Guidance on the Management of Menopause in Primary Care

Menopause is a biological stage in a woman’s life when menstruation ceases permanently due to the loss of ovarian follicular activity. The average age of the natural menopause is 51 years, but can occur much earlier or later. Menopause occurring before the age of 45 is called early menopause and before the age of 40 is premature menopause. Late menopause may also occur, but by the age of 54 years 80% of women will have stopped having periods. See appendix 4 for further definitions.

This guideline is aimed at assisting GPs in the diagnosis and treatment of menopause. Practitioners should adopt an individualised approach at all stages of diagnosis, investigation and management of menopause. These recommendations are based on NICE guidance NG23 Menopause: diagnosis and management.

Diagnosis of menopause

- Testing of follicle-stimulating hormone
  - Follicle-stimulating hormone (FSH) fluctuates considerably over short periods of time during the years leading up to menopause and so blood levels are not a helpful addition to what is a clinical diagnosis.
  - In younger women, FSH tests should not be used to diagnose menopause in those taking combined oestrogen and progestogen contraception or high-dose progestogen because these affect FSH measurements.
  - Consider using a FSH test to diagnose menopause only in women:
    - Aged 40-45 years with menopausal symptoms, including a change in their menstrual cycle.
    - Aged under 40 years in whom menopause is suspected.

- In otherwise healthy women over 45 years with menopausal symptoms, the diagnosis of menopause should be without laboratory tests in the following:
  - Perimenopause (based on vasomotor symptoms and irregular periods).
  - Menopause in women who have not had a period for at least 12 months and are not using hormonal contraception.
  - Menopause (based on symptoms in women without a uterus).

- Take into consideration that it may be difficult to diagnose menopause in women who are taking hormonal treatments, for example for the treatment of heavy periods.

Management of menopause

- Adopt an individualised approach at all stages of diagnosis, investigation and management of menopause.

- Pharmacological management
  - Women should be prescribed Hormone Replacement Therapy (HRT) only after being involved in discussions and being enabled to make informed decisions about their care.
  - Inform patients that non-hormonal alternatives are not as effective as HRT. Refer patients to the references in the patient resource section of this document for more information.
  - Allow three months on any treatment before making any changes as side effects often subside with use.
  - Women stopping HRT should be offered the choice of gradually reducing or immediately stopping treatment.
There is no clear evidence that Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs) ease low mood in menopausal women without a diagnosis of depression.

Patients should be informed of the importance of keeping up to date with nationally recommended health screening.

See appendix 3 for details on diagnosis and management of premature ovarian insufficiency.

**General prescribing advice on hormone replacement therapy**

- Do not use HRT as first line treatment in asymptomatic postmenopausal women for primary prevention of osteoporosis.

**Risks versus benefits**

- For the treatment of menopausal symptoms, the benefits of short-term HRT outweigh the risks in the majority of women, especially in those aged under 60 years. Experience of treating women over 65 years with HRT is limited. See appendix 1 for more information.
- The risks and benefits of long-term use of HRT should be assessed for each woman at regular intervals. See appendix 2 for more information.
- The risk of endometrial hyperplasia and carcinoma is increased when systemic oestrogens are administered alone for prolonged periods.
- HRT does not prevent coronary heart disease or protect against a decline in cognitive function and it should not be prescribed for these purposes. See appendix 2 for more information.

**Types of hormone replacement therapy**

- **Unopposed oestrogen** – suitable for continuous use in women without a uterus.
- **Combined oestrogen + progestogen** – for women with a uterus. Oestrogen relieves typical menopausal symptoms such as hot flushes. Progestogens are added to reduce the increased risk of endometrial hyperplasia and cancer which occurs with unopposed oestrogen.
  - **Sequential combined HRT** mimics the normal menstrual cycle with withdrawal bleed at the end of each cycle. It is used in perimenopause and during the first year or two after menopause.
  - **Continuous combined HRT** contains continuous progestogen with oestrogen, so there is no withdrawal bleed. It is not suitable for perimenopausal women or within 12 months of the last menstrual period. Usually, women start on sequential combined HRT and change to continuous combined HRT later.
  - **Tibolone** is a synthetic steroidal compound with oestrogenic, progestogenic and androgenic activity. It is taken continuously and there is no withdrawal bleed.

**Treatment choice and dosing**

- The type of HRT most suited to a woman will depend on a variety of factors, including her symptoms, her stage in the menopausal process, and whether or not she has had a hysterectomy.
- In terms of oestrogenic activity, natural oestrogens have a more appropriate profile for hormone replacement therapy than synthetic oestrogens
  - Natural oestrogens: estradiol (oestradiol), estrone (oestrone) and estriol (oestriol)
  - Synthetic oestrogens: ethinylestradiol (ethinyloestradiol) and mestranol.
- Use lowest effective dose of HRT to control menopausal symptoms.
- Oestrogen therapy is given cyclically or continuously for a number of gynaecological conditions.
• Tablets are more cost-effective.
• Transdermal patches are associated with fewer risks than oral HRT, but may have the added problem of detachment from the skin and local side effects. The transdermal route may be advantageous for women with diabetes, history of venous thromboembolism (VTE) and also those with thyroid disorders. In addition, transdermal HRT is preferable to those women with a history of migraine or gallbladder problems.
• Consider the transdermal route if:
  ▪ There is a clinical need to avoid first-pass metabolism of oestrogens (e.g. liver disease or an increased risk of venous thrombosis).
  ▪ A woman cannot tolerate tablets or expressed a strong preference for a non-oral preparation.
• Mirena® (intrauterine delivery system) provides contraception, and can be used in combination with oral or transdermal unopposed oestrogen preparations without additional exogenous progestogens. Mirena® should only be inserted by an appropriately trained practitioner and will be effective for 4 years.

See flowchart for general advice on prescribing, please note this does not cover Premature Ovarian Insufficiency.

**Review and referral**

➢ Review each treatment for short-term menopausal symptoms.

➢ Review at 3 months to assess efficacy and tolerability. Review annually thereafter unless there are clinical indications for an earlier review (such as treatment ineffectiveness, side effects or adverse events). Blood pressure and weight should be checked. Consider alternative osteoporosis treatments.

➢ Consider referring women to a healthcare professional with expertise in menopause if:
  • They have menopausal symptoms and contraindications to HRT (e.g. history of breast cancer)
  • There is uncertainty about the most suitable treatment options for their menopausal symptoms.

**Key counselling points**

➢ Reinforce the importance of adherence to medication.

➢ Remind women at the perimenopausal stage that HRT is not a contraceptive and that contraceptive precautions are still necessary.

➢ Inform women of the bleeding pattern that will occur with the chosen regime and emphasise that irregular bleeding is common in the first 3-6 months.

➢ Complementary therapies and unregulated preparations
  o Explain to patients that the safety and efficacy of unregulated compounded bioidentical are unknown.
  o There is some evidence that isoflavones or black cohosh may relieve vasomotor symptoms, however, multiple preparations are available and their safety is uncertain. Preparations may vary and interactions with other medicines have been reported.
  o Explain to patients that these preparations are not available on NHS prescriptions.
Management of side effects

Table 1. Management of oestrogenic and progestogenic side effects (adapted from Menopause Matters)

<table>
<thead>
<tr>
<th>Oestrogenic side effects</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast symptoms: breast tenderness, enlargement</td>
<td>If appropriate try a lower dose of oestrogen. Over-the-counter evening primrose oil or starflower oil may be of benefit. Note these preparations are not to be prescribed on NHS prescriptions.</td>
</tr>
<tr>
<td>Gastrointestinal symptoms: bloating, nausea</td>
<td>Take with food or consider an alternative route.</td>
</tr>
<tr>
<td>Other symptoms: leg cramps, headache</td>
<td>Change oestrogen type or route.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Progestogenic side effects</th>
<th>Management</th>
<th>Alternative preparations</th>
</tr>
</thead>
</table>
| Headache, depressed mood, PMS type symptoms, breast tenderness, lower abdominal pain, acne/greasy skin. | Change progestogen type | Testosterone derived – Norethisterone, Norgestrol or Levonogestrel  
Progestosterone derived - Medroxyprogesterone |
|                           | Change route | Progestogen by Mirena® or vaginal gel avoids side effects.                                |
|                           | Change drug class | If postmenopausal, change to continuous combined or tibolone. These avoid symptoms of progestogen fluctuation. |

Patient resources

Use materials such as NICE’s information for the public, NHS choices and the Women’s Health Concern leaflet to help support women to make informed decisions when advising them about HRT. Other useful resources can also be found on the Menopause Matters website (http://www.menopausematters.co.uk).

References


5. MIMS available at http://www.mims.co.uk [accessed 30/06/2017].
City and Hackney menopause pathway

**Menopause assessment**
1. Symptoms
2. Lifestyle
3. Medical Hx
4. Risk/benefit analysis

**Decision to start HRT**
- Systemic HRT
- Perimenopause

**Urogenital symptoms only**
- Yes

**Without uterus**
- Oestrogen only preparation
- Select appropriate formulation for patient
- Symptoms persist at 3 months
- Increase dose gradually
- Symptoms persist or other problems occur at 6 months
- Refer to gynae clinic

**With uterus**
- Systemic HRT
- Perimenopause
- Select appropriate formulation for patient
- After 2-5 years on sequential HRT OR >54
- Select appropriate formulation for patient
- Post-menopause >54 and / 1 year since last bleed
- Low dose continuous combined HRT
- Symptoms persist at 3 months
- High dose HRT
- Symptoms persist or irregular bleeding at 6 months
- Refer to gynae clinic

**Information and Advice**
Give information to menopausal women and their family members or carers (as appropriate) that includes:
- An explanation of the stages of menopause
- Common symptoms and diagnosis
- Lifestyle changes and interventions that could help general health and wellbeing
- Benefits and risks of treatments for menopausal symptoms
- Short and long-term health implications of menopause

**Low dose vaginal oestrogens e.g.**
1. Ovestin (0.1% estriol vaginal cream)
2. Vagifem (10 mcg vaginal tablet)

Explain to women that symptoms come back when treatment is stopped.

**Lifestyle advice to control symptoms**

**HOT FLUSHES and NIGHT SWEATS:**
- Taking regular exercise and losing weight (if applicable) may reduce the severity and frequency of flushes.
- Wearing lighter clothing, sleeping in a cooler room, reducing stress, and avoiding possible triggers (such as spicy foods, caffeine, smoking and alcohol) may also be helpful in reducing these symptoms.

**SLEEP DISTURBANCES:**
- Avoiding exercise late in the day and maintaining a regular bedtime can improve sleep.

**MOOD AND ANXIETY DISTURBANCES:**
- Adequate sleep, regular physical activity, and relaxation exercises may help.

**COGNITIVE SYMPTOMS:**
- Exercise and good sleep hygiene may improve subjective cognitive symptoms.

**Unopposed oestrogen (1 prescription charge)**
- 1st line oral standard strength: Elleste® Solo (all strengths)
- 2nd line oral standard strength: Premarin® (625 microgram and 1.25 mg)
- Low strength oestrogen: Premarin® (300 microgram)
- Patch: Evorel® (all strengths)

**Sequential combined (2 prescription charges)**
- 1st line oral standard strength: Elleste® Duet (all strengths)
- 2nd line oral standard strength: Clinorette® or Cycloprogynova®
- Low strength oestrogen: N/A
- Patch: Evorel® Sequi

**Continuous combined (1 prescription charge)**
- 1st line oral standard strength: Kliofem®
- 2nd line oral standard strength: Kliovance®
- Low strength oestrogen: Premique® Low Dose
- Patch: Evorel® Conti

Adjunctive progestogen to be considered in women with previous endometriosis, as endometrial foci may remain despite hysterectomy. Provera® 10 mg daily for the last 14 days of each 28-day oestrogen HRT cycle.
Table 2. Oral hormone replacement therapy products (prices according to MIMS and BNF, accessed Jun 2017)

<table>
<thead>
<tr>
<th>Brand</th>
<th>Active ingredients</th>
<th>Form</th>
<th>Cost/28 days</th>
<th>Prescribing notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sequential combined - oestrogen + progestogen</strong>&lt;br&gt;Use in women with a uterus in perimenopause and during the first year or two after menopause. Mimics the normal menstrual cycle with monthly bleed.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elleste-Duet® 1-mg</td>
<td>Estradiol 1mg + Norethisterone acetate 1mg</td>
<td>Tablets</td>
<td>£3.07</td>
<td></td>
</tr>
<tr>
<td>Elleste-Duet® 2-mg</td>
<td>Estradiol 2mg + Norethisterone acetate 1mg</td>
<td>Tablets</td>
<td>£3.07</td>
<td>Menopausal symptoms and osteoporosis prophylaxis.</td>
</tr>
<tr>
<td>Cyclo-progynova*</td>
<td>Estradiol valerate 2mg + Norgestrel 500microgram</td>
<td>Tablets</td>
<td>£3.11</td>
<td></td>
</tr>
<tr>
<td>Clinorette*</td>
<td>Estradiol 2mg + Norethisterone acetate 1mg</td>
<td>Tablets</td>
<td>£3.08</td>
<td></td>
</tr>
<tr>
<td><strong>Continuous combined – oestrogen + progestogen</strong>&lt;br&gt;Use in women with a uterus. Not suitable for perimenopausal women or within 12 months of last menstrual period. Cycle free (no monthly bleed).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Premique® Low dose</td>
<td>Conjugated oestrogens 300microgram Medroxyprogesterone acetate 1.5mg</td>
<td>Tablets</td>
<td>£2.17</td>
<td></td>
</tr>
<tr>
<td>Kliofem®</td>
<td>Estradiol 2mg + Norethisterone acetate 1mg</td>
<td>Tablets</td>
<td>£3.81</td>
<td>If changing from cyclical HRT, begin treatment at the end of scheduled bleed.</td>
</tr>
<tr>
<td>Kliovance*</td>
<td>Estradiol 1mg Norethisterone acetate 500microgram</td>
<td>Tablets</td>
<td>£4.40</td>
<td></td>
</tr>
<tr>
<td>Elleste-Duet Conti®</td>
<td>Estradiol 2mg + Norethisterone acetate 1mg</td>
<td>Tablets</td>
<td>£5.67</td>
<td>If changing from cyclical HRT, start treatment the day after finishing oestrogen plus progestogen phase.</td>
</tr>
<tr>
<td>Nuvelle® Continuous</td>
<td>Estradiol 2mg + Norethisterone acetate 1mg</td>
<td>Tablets</td>
<td>£6.33</td>
<td></td>
</tr>
<tr>
<td><strong>Unopposed oestrogen continuous</strong>&lt;br&gt;Suitable for use in women without a uterus. Add cyclical progestogen for 12–14 days of each cycle in women with a uterus.</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Premarin® 300microgram</td>
<td>Conjugated oestrogens 300microgram</td>
<td>Tablets</td>
<td>£2.02</td>
<td>In women with previous endometriosis, endometrial foci may remain despite hysterectomy and the addition of a progestogen should be considered. Premarin® 625microgram and 1.25mg are suitable for osteoporosis prophylaxis.</td>
</tr>
<tr>
<td>Premarin® 625microgram</td>
<td>Conjugated oestrogens 625microgram</td>
<td>Tablets</td>
<td>£1.34</td>
<td></td>
</tr>
<tr>
<td>Premarin® 1.25mg</td>
<td>Conjugated oestrogens 1.25mg</td>
<td>Tablets</td>
<td>£1.19</td>
<td></td>
</tr>
<tr>
<td>Elleste-Solo® 1-mg</td>
<td>Estradiol 1mg</td>
<td>Tablets</td>
<td>£1.69</td>
<td></td>
</tr>
<tr>
<td>Elleste-Solo® 2-mg</td>
<td>Estradiol 2mg</td>
<td>Tablets</td>
<td>£1.69</td>
<td></td>
</tr>
<tr>
<td><strong>Continuous mixed oestrogenic, progestogenic and weak androgenic activity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Livial®</td>
<td>Tibolone</td>
<td>Tablets</td>
<td>£10.36</td>
<td>Unsuitable for use in premenopause (unless being treated with gonadotrophin-releasing hormone analogue) and as (or with) an oral contraceptive; also unsuitable for use within 12 months of last menstrual period (may cause irregular bleeding). If transferring from cyclical HRT, start at end of regimen; if transferring from continuous-combined HRT, start at any time.</td>
</tr>
<tr>
<td><strong>Adjunctive progestogen</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Provera® 10mg</td>
<td>Medroxyprogesterone acetate 10mg</td>
<td>Tablets</td>
<td>£3.46</td>
<td>Use during the last 14 days of each 28-day oestrogen HRT cycle.</td>
</tr>
</tbody>
</table>
### Table 3. Oral hormone replacement therapy products being discontinued

<table>
<thead>
<tr>
<th>Brand</th>
<th>Active ingredients</th>
<th>Form</th>
<th>Alternative brands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premique® (continuous combined)</td>
<td>Conjugated oestogens 625 microgram Medroxyprogesterone acetate 1.5 mg</td>
<td>Tablets</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; line – Kliofem&lt;sup&gt;®&lt;/sup&gt; 2&lt;sup&gt;nd&lt;/sup&gt; line – Kliovance&lt;sup&gt;®&lt;/sup&gt;</td>
</tr>
<tr>
<td>Prempak-C® 0.625 Calendar pack (sequential combined)</td>
<td>Conjugated oestrogens 625 microgram Norgestrel 150 microgram</td>
<td>Tablets</td>
<td>Elleste-Duet&lt;sup&gt;®&lt;/sup&gt; 2 mg</td>
</tr>
<tr>
<td>Prempak-C 1.25 Calendar pack (sequential combined)</td>
<td>Conjugated oestrogens 1.25 mg Norgestrel 0.15 mg</td>
<td>Tablets</td>
<td>Elleste-Duet&lt;sup&gt;®&lt;/sup&gt; 2 mg</td>
</tr>
</tbody>
</table>

### Table 4. Hormone replacement therapy patches (prices according to MIMS and BNF, accessed Jun 2017)

<table>
<thead>
<tr>
<th>Brand</th>
<th>Active ingredients</th>
<th>Form</th>
<th>Dose</th>
<th>Cost per pack</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Use in women with a uterus</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evorel® Conti (continuous combined)</td>
<td>Estradiol approx. 50 micrograms/24 hours and norethisterone acetate approx. 170 micrograms/24 hours.</td>
<td>Patches</td>
<td>1 patch to be applied twice weekly continuously.</td>
<td>8-patch pack = £13.00</td>
</tr>
</tbody>
</table>
| Evorel® Sequi combination pack (sequential combined) | Evorel® - Estradiol approx. 50 micrograms/24 hours.  
Evorel® Conti - estradiol approx. 50 micrograms/24 hours and norethisterone acetate approx. 170 micrograms/24 hours. | 2 different patches | 1 Evorel® 50 patch to be applied twice weekly for 2 weeks, starting within 5 days of onset of menstruation (or at any time if cycles have ceased or are infrequent), followed by 1 Evorel® Conti patch twice weekly for 2 weeks; subsequent courses are repeated without interval. | 8-patch pack = £11.09 |
| **Unopposed oestrogen continuous – use in women without a uterus** |                   |      |                                                                      |               |
| Evorel® 25 | Estradiol, ‘25’ patch (releasing approx. 25 micrograms/24 hours) | Menopausal symptoms and osteoporosis prophylaxis. | 1 patch to be applied twice weekly continuously starting within 5 days of onset of menstruation (or at any time if cycles have ceased or are infrequent), with cyclical progestogen for 12–14 days of each cycle in women with a uterus; therapy should be initiated with Evorel 50 patch; subsequently adjust according to response; dose may be reduced to Evorel 25 patch after first month if necessary for menopausal symptoms | 8-patch pack = £3.42 |
| Evorel® 50 | Estradiol, ‘50’ patch (releasing approx. 50 micrograms/24 hours) | | | 8-patch pack = £3.88 |
| Evorel® 75 | Estradiol, ‘75’ patch (releasing approx. 75 micrograms/24 hours) | | | 8-patch pack = £4.12 |
| Evorel® 50 | Estradiol, ‘100’ patch (releasing approx. 100 micrograms/24 hours) | | | 8-patch pack = £4.28 |
Table 5. Intravaginal hormone replacement therapy products (prices according to MIMS and BNF, accessed Jun 2017)

<table>
<thead>
<tr>
<th>Brand</th>
<th>Active ingredients</th>
<th>Form</th>
<th>Dose</th>
<th>Cost/pack</th>
<th>Prescribing notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estring®</td>
<td>Estradiol approx. 7.5 micrograms/24 hours</td>
<td>Vaginal ring</td>
<td>To be inserted into upper third of vagina and worn continuously; replace after 3 months; max. duration of continuous treatment is 2 years.</td>
<td>1-ring pack = £31.42</td>
<td>Postmenopausal urogenital conditions (not suitable for vasomotor symptoms or osteoporosis prophylaxis).</td>
</tr>
<tr>
<td>Ovestin® 0.1%</td>
<td>Estriol 0.5mg per 1 applicatorful</td>
<td>Intravaginal cream with applicator</td>
<td>Insert 1 applicatorful daily for 2-3 weeks and then reduce to 1 applicatorful twice a week.</td>
<td>15g = £4.45</td>
<td>Effect on latex condoms and diaphragms not yet known. Discontinue every 2-3 months for 4 weeks to assess need for further treatment.</td>
</tr>
<tr>
<td>Gynest® 0.01%</td>
<td>Estriol 0.5mg per 1 applicatorful</td>
<td>Intravaginal cream with applicator</td>
<td>Insert 1 applicatorful daily, preferably in the evening until improvement occurs, and then reduce to 1 applicatorful twice a week.</td>
<td>80g = £4.67</td>
<td>Contains arachis (peanut) oil. Attempts to discontinue should be made at 3–6 month intervals with re-examination.</td>
</tr>
<tr>
<td>Vagifem®</td>
<td>Estradiol 10 microgram</td>
<td>Vaginal tablets with applicators</td>
<td>Insert 1 vaginal tablet daily for 2 weeks then reduce to 1 tablet twice weekly</td>
<td>24-applicator pack = £16.72</td>
<td>No evidence of damage to latex condoms and diaphragms.</td>
</tr>
<tr>
<td>Mirena®</td>
<td>Levonorgestrel 20 micrograms/24 hours</td>
<td>Intra-uterine system</td>
<td>Insert during last days of menstruation or withdrawal bleeding or any time if amenorrhoeic, effective for 4 years.</td>
<td>1 = £88.00</td>
<td>Prevention of endometrial hyperplasia during oestrogen replacement therapy. No monthly bleeds, provides contraception.</td>
</tr>
</tbody>
</table>
Appendix 1: Management of short-term menopausal symptoms

Treatment should be adapted as needed according to a woman’s symptoms. These recommendations do not cover Premature Ovarian Insufficiency (POI).

Vasomotor symptoms

- Offer women HRT for vasomotor symptoms after discussing with them the short-term (up to 5 years) and longer-term benefits and risks.

- Do not routinely offer Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs) or clonidine as first-line treatment for vasomotor symptoms alone.

- There is some evidence that isoflavones or black cohosh may relieve vasomotor symptoms, however multiple preparations are available and safety is uncertain and interactions with other medicines have been reported.

Psychological symptoms

- Consider HRT to alleviate low mood that arises as a result of the menopause.

- Consider Cognitive Behavioural Therapy (CBT) to alleviate low mood or anxiety that arise as a result of the menopause.

- There is no clear evidence that SSRIs or SNRIs ease low mood in menopausal women who have not been diagnosed with depression.

Altered Sexual function

- Consider testosterone supplementation for menopausal women with low sexual desire if HRT alone is not effective. If offered, it should be prescribed by specialists after obtaining and documenting informed consent.

Urogenital atrophy

- Vaginal oestrogen:
  - Should be offered to women with urogenital atrophy (including those on systemic HRT) and continue treatment for as long as needed to relieve symptoms.
  - Should be considered in women with urogenital atrophy in whom systemic HRT is contraindicated, after seeking advice from a healthcare professional with expertise in menopause.

- If vaginal oestrogen does not relieve symptoms of urogenital atrophy, consider increasing the dose after seeking advice from a healthcare professional with expertise in menopause.
Explain to women with urogenital atrophy that symptoms often come back when treatment is stopped, adverse effects from vaginal oestrogen are very rare and women should report unscheduled vaginal bleeding to their GP.

Advise women with vaginal dryness that moisturisers and lubricants can be used alone or in addition to vaginal oestrogen.

Do not offer routine monitoring of endometrial thickness during treatment for urogenital atrophy.

**Women with or at high risk of breast cancer**

See section 1.13 of the NICE guideline on [early and locally advanced breast cancer](#) and 1.7 of the NICE guideline on [familial breast cancer](#).

- Offer menopausal women with, or at high risk of, breast cancer:
  - Information on all available treatment options.
  - Information that the SSRIs paroxetine and fluoxetine should not be offered to women with breast cancer who are taking tamoxifen.
  - Referral to a healthcare professional with expertise in menopause.

**Appendix 2: Long-term risks of hormone replacement therapy**


For absolute rates of risk for different types of HRT compared with no HRT refer to NICE guidelines: [NICE guidance NG23 Menopause: diagnosis and management section 1.5](#).

**Venous Thromboembolism**

- The risk of venous thromboembolism (VTE) is increased by oral HRT compared with baseline population risk.

- The risk associated with transdermal HRT given at standard therapeutic doses is no greater than baseline population risk.

- Consider transdermal rather than oral HRT for menopausal women who are at increased risk of VTE, including those with a BMI over 30 kg/m².

- Consider referring menopausal women at high risk of VTE (for example, those with a strong family history of VTE or a hereditary thrombophilia) to a haematologist for assessment before considering HRT.

**Cardiovascular disease**

- HRT does not increase cardiovascular disease risk when started in women aged under 60 years and does not affect the risk of dying from cardiovascular disease.
Be aware that the presence of cardiovascular risk factors is not a contraindication to HRT as long as they are optimally managed.

The baseline risk of coronary heart disease and stroke for women around menopausal age varies from one woman to another according to the presence of cardiovascular risk factors.

HRT with oestrogen alone is associated with no, or reduced, risk of coronary heart disease.

HRT with oestrogen and progestogen is associated with little or no increase in the risk of coronary heart disease.

Taking oral (but not transdermal) oestrogen is associated with a small increase in the risk of stroke.

**Type 2 diabetes**

HRT (either orally or transdermally) is not associated with an increased risk of developing type 2 diabetes.

HRT is not generally associated with an adverse effect on blood glucose control.

Consider HRT for menopausal symptoms in women with type 2 diabetes after taking comorbidities into account and seeking specialist advice if needed.

**Breast Cancer**

The baseline risk of breast cancer for women around menopausal age varies according to the presence of underlying risk factors.

HRT with oestrogen alone is associated with little or no change in the risk of breast cancer.

HRT with oestrogen and progestogen can be associated with an increase in the risk of breast cancer.

Any increase in the risk of breast cancer is related to treatment duration and reduces after stopping HRT.

**Osteoporosis**

Give women advice on bone health and discuss these issues at review appointments.

Explain to women that their risk of fragility fracture is decreased while taking HRT and that this benefit is maintained during treatment, but decreases once treatment stops, and may continue for longer in women who take HRT for longer.
Appendix 3: Diagnosis and management of premature ovarian insufficiency

Diagnosis
- Take into account the woman’s clinical history when diagnosing premature ovarian insufficiency.
- Diagnose premature ovarian insufficiency in women aged under 40 years based on menopausal symptoms, including no or infrequent periods (taking into account whether the woman has a uterus) and elevated FSH levels on 2 blood samples taken 4–6 weeks apart.
- Do not diagnose premature ovarian insufficiency on the basis of a single blood test.
- Do not routinely use anti-Müllerian hormone testing to diagnose premature ovarian insufficiency.
- If there is doubt about the diagnosis of premature ovarian insufficiency, refer the woman to a specialist with expertise in menopause or reproductive medicine.

Management
- Offer sex steroid replacement with a choice of HRT or a combined hormonal contraceptive to women with premature ovarian insufficiency, unless contraindicated (for example, in women with hormone-sensitive cancer).
- Explain to women with premature ovarian insufficiency:
  - The importance of starting hormonal treatment either with HRT or a combined hormonal contraceptive and continuing treatment until at least the age of natural menopause (unless contraindicated).
  - That the baseline population risk of diseases such as breast cancer and cardiovascular disease increases with age and is very low in women aged under 40.
  - That HRT may have a beneficial effect on blood pressure when compared with a combined oral contraceptive.
  - That both HRT and combined oral contraceptives offer bone protection.
  - That HRT is not a contraceptive.
- Give advice to women with premature ovarian insufficiency and contraindications to hormonal contraception; include information on bone, cardiovascular health and symptom management.
- Consider referring women with premature ovarian insufficiency to healthcare professionals who have the relevant experience to help them manage all aspects of physical and psychosocial health related to their condition.
Appendix 4: Definitions

**Menopause** - a biological stage in a woman's life that occurs when she stops menstruating and reaches the end of her natural reproductive life. Usually it is defined as having occurred when a woman has not had a period for 12 consecutive months (for women reaching menopause naturally). The changes associated with menopause occur when the ovaries stop maturing eggs and secreting oestrogen and progesterone.

**Perimenopause** - the time in which a woman has irregular cycles of ovulation and menstruation leading up to menopause and continuing until 12 months after her final period. The perimenopause is also known as the menopausal transition or climacteric.

**Postmenopause** - the time after menopause has occurred, starting when a woman has not had a period for 12 consecutive months.

**Menopausal women** - this includes women in perimenopause and postmenopause.

**Premature ovarian insufficiency** - menopause occurring before the age of 40 years (also known as premature ovarian failure or premature menopause). It can occur naturally or as a result of medical or surgical treatment.

**Bioidentical hormone therapy** – unregulated custom-compounded recipes prepared by a pharmacist following an individual prescriber’s order for a specific patient.