undesirable effects (> 10 %) in clinical trials were application site reactions, e.g. pruritus, erythema, eczema, urticaria, oedema and changes in skin pigmentation. They were mostly mild skin reactions and usually disappeared 2 – 3 days after patch removal. **Common ADRs (≥ 1/100, < 1/10):** Headache, breast discomfort. **Uncommon ADRs (≥ 1/1,000, < 1/100):** Hair changes, sweating increased, Arthralgia, leg cramps, dizziness, paraesthesia, migraine, anxiety, appetite increase, depression, insomnia, nervousness, nausea, dyspepsia, abdominal pain, vomiting, blood pressure changes, chest pain, vein disorders, vaginal discharge, breakthrough bleeding, oedema, fatigue, weight changes. **Rare (≥ 1/10 000, < 1/1 000):** Worsening of uterine fibroids. Refer to SmPC for information on adverse effects of HRT, including breast and ovarian cancer, VTE, and cardiovascular risks. **Package Quantities & Cost:** Each container (primary packaging) consists of a sealed laminated sachet. Package sizes: Carton of 4 patches. Cost: 50 (1x4) £6.04; 75 (1x4) £6.98; 100 (1x4) £7.28. **Marketing authorisation number:** FemSeven 50 PL 49876/0007; FemSeven 75 PL 49876/0008; FemSeven 100 PL 49876/0009. **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: FEM7_HQ-UK_EN_21147_v1.

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

Presentation: FemSeven Conti 1.5 mg of estradiol hemihydrate and 0.525 mg levonorgestrel transdermal patch, releasing 50 mcg of estradiol and 7 mcg of levonorgestrel per 24 hours **Indication:** Hormone replacement therapy (HRT) for oestrogen deficiency symptoms in postmenopausal women more than one year after menopause. **Dosage & administration**: For transdermal use. FemSeven Conti has to be applied once a week. FemSeven Conti is a continuous combined HRT treatment without a treatment-off phase. In women with amenorrhoea and not taking HRT or women transferring from another continuous combined HRT product, treatment with FemSeven Conti may be started on any convenient day. In women transferring from sequential HRT regimens, treatment should start right after their withdrawal bleeding has ended. For initiation and continuation of treatment of menopausal symptoms, the lowest effective dose for the shortest duration should be used. **Method of Administration:** FemSeven Conti should be applied to clean, dry, healthy skin, free from any cream, lotion or other oily product. The patch should be applied to an area of skin without major skin folds, i.e. the buttocks or hips, and not subject to chafing by clothing (avoid the waist and also avoid wearing tight clothing that could loosen the transdermal patch). FemSeven Conti must not be applied either on or near the breasts. It is advisable to avoid applying the patch to the same site twice running. At least one week should be allowed to elapse between applications to the same site. The patch must be applied directly to the skin and must be firmly pressed with the palm of the hand for at least 30 seconds, concentrating on the edges. Once applied, the transdermal patch has to be covered by clothes to avoid direct exposure to sunlight. Removal of the transdermal patch should be carried out slowly to avoid irritating the skin. **Contraindications:** Known or suspected oestrogen-dependent malignant tumours or pre-malignant tumours. Undiagnosed genital bleeding. Untreated endometrial hyperplasia.. Previous or current venous thromboembolism (VTE) (deep venous thrombosis, pulmonary embolism). 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. Known hypersensitivity to the active substances or to any of the excipients. Porphyria. **Special warnings and precautions for use**: Before initiating or re-instituting HRT, a complete personal and family medical history should be taken. ***Conditions which need supervision:*** If any of the following conditions are present, occurred previously, have been aggravated during pregnancy or previous hormone treatment, supervise patient closely. Conditions may recur or be aggravated during treatment, in particular: Leiomyoma or endometriosis, risk factors for thrombo-embolic disorders or 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. ***Therapy should be discontinued if a contraindication is discovered and in the following situations:*** jaundice/deterioration in liver function, significant increase in blood pressure, new onset of migraine-type headache, pregnancy. The overall evidence suggests an increased risk of breast cancer in women using oestrogen-progestogen HRT, that is dependent on the duration of taking HRT. 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:** The metabolism of oestrogens and progestogens may be increased by concomitant use of substances known to induce drug-metabolising enzymes, specifically cytochrome P450 enzymes, such as anticonvulsants and anti-infectives. Ritonavir, nelfinavir and herbal preparations containing St. John's Wort may induce the metabolism of oestrogens and progestogens. At transdermal administration, the first-pass effect in the liver is avoided and, thus, transdermally applied oestrogens and progestogens might be less affected than oral hormones by enzyme inducers. Clinically, an increased metabolism of oestrogens and progestogens may lead to decreased effect and changes in the uterine bleeding profile. 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**. Fertility**, **Pregnancy and lactation:** 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 frequently reported undesirable effects (> 10 %) in clinical trials were application site reactions, breast tenderness and bleeding or spotting. **Common ADRs (≥ 1/100; < 1/10):** Headache, dyspepsia and mastodynia. **Uncommon ADRs (≥ 1/1 000; < 1/100):** Fluid retention/ oedema/weight increase/loss, fatigue, leg cramps, dizziness, migraine, bloating, abdominal cramps, nausea, hypertension, endometrial hyperplasia benign breast tissue changes and depression. **Rare (≥ 1/10 000; < 1/1 000):** Cholelithiasis, cholestatic jaundice and increase in size of uterine fibrosis. Refer to SmPC for information on adverse effects of HRT, including breast and ovarian cancer, VTE, and cardiovascular risks. **Package Quantities & Cost:** the container consists of a sealed laminated sachet. Each carton box has 4 transdermal patches. Cost: 1x4 £15.48. **Marketing authorisation number:** PL 49876/0010. **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: FEM7_HQ-UK_EN_21168_v1.

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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

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