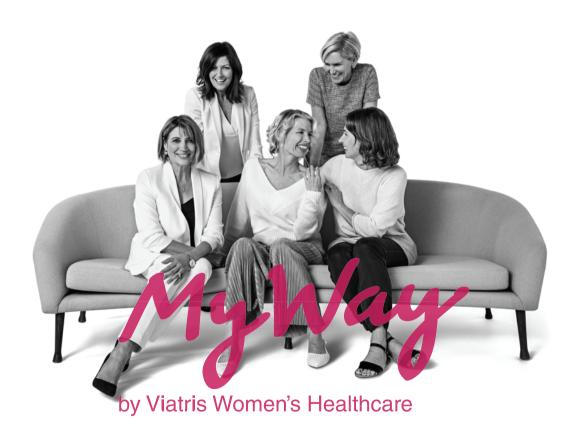
Hormone Replacement Therapy: Cost Comparison



Could you Prescribe Femoston®?

estradiol/dydrogesterone

The only HRT range with dydrogesterone



Visit our website to find out more about our HRT range www.mywayhub.co.uk









Patient case studies

Emma, Age: 46

Situation: First visit to GP

Symptoms: No periods for 6 months, previously erratic periods, "brain fog", irritable,

hot flushes

Concern: Aunt had breast cancer at age 55* Taking: Over the counter herbal remedies





Initiate with: Femoston® 1/10 mg

Jill, Age: 55

Situation: Visited GP twice before seeing a specialist now at 6-month HRT review

Prescribed: Continuous micronised

progesterone & gel

Review notes: Symptoms improved, patient dislikes treatment regimen as she finds gel messy and does not like taking the micronised progesterone





Consider: Femoston®-conti 1/5 mg

Deborah, Age: 52

Situation: 3-month HRT review **Prescribed:** Sequential combined

transdermal patch

Review notes: Symptoms improved, but experiencing androgenic side effects, patch causing irritation and patient found it difficult to use



Consider: Femoston® 1/10, or 2/10 mg



KEY CONSIDERATIONS

Emma, 46 1. Worried about risk of breast cancer -- consider the progestogen

Jill, 55 1. Transdermal gel messy → consider the route and patient choice 2. Problems with patient compliance risk of endometrial hyperplasia/cancer

Deborah, 52 1. Transdermal patch causing irritation -> consider the route 2. Androgenic side effects → consider the progestogen

The patient case studies above are intended to aid and not replace clinical decision making. Below are some examples of other factors which should be considered when prescribing HRT.

Factors to consider when prescribing HRT:1-4

- Presence/absence of uterus
 Time since last menstrual period
 - Patient choice
- Contraindications to HRT

• Type of hormone(s)

• Age of menopause

- Risk factors for VTE
- Need for contraception
- Severity of symptoms

HRT: Hormone replacement therapy; VTE: Venous thromboembolism.

*For full information on familial breast cancer risk, please refer to NICE Clinical Guideline [CG164] available at www.nice.org.uk/guidance/cg164.

What is the monthly cost** of treating patients with the most common combined HRT regimes?^{5,6}

Table contains commonly prescribed combined HRT regimes, and is not intended as a clinical prescribing guide. It is not an exhaustive list and note that other HRT options are available including, combinations using LNG52mg IUS. Clinical prescribing should be guided by the clinical judgement and individual assessment of each patient.

| Trade name(s) | Elleste Duet™ (E2 1mg, 2mg) & (NETA 1mg) | Kliofem® (E2 2mg) & (NETA 1mg) | Kliovance® (E2 1mg) & (NETA 500mcg) | Femoston® (E2 1mg, 2mg) & (DYD 10mg) | Elleste Duet™ Conti (E2 2mg) & (NETA 1mcg) | Femoston® -conti (E2 500mcg, 1mg) & (DYD 2.5mg, 5mg) | Utrogestan® (MP 100mg) + Evorel® (E2 50mcg) | Utrogestan® (MP 100mg) + Oestrogel® (E2 0.06%) | Evorel® Sequi (E2 50mcg) & (NETA 170mcg) | Evorel® Conti (E2 50mcg) & (NETA 170mcg) |
|--------------------|--|-----------------------------------|---------------------------------------|--|--|--|--|--|--|--|
| Treatment regimen | Sequential combined therapy | Continuous combined therapy | Continuous combined therapy | Sequential combined therapy | Continuous combined therapy | Continuous combined therapy | Sequential/ continuous combined therapy | Sequential/ continuous combined therapy | Sequential combined therapy | Continuous combined therapy |
| Treatment duration | 28 days | | | | | | | | | |
| Total cost** | £3.07 | £3.81 | £4.40 | £5.39 | £5.67 | £8.14 | £4.28 + £3.88 = £8.16 | £4.28 + £4.20 = £8.48 | £11.09 | £13.00 |

Kliofem® and Kliovance® are trade names of Novo Nordisk Limited; Utrogestan® and Oestrogel® are trade names of Besins Healthcare (UK) Ltd; Evorel®, Evorel® Segui and Evorel® Conti are trade names of Theramex UK Limited

Costs** are based on 28 days of treatment

"But doctor, are all progestogens the same?"

- Overall evidence shows an increased risk of breast cancer in women taking combined estrogen-progestogen or estrogen-only HRT, that is dependent on the duration of taking HRT.^{3,7-9}
- The Women's Health Initiative (WHI) study and a meta-analysis are consistent in finding an increased risk of breast cancer in women taking combined estrogen-progestogen for HRT that becomes apparent after about 3 (1–4) years.^{3,7-9}

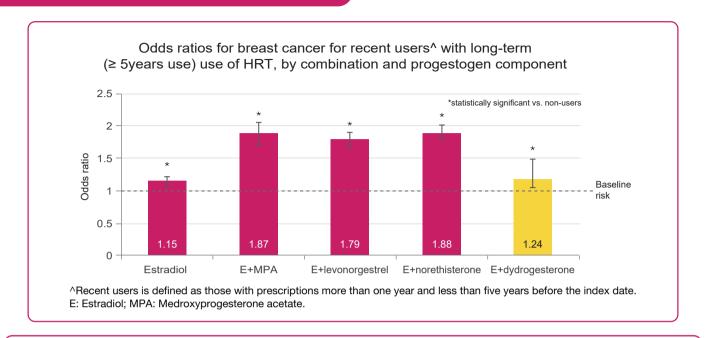
Additional results of observational studies and a recent meta-analysis show that **different** progestogens may have different risk profiles when it comes to breast cancer risk.¹⁰⁻¹³



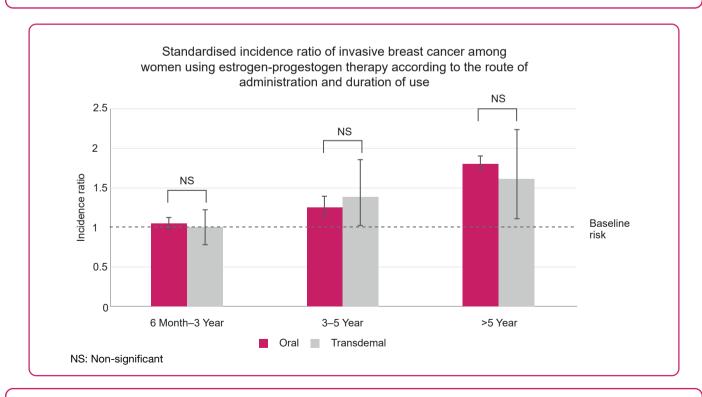
DYD: Dydrogesterone; E2: Estradiol; HRT: Hormone replacement therapy; IUS: Intrauterine system; LNG: Levonorgestrel; MP: Micronised progesterone; NETA: Norethisterone.

^{**}These prices are based on 28 days of treatment taken from the MIMS HRT table.⁶ Prices last accessed in January 2021. They are approximations only and exact cost prices may vary depending on the product and usage. Some products are only available in either 1 or 3 monthly packs.

Breast cancer data 10,13



Conclusion: A recent nested case-control study reported that in recent users^ with long-term use (>5 years), the increased risk was **highest for norethisterone** (OR: 1.88, Cl 1.79 to 1.99) and **lowest for dydrogesterone** (OR: 1.24, Cl 1.03 to 1.48). 13



Conclusion: A Finnish Cohort study, which included 221,551 postmenopausal women, reported that there was **no difference between the route of administration (oral vs. transdermal)** when it comes to breast cancer risk.¹⁰

HRT: Hormone replacement therapy.

References

- 1. Hamoda H, Panay N, Pedder H, et al. The British Menopause Society & Women's Health Concern 2020 recommendations on hormone replacement therapy in menopausal women. Post Reprod Health. 2020;26(4):181-209.
- Anderson Jr FA, Spencer FA. Risk factors for venous thromboembolism. Circulation. 2003 Jun 17;107(23 suppl 1):1-9.
- Femoston® 1/10 mg Summary of Product Characteristics.
- NICE NG23. Menopause: diagnosis and management. NG23. Available at: www. nice.org.uk/guidance/ng23 (Last accessed December 2020).
- 5 Viatris data on file 2020
- MIMS Online. Hormone Replacement Therapy Table, accessed on https:// www.mims.co.uk/table-hormone-replacement-therapy-hrt/womens-health/ article/1415738. Last accessed, December 2020.
- Femoston® 2/10 mg Summary of Product Characteristics.
- Femoston®-conti 0.5 mg/2.5 mg Summary of Product Characteristics.

- 9. Femoston®-conti 1 mg/5 mg Summary of Product Characteristics.
- 10. Lyytinen H, Pukkala E, Ylikorkala O. Breast cancer risk in postmenopausal women using estradiol-progestogen therapy. Obstet Gynecol. 2009;113(1):65-73.
- 11. Collaborative Group on Hormonal Factors in Breast Cancer. Lancet 2019; published online: August 29, 2019. https://www.thelancet.com/journals/lancet/ article/PIIS0140-6736(19)31709-X/fulltext (Last accessed December 2020).
- 12. Fournier A, Berrino F, Clavel-Chapelon F. Unequal risks for breast cancer associated with different hormone replacement therapies: Results from the E3N cohort study. Breast Cancer Res Treat. 2008; 107:103-111.
- 13. Vinogradova Yana, Coupland Carol, Hippisley-Cox Julia. Use of hormone replacement therapy and risk of breast cancer: nested case-control studies using the QResearch and CPRD databases. BMJ. 2020; 371 :m3873





PRESCRIBING INFORMATION (combined)

Femoston® 1/10 mg film-coated tablets

Femoston®-conti 0.5 mg/2.5 mg film-coated tablets Femoston®-conti 1 mg/5 mg film-coated tablets

Refer to the Summary of Product Characteristics for full information.

Refer to the Summary of Product Characteristics for full information.

Presentation: Femoston®-contil 0.5 mg/2.5 mg film-coated tablets containing 0.5 mg estradiol (as hemilydrate) and 2.5 mg dydrogesterone. Femoston®-0.011 mg/5 mg film-coated tablets containing 1 mg estradiol (as hemilydrate) and 5 mg dydrogesterone. Femoston®-0.011 mg/5 mg film-coated tablets containing 1 mg estradiol (as hemilydrate) and 10 mg dydrogesterone. Femoston®-0.011 mg/5 mg film-coated tablets containing 1 mg estradiol (as hemilydrate) and 10 mg dydrogesterone. Femoston®-0.011 mg/5 mg film-coated tablets. Description of 10 mg dydrogesterone. Femoston®-0.011 mg/5 mg film-coated tablets. Hormone replacement therapy (HRI) or estrogen deficiency symptoms in postmenopausal women at least 12 months since last menses. Femoston®-0.011 mg/5 mg film-coated tablets. Hormone replacement therapy (HRI) for estrogen deficiency symptoms in postmenopausal women at least 18 months since last menses. Femoston®-0.011 mg/5 mg femoston®-1/10 mg and 2/10 mg film-coated tablets are under the contraindicated for other medicinal products approved for the prevention of soleoprosis in postmenopausal women at least 18 months since last menses. Femoston®-0.011 mg/5 mg femoston®-1/10 mg and 7/10 mg film-coated tablets are sent as ordinated soleoprosis in postmenopausal women at high risk of the returns with part of the prevention of soleoprosis in postmenopausal women at high risk of the returns with part of the prevention of soleoprosis in postmenopausal women at high risk of the returns with part of the prevention of soleoprosis in postmenopausal women at high risk of the returns with part of the prevention of soleoprosis in postmenopausal women at high risk of the returns with part of the prevention of soleoprosis in postmenopausal women at high risk of the returns with part of the prevention of soleoprosis in postmenopausal women at high risk of the returns with part of the returns wit ommended 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 uruse. Ceratifuly supervise if leinorymour or endometrious, risk factors for thromboemhobic disorders or estogen-dependent purpose, investigations, liver disorders, diabetes melitus, cholelithiasis, migraine or severe headaches, systemic lupus erythematous, history of endometrial hyperplasia, epilepsy, asthma, dioselerosis and menioginam conditions are present or have previously occurred and/or have been agravated during proxy or previous hormone treatment. Therapy should be discontinued in case a contraindication is discovered and in the following situations; audice or deterioration in liver function, significant increase in bod or pressure, envous of migraine-hype headache, prepanacy Investigate breakthrough bleeding, an increased risk of breast cancer has been reported that is dependent on the length of treatment. HRT can increase the density of mammographic images which may affect ardiological detection of breast cancer. The use of estrogen-only or combined estrogen-progestogen HRT has been associated with an increased relative risk of venous thromboemholism (VTE) i.e. deep vein thrombosis or pulmonary embolism.

Patients with known thrombophilic states have an increased risk of VTE and HRT may add to this risk. HRT is therefore contraindicated in these patients Generally recognised risk factors for VTE include use of estrogens, older age, major surgery, prolonged immobilisation, obesity (BMIs-30 kg/m²), preparancy postpartum period, systemic fupus exprehenators (SCI, and cancer IVTE develops after inflating therapy the fruity should be licensed, observed. Relative risk of coronary artery disease is raised with estrogen-propestogen therapy, but randomised controlled trials have not shown an increase with estrogen-pronyestogen therapy is associated with an up to 1.5-fold increased relative risk of ischaemic stroke. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malbasoprotion should not take this medicine. Estrogen-projestogen streamy is associated with an up to 1.5-fold increased relative risk of ischaemic stroke. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malbasoprotion should not take this medicine. Estrogen-projestogen smay be increased by concomitant use of P450 enzymes such as anticonvulsants and anti-inectives. Rithouris, relitariary and therapt preparations containing SL. John Van yillower the metabolism of estrogens and progestogens. Clinically, an increased metabolism of estrogens and progestogens may lead to decreased effect and changes in the uterine beeding profile. Femous **10 fold programs** 10 fold programs** Patients with known thrombonbilic states have an increased risk of VTE and HRT may add to this risk. HRT is therefore contraindicated in these natients Marketing Authorisation Holder: Mylan Products Ltd., 20 Station Close, Potters Bar, Herts, EN6 1TL, UK.

Marketing Authorisation Number: Femoston® 1/10 mg film-coated tablets PL 46302/0035; Femoston® 2/10 mg film-coated tablets PL 46302/0036; Femoston® 2/10 mg film-coated tablets PL 46302/0036; Femoston®-contil 0.5 mg/2.5 mg film-coated tablets PL 46302/0037; Femoston®-contil 1 mg/5 mg film-coated tablets PL 46302/0038

Basic NHS price: Femoston®-conti £24.43 (84 tablets) & Femoston® £16.16 (84 tablets

Legal Category: POM

Date of Last Revision: October 2020

Veeva Reference: FFM-2020-0409

The SmPC for this product, including adverse reactions, precautions, contra-indications, and method of use can befound at: http://www.mhra.gov.uk/ tylinformation/Nedsicinesinformation/SPCand/Psindex.htm and from Mylan Medical information, Building 4, Trident Place, Hatfield Business Park, Mo Way, Hatfield, Hertfordshire, ALI of 90L, phone no. 0.1707 83000, Email: Info@mylan.cu & MicroBorghian.cu & MicroBorghi

Adverse Drug Reactions 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 be reported to UK Pharmacovigilance, Mylan, Building 4, Trident Place, Hatfield Business Park, Mosquito Way, Hatfield, Hertfordshire, AL10 9UL, on phone no. +44 (0) 800 121 8267, Emait: ukpharmacovigilance@mylan.com



PRESCRIBING INFORMATION

ELLESTETM (estradiol +/- norethisterone acetate)
Please refer to Summary of Product Characteristics (SmPC) before prescribing.

ELLESTE" (estradiol +/- norethisterone acetate)
Please refer to Summary of Product Chracteristics (SmPC) before prescribing.

Presentation: Ellests Solo™ 1 mg and 2 mg film-coated tablets containing estradiol hemihydrate 1 mg and 2 mg respectively. Ellests Solo™ MK 40 mg transfermal patch containing 1.25 mg estradiol hemihydrate 1 mg and 2 mg respectively. Ellests Solo™ MK 40 mg transfermal patch containing 1.25 mg estradiol hemihydrate 1 mg film-coated tablets containing estradiol hemihydrate 1 mg (white tablets) and estradiol hemihydrate and Elleste Solo™ MK 40 mg transfermal patch containing 1.25 mg estradiol hemihydrate 2 mg (pransfermal patch containing 1.25 mg estradiol hemihydrate 2 mg (pransfermal patch containing 1.25 mg estradiol hemihydrate 2 mg (pransfermal patch containing 1.25 mg estradiol hemihydrate 2 mg mestadol 2 mg mestadol hemihydrate 2 mg mestadol hemihydrate 2 mg mestadol 2 mg me progestogen for at least 12 days per cycle in non-hysterectomised women. Investigate breakthrough bleeding. An increased risk of breast cancer has been reported that is dependent on the length of treatment. HTC can increase the density of mammorgraphic images which may affect radiological detection of breast cancer. HTC is associated with an increased relative risk of venous thromboembolism VTE) or pulmonary embolism (PE, Risk factors include personal or family history of thrombosis, severe deseity, systemic luque erythematouss, immobilisation, major trauma and major surgery soft der disconsistance in the properties of the properties of the descending surgery. There is an increased risk of cardiovascular morbidity during the first year of use of HTL HTC is associated with an up to 1.5-foil increased risk of strike. Long term use of estrogens in women has been associated with an increased risk of orarian cancer. Estrogens may cause fluid retention. Women with pre-existing hyper-triglycendemia should be followed closely (risk of pancreatitis). Certain endocrine tests may be affected. No evidence for improvement in cognitive function. Increased risk of gallibateder disease. Liver tumours leading to intra-abdominal haemorrhage have been reported. Patients with rare hereatilary disorders of

galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. Eleste "Duet 2 mg film-coated tablets and Elieste" Solo 2 mg film-coated tablets contain sunset yellow colouring (E110) which can cause allergic reactions. May interact with other medicines. Please refer SmPC for further information. Interaction with other medicinal products: The metabolism of estrogens and progestogens may be increased by concomitant uses of substances known to induce drug-metabolising newnymes, specifically cyclorhorne P405, such as anticonvulsants (e.g. phenodarbital), phenytion, carbamazepine) and anti-infectives (e.g. rifampicin, rifabutin, nevirapine, efavirenz). Ritonavir, telaprevir, nefilmavir and herbal preparations containing St.Johns Wort may induce the metabolism of estrogens and progestogens. Please refer SmPC for further information. Pregnancy and lactations Not recommended. If pregnancy occurs, withdraw treatment immediately. Effects an ability to drive and use machines. No influence on the ability to drive and use machines. Wheterabolism de effects. Very common sofie effects [1-110], Headacher, breast pair and tenderness, dysmemorthee, mensitual dissortance of the effects of the programment of the effects. Very common sofie effects [1-110], Headacher, breast pair and tenderness, dysmemorthee, mensitual dissortance in the effects of the effects o

Legal Category: POM Marketing Authorisati

Legal Category: POM Marketing Authorisation Numbers and Basic NHS Price: Elleste Solo™ 1mg; PL 46302/0169; 3 x 28 film-coated tablets £5.06. Elleste Solo™ 2mg; PL 46302/0167; 8 patches £5.19. Elleste Solo™ 2mg; PL 46302/0167; 8 patches £5.19. Elleste Solo™ MN 8 mog; PL 46302/0168; 8 patches £5.19. Elleste Solo™ MN 8 mog; PL 46302/0168; 8 patches £5.19. Elleste Solo™ 2mg; PL 46302/0168; 8 patches £5.19. Elleste Dute™ 1mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste Dute™ 2mg; PL 46302/0166; 3 x 28 film-coated tablets £3 22. Elleste

Date of Last Revision: October 2020 Veeva Reference: ELL-2020-0087

The SmPC for this product, including adverse reactions, precautions, contra-indications, and method of use can be found at http://www.mhra.gov.uk/Safelyinformatio MedicinesinformationSPCandPlus/index.htm and from Mylan Medical Information, Building 4, Trident Place, Hatfield Business Park, Mosquito Way, Hatfield, Hertfordshir ALT 199U, phone on 07170 853000, Email: Info@mylan.co.uk

Adverse Drug Reactions 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 be reported to UK Pharmacovigilance, Mylan, Building 4, Trident Place, Hatfield Business Park, Mosquito Way, Hatfield, Hertfordshire, AL10 9UL, on phone no. +44 (0) 800 121 8267, Email: ukpharmacovigilance@mylan.com



