

**Evorel Supply Update: August 2020**

Following the acquisition of Evorel by Theramex in October 2019, we have worked tirelessly with multiple manufacturing partners to resupply the product in the UK market. Since February 2020, we have produced over 800,000 packs across the Evorel portfolio. There has been unprecedented demand for all of the products and we are are working with our manufacturing partners to continuously increase capacity in order to ensure that Evorel is readily available to every patient who needs it.

We would like to thank both patients and healthcare professionals for their patience as we focus our attention on building a stable supply chain. In addition, we thank GPs across the UK for continuing to prescribe responsibly as we replenish the market and build a solid inventory of product.

Evorel 50, Evorel 100, Evorel Conti and Evorel Sequi are all currently available. There will be intermittent supply of Evorel 25 and Evorel 75 during the first half of August.

|  |  |  |
| --- | --- | --- |
| **Country** | **Product Name** | **Dates of Availability** |
| **UK** | 1. Evorel 25
2. Evorel 50
3. Evorel 75
4. Evorel 100
5. Evorel Conti
6. Evorel Sequi
 | 1. Intermittent supply first half of August
2. Available
3. Intermittent supply first half of August
4. Available
5. Available
6. Available
 |
|  |  |  |

**Note to pharmacists**

In order to ensure the widest possible reach of the available stock, Alliance Healthcare have applied monthly quotas to the volume of stock available to individual pharmacists. If you require additional stock above this quota, in order to fulfil prescriptions, please contact Alliance Healthcare Customer Service by telephone *0330 100 0448* or email *customerservice@alliance-healthcare.co.uk*.

**Further information**

Patients who have any questions with regards to their treatment options should speak to their general practitioner.

For pharmacists and healthcare professionals who wish to place orders for the Evorel range of products, please contact Alliance Healthcare via your usual channels.

**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:** 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. 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*.* Should not be applied on or near the breasts. 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 in children. ***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 or pre-malignant tumours. Undiagnosed genital bleeding. Previous idiopathic or current VTE. Active or recent past 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:** 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, 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. For Evorel 75 and 100 the endometrial safety of added progestogens has not been studied. **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, treatment should be withdrawn immediately. **Side effects:** Adverse reactions observed in clinical trials: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); and not known (cannot be estimated from the available clinical trial data). **Very common:** Application site pruritus, Application site rash. **Common:** 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 increased. **Uncommon include:** Genital candidiasis,Hypersensitivity, Palpitations, Myalgia, Dysmenorrhoea, Oedema, Oedema peripheral. **Rare:** Breast cancer, Epilepsy, Thrombosis, Abdominal distension, Cholelithiasis, **Frequency not known:** Endometrial cancer**,** Cerebrovascular accident, Myocardial infarction, Deep vein thrombosis, Pulmonary embolism, Angioedema. **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) £3.42; 50 (1x8) £3.88; 50 (1x24) £11.66; 75 (1x8) £4.12; 100 (1x8) £4.28. **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 LTD, Sloane Square House, 1 Holbein Place, London SW1W 8NS, UK. **Legal classification:** POM. **Date of Preparation:** January 2020: THX\_GB\_PI\_001472.

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**

**Adverse events should be reported. Reporting forms and information can be found at**

[**www.mhra.gov.uk/yellowcard**](http://www.mhra.gov.uk/yellowcard) **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: 0333 0096795**

**Presentation:** Evorel Conti 3.2 mg of estradiol hemihydrate, 11.2 mg of norethisterone acetate transdermal patch. **Indication:** HRT for oestrogen deficiency symptoms in post-menopausal 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, the usual day of changing Evorel Conti patches should be maintained. ***Children*:** Not indicated in children. ***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. Previous idiopathic or current VTE. Active or recent past 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:** 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, 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 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. **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); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); and not known (cannot be estimated from the available clinical trial data). **Very common:** Application site erythema, Application site pruritus, Application site rash, Application site reaction. **Common:** 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. **Uncommon include:** Candidiasis,Myalgia, Oedema, Oedema peripheral. **Rare:** Epilepsy, Thrombosis. **Frequency not known include:** 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 TDSs in individual foil-lined sachets. Cost – 1x8 £13.00; 1x24 £37.22. **Marketing authorisation number:** PL 49105/0009 **Marketing authorisation holder:** Theramex HQ UK LTD, Sloane Square House, 1 Holbein Place, London SW1W 8NS, UK. **Legal classification:** POM. **Date of Preparation:** January 2020: THX\_GB\_PI\_001473.

* EVOREL® Conti (estradiol hemihydrate norethisterone acetate) Abbreviated Prescribing Information
* **Please consult the Summary of Product Characteristics for other adverse reactions and full prescribing information**

**Adverse events should be reported. Reporting forms and information can be found at**

[**www.mhra.gov.uk/yellowcard**](http://www.mhra.gov.uk/yellowcard) **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: 0333 0096795**

**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:** 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 at all times, without interruption. 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. Wearing a patch for more than 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 VTE. Active or recent past 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:** 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, 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. **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); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); and not known (cannot be estimated from the available clinical trial data). **Very common:** Application site erythema, Application site pruritus, Application site rash, Application site reaction. **Common:** 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. **Uncommon include:** Candidiasis,Breast cancer, Fibroadenoma of breast, Hypersensitivity, Paraesthesia, Palpitations, Endometrial hyperplasia, Metrorrhagia, Oedema. **Rare include:** Epilepsy, Thrombosis, Stevens-Johnson syndrome. **Frequency not known include:** Endometrial cancer**,** Cerebrovascular accident, Epilepsy, Deep vein thrombosis, Thrombosis, Pulmonary embolism, Abdominal distension, Cholelithiasis, 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: £11.09. **Marketing authorisation number:** PL 49105/0010. **Marketing authorisation holder:** Theramex HQ UK LTD, Sloane Square House, 1 Holbein Place, London SW1W 8NS, UK. **Legal classification:** POM. **Date of Preparation:** January 2020: THX\_GB\_PI\_001474.

**Adverse events should be reported. Reporting forms and information can be found at**

[**www.mhra.gov.uk/yellowcard**](http://www.mhra.gov.uk/yellowcard) **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: 0333 0096795**

* EVOREL® Sequi (estradiol hemihydrate norethisterone acetate) Abbreviated Prescribing Information
* **Please consult the Summary of Product Characteristics for other adverse reactions and full prescribing information**