HRT Formulary Treatment Options

NHS Wiltshire Clinical Commissioning Group

NHS Bath and North East Somerset Clinical Commissioning Group

See the British Menopause Society (BMS) website for further advice on the following:

For healthcare professionals: NICE: Menopause Diagnosis and Management from Guideline to Practice – Guideline Summary ; HRT Guide

For women: Women's Health Concern factsheets https://www.womens-health-concern.org/help-and-advice/factsheets/ ; Pt info leaflets: http://www.menopausematters.co.uk/oestrogens.php

TRANSDERMAL TREATMENT OPTIONS

Oestrogen Only
(no uterus)
1 prescription charge

- **Evorel** patches . Change TWICE per week
  25, 50, 75, 100mcg estradiol
- **Estradot** patches. Change TWICE per week
  25, 37.5, 50, 75, 100mcg estradiol
- **Oestrogel** 0.06% oestradiol gel, 0.75mg estradiol per measure, 2 measures= standard regime

Sequential combined
(uterus - monthly bleed)
2 prescripton charges

- **Evorel Sequi** patches
  Change TWICE per week
  50mcg estradiol + 170mcg norethisterone

Continuous combined
(uterus - no bleed)
1 prescription charge

- **Evorel-Conti** patches
  Change TWICE per week
  50mcg estradiol + 170mcg norethisterone

Utrogestan 100mg oral capsules*. Micronised progesterone for progestogenic opposition of oestrogen in women with intact uterus where patient is at increased risk of VTE or breast cancer and unable to tolerate an alternative progestogen (either oral or patch combined product) and has declined LNG-IUS (see overleaf).

The transdermal route should be considered as first choice route of estradiol administration, particularly in women with risk factors, including those with a BMI >30 kg/m2. Transdermal administration of estradiol is unlikely to increase the risk of VTE or stroke above that in non-users and is associated with a lower risk compared with oral administration of estradiol. See NICE menopause guidance and BMS recommendations on HRT for further details.

ORAL TREATMENT OPTIONS

Oestrogen Only
(no uterus)
1 prescription charge

- **Elleste Solo -** 1mg or 2mg estradiol
- **Premarin** - 0.625mg or 1.25mg conjugated oestrogen

Older women (60yrs plus) may require less oestrogen as found in the following low dose preparations:

- Oestrogen only
  - Evorel 25 patch 25mcg/24hrs
  - Oestrogel (estradiol 0.75mg per pump. 1 pump = low dose)
  - Premarin 300mcg (conjugated oestrogen)
- Continuous combined
  - Femoston Conti low dose (0.5mg estradiol + 2.5mg dydrogesterone)
  - Kliovance (estradiol 1mg and norethisterone acetate 500mcg)
  - Premique low dose 300mcg (conjugated oestrogen + medroxyprogesterone acetate 1.5mg)

Progestogenic side effects: *e.g. PMS type symptoms, Breast tenderness, Lower abdominal pain, Backache, Depressed mood, Acne/greasy skin, headache*

Sequential combined
(uterus - monthly bleed)
2 prescripton charges

- **Elleste Duet**
  1mg or 2mg estradiol + 1mg norethisterone
- **Progestogenic side effects: Femoston**
  1mg or 2mg estradiol + dydrogesterone 10mg

Modifiable lifestyle factors - *ensure these are addressed:*
- Women should be advised to eat a healthy balanced diet, to maintain a healthy BMI, to ensure they eat sufficient dietary calcium and undertake regular weight-bearing exercise.
- Ensure that a discussion occurs with the patient in order to address stopping smoking, reducing alcohol intake.
- Ensure optimum treatment of conditions such as diabetes and blood pressure as applicable .

Urogenital Atrophy
Ovestin (0.1% estriol vaginal cream)
or Vagifem (10mcg vaginal tablet)
To initiate (reducing course):
- Use once a night for 14 nights
- Then alternate nights for 14 nights †
- Twice per week thereafter
- Continue while therapeutic benefit

Or Estring (7.5mcg /24hrs vaginal delivery system) 3 month device

Continuous combined
Women should have had NO periods for 2 yrs if <50yrs old, 1 year if >50 yrs old or be 54
(uterus - no bleed)
1 prescription charge

- **Kliofem**
  2mg estradiol + 1mg norethisterone
- **Elleste Duet Conti**
  2mg estradiol + 1mg norethisterone
- **Tibolone (Livial)**
  (See text overleaf for full guidance)

Progestogenic side effects:
Femoston Conti ‡
1mg estradiol + 5mg dydrogesterone
OR Femoston Conti (low dose) ‡
0.5mg estradiol + 2.5mg dydrogesterone (lowest effective dosed HRT preparation)
OR Indivina
1mg or 2mg estradiol + 2.5mg or 5mg medroxyprogesterone acetate

*200 mg OD on days 15–26 of each 28-day cycle (sequential combined) OR 100 mg OD on days 1–25 of each 28-day cycle (continuous combined).
†This is an extra step which allows slower reduction than the license, as recommended by local specialists. ‡ Dydrogesterone is useful if patient has had side effects with other progestogens. If patient has menopausal symptoms (e.g. hot flushes) on this preparation, the estradiol may need increasing to 2mg by adding in a 1mg elleste solo tablet.

Medicines Management Team
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Additional information

Levonorgestrel Intrauterine System (LNG-IUS) (Mirena® Coil)

- Can be a useful treatment option if progestogenic side effects are an issue with systemic treatment.
- It is licensed as a contraceptive, to treat menorrhagia and to give endometrial protection as part of HRT.
- Once in place, if being used as part of a HRT regime, additional oestrogen HRT is needed as a tablet, patch or topical gel.
- In a HRT regime, Mirena® has a 4 year license. Other LNG-IUS products (Jaydess® and Levosert®) are not licensed for use as part of a HRT regime.
- Irregular bleeding is common in the first few months of use.
- An IUS should only be inserted after an appropriate gynaecological/menstrual history and after appropriate assessment/investigation.
- Once in-situ, periods may be reduced by >95% by 6 months and approximately 20% of users will be fully amenorrheic.

Tibolone (gonadomimetic)

- Tibolone is a synthetic steroid with oestrogenic, progestogenic and androgenic activity so is a type of continuous combined HRT and so this is a no bleed preparation. Because of its androgenic activity, it has been shown to have a positive effect on libido.
- Tibolone has been shown to be as/or more effective than oestradiol in controlling menopausal symptoms.
- Although 85% of Tibolone users are amenorrhoeic, there is an 11% chance of irregular bleeding, which may require gynaecological investigation.
- Long-term use of tibolone is thought to be associated with a similar increased risk of breast cancer to that of estrogen alone, which is less than that of estrogen plus progestogen.

Herbal Medicines

- There are non-hormonal alternatives for menopause treatment, but none are as effective as HRT. There is some evidence that isoflavones or black cohosh may relieve vasomotor symptoms, however long term safety and efficacy has not been established.
- These are therefore not available on the NHS and should not be prescribed on a FP10. See www.menopausematters/remedies.php for info.

Testosterone

- The BMS recommend testosterone as a treatment option for loss of libido, but no licensed treatments for women are available in the UK.
- Testosterone for this unlicensed indication is TLS RED so secondary care initiation and continuation [RUH ONLY]. Alternatively, patients can pursue this option privately.

Follow-up/Annual Review/Duration of treatment

- Follow up after 3/12 of treatment to assess effect, enquire about side effects & bleeding pattern.
- Unscheduled vaginal bleeding is a common side-effect of HRT within the first 3 months of treatment, but should be reported promptly if it occurs after the first 3 months (see recommendations on endometrial cancer in the NICE guideline on suspected cancer (reference section below)).
- At annual review check efficacy, side-effects, ensure correct dose, optimal route of delivery and compliance. Also check:
  - Pros & cons of continuing HRT, increased risk of breast cancer with long-term use, do benefits outweigh risks?
  - Check blood pressure, encourage breast awareness/attendance of screening mammography
  - Assess osteoporosis risk & consider the need for investigation/monitoring
  - Ensure cervical screening is up to date
  - Enquire about symptoms of urogenital atrophy
- Duration of treatment:
  - Most guidelines recommend that HRT for around 5 years in women as they enter menopause (i.e. in late 40's/early 50's) is likely to confer benefit and not harm
  - There are no reasons to place mandatory limitations on duration of HRT, which should be decided with a well informed woman & her heath professional, dependent on specific goals & objective estimate of risks & benefits.
  - Withdrawing HRT slowly may reduce the chance of recurrent symptoms. It should be noted that 5% of women will have hot flushes for life.

Contra-indications - see http://www.medicines.org.uk/emc

- See individual products Summary of Product Characteristics for full information

- Porphyria
- Undiagnosed abnormal vaginal bleeding
- Suspected or active breast or endometrial cancer
- Dubin-Johnson and Rotor syndromes (or monitor closely)
- Active liver disease with abnormal liver function tests.
- Previous idiopathic or current VTE unless the woman is already on anticoagulant
- Pregnancy
- Oestrogen sensitive cancer
- Untreated endometrial hyperplasia
- Active thromboembolic disorder or acute-phase myocardial infarction.
- Hypersensitivity to any of the active constituents or excipients
- Untreated hypertension
- Undiagnosed genital bleeding
- Porphyria cutanea tarda

Risks of HRT

- The NICE clinical guideline on menopause from 2015 is the best source to look at the risks of long-term HRT use, in order to explain such risks to your patient. See section 1.5 (p11) and tables 1 to 4: https://www.nice.org.uk/guidance/ng23

References:

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