Primary Care Women's Health Forum

PRIMARY CARE WOMEN'S HEALTH FORUM GUIDELINES

Menopause – Guidance on management and prescribing HRT for GPs based on NICE guidance 2015

Written by Dr Imogen Shaw

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This guidance is designed to support you when initiating therapy or to assist in choosing alternative preparations, for the treatment of symptoms of the menopause.

Enclosed are guides to:

1. Short summary of the 2015 NICE guidance (including Ovarian Cancer - not covered in NICE guidelines)
2. The type of progestogens used in HRT
3. A flow chart to guide you in choosing appropriate treatment
   - Remember all women are different and this is a guide only, treatment must be individualised. There is a large variation in the individual's response to different types and routes of oestrogen for symptom control.
   - The following websites are good resources:
     www.menopauseacademy.co.uk
     www.menopausematters.co.uk
4. Possible medications to use - these are the drugs frequently used by the author, alternatives are available.

1. SUMMARY 2015 NICE GUIDANCE: MANAGEMENT OF THE MENOPAUSE

Diagnosis

Diagnosis can be made without laboratory tests in otherwise healthy women aged over 45 years with appropriate symptoms:

- Peri-menopause 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. Or,

  – Symptoms in women without a uterus.

Consider using a FSH test to diagnose menopause only:

- In women aged 40 to 45 years with menopausal symptoms, including a change in their menstrual cycle.
- In women aged under 40 years in whom menopause is suspected.
- If possible, test day 2-5 of cycle.
- Two FSH levels over 30mIU/ml taken 6 weeks apart in women using hormonal contraception rendering them amenorrhoeic (IUS, POP, Nexplanon), can be used to determine when contraception can be stopped (after a further 12 months in women over 50 years).
- Some women may have normal levels of FSH during the menopausal transition, so this should not exclude peri-menopause as a cause of their symptoms.

Vasomotor symptoms

- Offer women HRT for after discussing with them the short-term (up to 5 years) and longer-term benefits and risks.
  Offer a choice of preparations as follows:
  - Oestrogen and Progestogen to women with a uterus
  - Oestrogen alone to women without a uterus.

Do not offer selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs) or Clonidine as first-line treatment for vasomotor symptoms alone. Consider testosterone supplementation for menopausal women with low sexual desire if HRT alone is not effective.

Urogenital atrophy

Vaginal oestrogen can be given to women with urogenital atrophy (including those on systemic HRT) and continued for as long as needed to relieve symptoms. Treatment should be started early before irreversible changes have occurred.

- 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. Vaginal moisturisers and lubricants can be used alone or in addition to vaginal oestrogen.
- There is no need for monitoring of endometrial thickness during treatment of urogenital atrophy with vaginal oestrogens. But advise women they should report unscheduled vaginal bleeding promptly.

Venous thromboembolism

The risk of venous thromboembolism (VTE) is increased (RR=2) by oral HRT compared with baseline population risk.

The risk associated with transdermal HRT given at standard therapeutic doses (under 50mcg/24h) does not appear to be 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.

Refer menopausal women at high risk of VTE (for example, those with a strong family history of VTE or a hereditary thrombophilia) to a haematologist or local specialist/GPSI with an interest in the menopause for assessment, before considering HRT.

Cardiovascular disease

HRT does not increase coronary heart disease risk when started in women aged under 60 years, and does not affect the risk of dying from cardiovascular disease.

- 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 according to their personal 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 Oestrogen (but not transdermal under 50mcg/24hr) is associated with a small increase in the risk of stroke, but the baseline population risk of stroke in women aged under 60 years is very low, so the increased risk is non significant.

Type 2 diabetes

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

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

Osteoporosis

Give women advice on bone health and discuss any risk factors for osteoporosis.

- The baseline population risk of fragility fracture for women around menopausal age in the UK is low and varies according to their personal and familial risk factors.
- Risk of fragility fracture is decreased while taking HRT but increases once treatment stops, although may persist for a while in women who take HRT for longer.

Loss of muscle mass and strength

There is limited evidence suggesting that HRT may improve muscle mass and strength, which otherwise tends to decrease after the menopause. Muscle mass and strength is also maintained through daily activities and weight bearing exercise.

Breast cancer

HRT does not affect the risk of dying from breast cancer.

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

- HRT with Oestrogen alone is associated with little or no increase in the risk of breast cancer.
- HRT with Oestrogen and Progestogen can be associated with an increase in the risk of breast cancer, however any increase in risk of breast cancer is related to treatment duration and reduces after stopping HRT.

The Woman's Health institute study suggests if 1000 women used HRT for 5 years there would be 4 extra cases of breast cancer with combined HRT use, and 4 fewer cases with Oestrogen only use, on a baseline risk of 15 cases per 1000 women over 5 years.

Ovarian cancer
(not in NICE guidelines)

A 2015 meta-analysis of 52 epidemiological studies has shown an increased risk of ovarian cancer with Oestrogen only and combined HRT. Whilst this study provides evidence of an association between HRT use and some tumour subtypes, it provides insufficient evidence to claim that HRT causes ovarian cancer.

When counselling patients, it is important to discuss these findings in terms of absolute risk.

With 5 years of HRT use, there could be 1 additional ovarian cancer per 1,000 users and 1 additional death per 1,700 users among women of all ages.

A better way of framing it is to point out that, after 5 years of HRT there is only a 0.1% increase in ovarian cancer and less than 0.6% additional deaths.

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Premature ovarian insufficiency

In women with premature ovarian insufficiency (menopause under 40 years) it is important to start hormonal treatment either with HRT or a combined hormonal contraceptive.

This treatment should be continued until at least the age of natural menopause (unless contraindicated) to protect against the increased risk of dementia, cognitive decline, cardiovascular disease and osteoporosis seen in these women.

- HRT has a negligible effect on blood pressure and beneficial effects on metabolic parameters, when compared with a combined oral contraceptive.
- Both HRT and combined oral contraceptives offer bone protection.
- HRT is not a contraceptive.

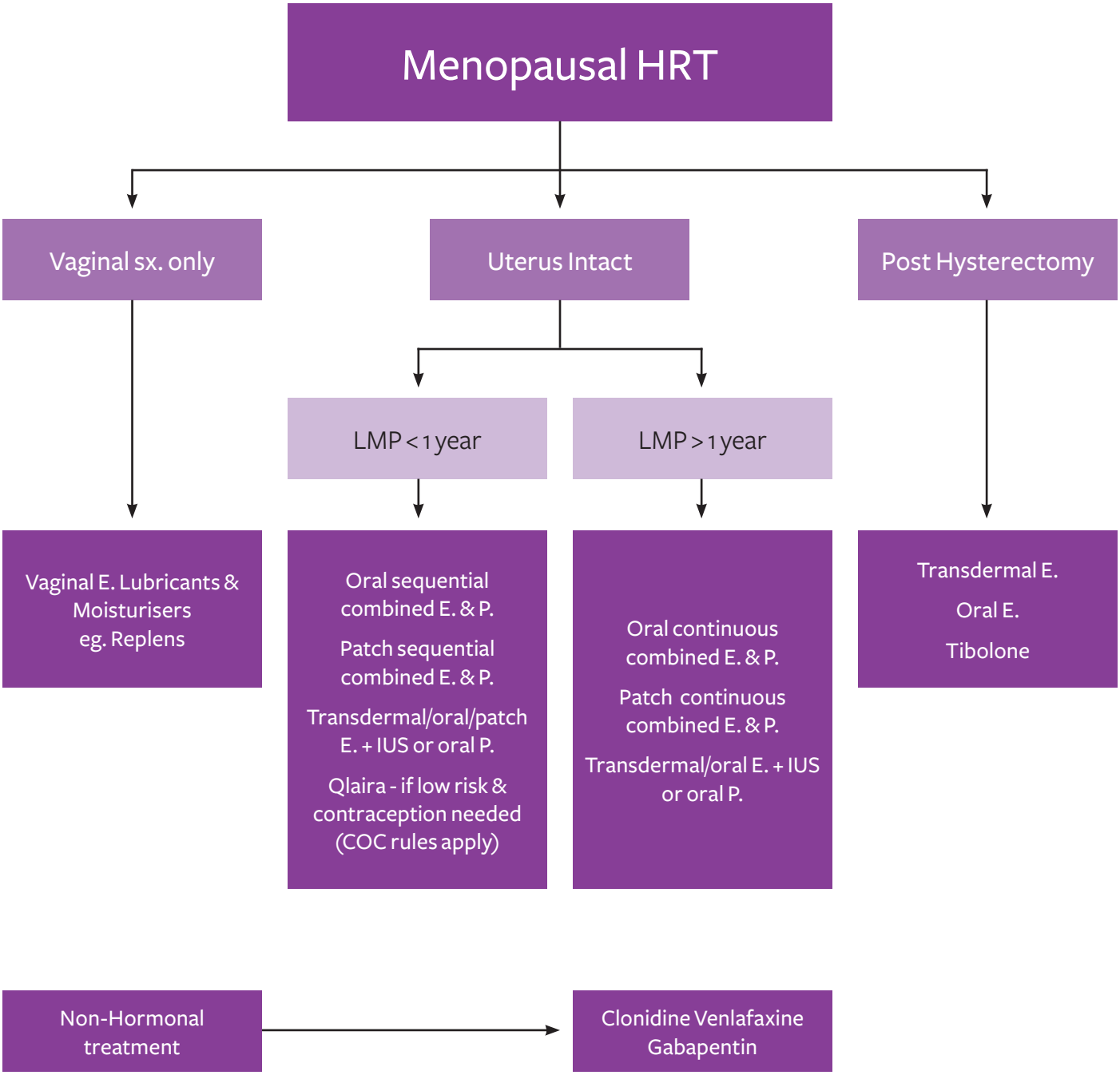
Consider referring women with premature ovarian insufficiency to healthcare professionals who have the relevant experience to help them manage all aspects of physical and psychosocial health related to their condition.

REVIEW EACH TREATMENT FOR MENOPAUSAL SYMPTOMS	At 3 months to assess efficacy and tolerability Annually thereafter unless there are clinical indications for an earlier review (such as treatment ineffectiveness, side effects or adverse effects).

2. PROGESTOGENS

Synthetic Progestogens	Features	Natural Progestogens	Features
c19 testosterone derivatives			
Norethisterone Norgestrel Levonorgestrel	Better cycle control Androgenic (good for libido) Unfavourable effect on lipids	Micronised Progesterone (Utrogestran)	Fewer progestogenic side effects No androgenic or glucocorticoid activity No impact on lipids Less effective cycle control
c21 testosterone derivatives			
Medroxyprogesterone acetate	Can be added to oral or transdermal oestrogen (Androgenic so may be good for libido) Unfavourable effect on lipids		
Dydrogesterone	Non Androgenic Not available as single preparation		
IUS = Levonorgestrel	Replace after 5 years as per FSRH guidance There is minimal systemic absorbtion		

3. FLOW CHART FOR HRT PRESCRIBING



4. POSSIBLE MEDICATIONS TO USE

There are alternatives available. See the BNF.

HRT	TABLETS*	2nd LINE*	TRANSDERMAL*
Sequential preparations For patients with: • intact uterus • perimenopausal-under 1yr or amenorrhoea	ELLESTE DUET 1mg (£9.20) ELLESTE DUET 2mg (£9.20) *Norethisterone*	FEMOSTON 1/10 (£16.16) FEMOSTON 2/10 (£16.16) *Dydrogesterone* (Non androgenic)	FEMSEVEN SEQUI 50mcg (£37.54) *Levonorgestrel* EVOREL SEQUI 50mcg (£33.27) *Norethisterone*
Continuous combined Bleed free HRT use if: • amenorrhoeic > 1yr • > 54y • > 3yrs on sequential HRT	ELLESTE DUET CONTI 2mg (£17.02) *Norethisterone* FEMOSTON CONTI 0.5mg (£24.43) FEMOSTON CONTI 1mg (£24.43) *Dydrogesterone*	TIBOLONE 2.5mg (£31.08) Can be useful if: • Bloating on oestrogen • Poor libido • Endometriosis	FEMSEVEN CONTI 50mcg (£44.12) *Levonorgestrel* EVOREL CONTI 50mcg (£37.22) *Norethisterone*
Unopposed Oestrogen Post hysterectomy	ELLESTE SOLO 1mg (£5.06) ELLESTE SOLO 2mg (£5.06)		ESTRADOT PATCH 25mcg (£17.97) 37.5mcg (£18.00) 50mcg (£18.06) 75mcg (£21.00) 100mcg (£21.81) OESTROGEL (£14.40) SANDRENA GEL 500mcg (£15.24) 1mg (£17.57)
Topical vaginal oestrogen			VAGIFEM 10mcg 24 pessaries (£16.72) OVESTIN CREAM (£4.45)
Progestogen adjunct to topical oestrogen if no hysterectomy	MPA 5 or 10mg (£9.81) *Medroxyprogesterone* 10mg d14-28 or 5mg dailyÐ Utrogestan 100mg (£15.39) *Micronised progesterone* 200 mg d14-28 or 100mg daily#	Mirena – IUS (£88) *Levonorgestrel* Replace after 5 years as per FSRH guidance	

Progestogen component in grey. Prices for 3 months treatment

*Use lowest dose to control symptoms.
#Day 14-28 (sequential – i.e. still giving periods), daily for continuous combined (bleed free)

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