MENOPAUSE

INTRODUCTION

- Menopause is defined as the cessation of the menstrual cycle and is caused by ovarian failure
- Reproductive ageing is the process by which the ovaries become less responsive to gonadotrophins (LH and FSH) and estradiol levels begin to fall
- Median age at which the menopause occurs in the UK is 51 years
- The menopausal age is determined by a combination of genetic and environmental factors

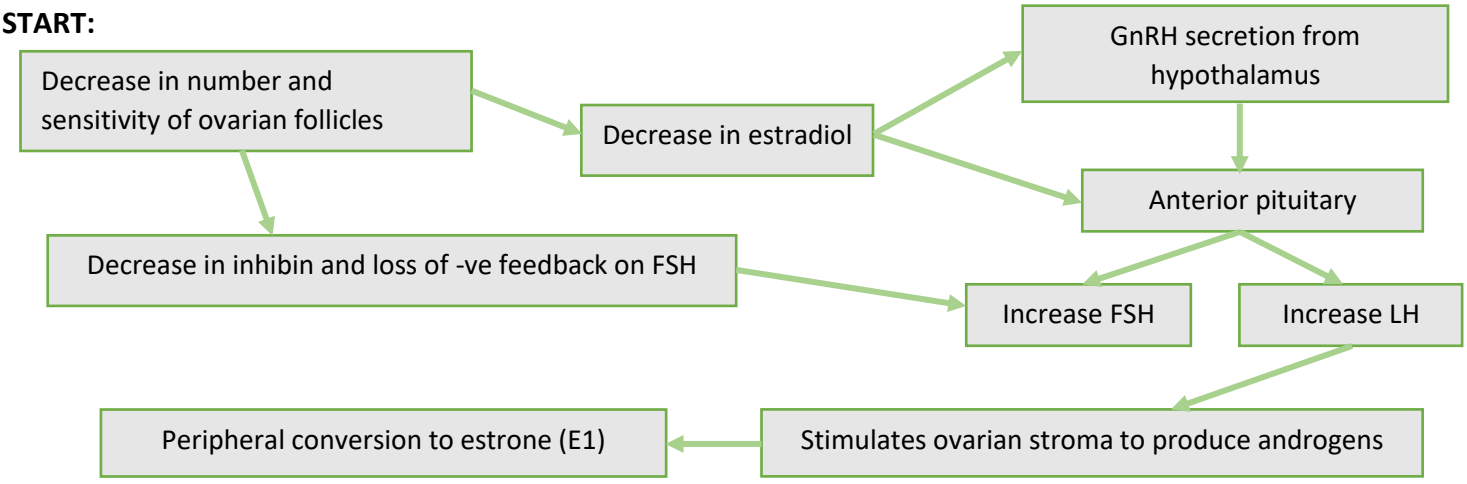
DEFINITIONS

- **Menopause** – permanent cessation of menstruation that results from loss of ovarian follicular activity. Natural menopause is a retrospective diagnosis after 12 consecutive months of amenorrhoea (with no other cause identified)
- **Perimenopause** – the period starting with the first features of menopause such as irregular cycles, menopausal symptoms and ending 12 months after the last menstrual period (also known as menopausal transition or climacteric)
- **Premature ovarian insufficiency** - menopause occurring before the age of 40 years. It can occur naturally or because of medical or surgical treatment.
- **Induced/Iatrogenic menopause** – cessation of menstruation following surgical oophorectomy or ablation of ovarian function by chemotherapy, radiotherapy, or GnRH analogues.
- **Early menopause** – a menopause that occurs between 40 and 45 years of age.

PHYSIOLOGY OF THE MENOPAUSE

- Women are born with a finite number of oocytes which peak at 20-28 weeks gestation and by menarche around 400,000 remain. This number decreases with each menstrual cycle and the menopause signifies the inevitable depletion of the oocyte stores.
- The ovarian cycle is controlled by the hypothalamic-pituitary-ovarian (HPO) axis
- In premenopausal women, follicle stimulating hormone (FSH) and Luteinising hormone (LH) released from the anterior pituitary gland cause the production and secretion of estradiol, progesterone and testosterone from the ovaries.
- During the perimenopause, the ovaries become less responsive to gonadotrophins causing a reduction in oestrogen and inhibin levels, and reduced negative feedback to the pituitary causes FSH and LH levels to rise.
- Decreasing oestrogen levels start to disrupt the menstrual cycle and menopausal symptoms develop
- Eventually, amenorrhoea and the menopausal pattern of low oestrogen and persistently high FSH and LH levels is established.

START:



SYMPTOMS OF THE MENOPAUSE

- The perimenopause usually begins with a change to the menstrual pattern. Cycle length may get shorter or longer and the amount of menstrual blood loss may change.
- Menopausal symptoms are common and are mostly caused by estrogen deficiency with 70% of women experiencing vasomotor symptoms.
- The median duration of symptoms is 7 years but symptoms can persist beyond age 60.
- Symptoms are usually the most prevalent in the first year after the final menstrual period however some symptoms such as urogenital symptoms may only appear many years after the onset of menopause.

Symptoms can be broadly split into four categories:

PHYSICAL/VASOMOTOR	UROGENITAL
Hot flushes Night sweats Dry skin and Hair Arthralgia Headaches	Vaginal dryness Dyspareunia Recurrent UTI Note: Symptoms may appear > 10yrs after LMP
PSYCHOLOGICAL	**SEXUAL DYSFUNCTION**
Depression Anxiety Irritability Mood swings Lethargy / exhaustion	Dyspareunia Low libido Vaginal dryness Note: Often multifactorial physical and psychological causes

LONG TERM IMPLICATIONS OF THE MENOPAUSE

Postmenopausal women (including those with untreated POI) are at increased risk of osteoporosis, CVD, stroke, and atrophic changes in the vagina and bladder, due to oestrogen depletion as well as natural ageing.

As a direct consequence of loss of estrogen, the woman is:

- less able to conserve her collagen in bone (leading to osteoporosis), skin, nails, vagina, and pelvic ligaments
- less able to maintain a healthy endothelium: development of hypertension and atherosclerosis
- less able to synthesise neurotransmitters, particularly acetyl choline (cognition), serotonin and dopamine (low moods, irritability, insomnia)
- sustains changes to adrenergic and noradrenergic transmission with development of panic attacks and palpitations

ASSESEMENT AND DIAGNOSIS

HISTORY AND EXAMINATION

History

- Full gynae history including PMH and FH
- Specifically enquire about LMP, current bleeding pattern and menopausal symptoms
- Exclude pathology
- Full social history to include effect of symptoms on lifestyle, exercise, diet, social stressors, occupation
- Assess risk factors for breast and endometrial cancer, osteoporosis, VTE, CVD
- Assess contraceptive and sexual health needs, smear and mammogram history
- Ensure to cover all 4 areas of symptoms (vasomotor/urogenital/sexual/psychological) as often they won't be volunteered without direct questioning

Examination

- PV/breast exam if indicated
- Baseline BP and BMI

DIAGNOSIS

Diagnosis can be purely clinical where appropriate or based on a typical history with an elevated FSH level. The diagnosis of menopause differs according to the age of the woman at the time of presentation

>45years

If symptoms are **typical**, there are no red flags and the patient is otherwise healthy lab tests are not required and the diagnosis is clinical.

- **Perimenopause** — if the woman has vasomotor symptoms and irregular periods.
- **Menopause** — if the women has not had a period for at least 12 months or based on symptoms in women without a uterus.

Consider FSH if:

- Atypical symptoms
- Amenorrhoeic with Progestogen-only contraception
- History of ablation or hysterectomy

40-45years

Symptoms suggestive of menopause and cycle change:

- Consider day 1-5 FSH to support diagnosis

<45 years

Symptoms suggestive of menopause:

- 2 x FSH 4-6 weeks apart
- See pathway on POI

FSH testing

- FSH Testing in women over 45years is not generally advised as diagnosis is made clinically
- FSH is not reliable on those taking Combined hormonal contraception (CHC), high dose progestogens and HRT but can be done on those using POP or LNG-IUS
- A serum FSH level >30 IU/L indicates a degree of ovarian insufficiency, but not necessarily sterility.

Other Investigations

- LH, oestradiol, progesterone, testosterone, inhibin, AMH, AFC should not be used in the diagnosis of menopause in those more the 45years old
- In women reporting lack of libido, a testosterone level (either total testosterone or free androgen index)is of some use, but there is a lack of guidance on this and levels do not always correlate with symptoms (see below section on libido and testosterone.
- FBC, TFT's, fasting glucose, autoantibody screen, catecholamine screening if indicated clinically

MANAGEMENT OF THE MENOPAUSE

INFORMATION GIVING

Counselling:

- Explain stages of the menopause and the common symptoms
- Overview of treatments including HRT, non-hormonal treatments, non-pharmacological treatments (CBT) and the risks and benefits of each (see pages on treatment)
- Advice on contraception, including that HRT does not provide contraception and that a woman is considered potentially fertile for 2 years after her last menstrual period if she is younger than 50 years, and for 1 year if she is over 50 years.
- Peer support www.menopausematters.co.uk

Health promotion:

- Maintain a healthy BMI between 18.5-25kg/m2
- Smoking cessation and reduce alcohol consumption to less than 2 units per day
- Diet high in fibre (wholegrain rice, pasta, bread) and protein (oily fish, lean meat, eggs, beans, soy), Reduce saturated fats, refined sugar and salt.
- Regular exercise (aim for 150 minutes of moderate intensity) and importance of pelvic floor exercises
- Screening – Cardiovascular risk screening (QRISK2), Cancer screening (cervical, breast, bowel) as per national screening programmes
- bone health – calcium 700mg/day and vit d 10 mcg/day

Lifestyle modifications to reduce menopausal symptoms:

- Hot flushes and night sweats — regular exercise, weight loss, lighter clothing, sleeping in a cooler room, reducing stress, and avoiding possible triggers (such as spicy foods, caffeine, smoking, and alcohol).
- Sleep disturbances — avoiding exercise late in the day and maintaining a regular bedtime.
- Mood and anxiety disturbances — adequate sleep, regular physical activity, and relaxation exercises
- Cognitive symptoms — exercise and good sleep hygiene

SEXUAL HEALTH AND CONTRACEPTIVE ADVICE

Contraception

- During the perimenopause, isolated FSH, LH and estradiol levels can be misleading and should not be used to guide advice about stopping contraception as ovulation may still occur with risk of pregnancy
- Contraception should be continued for at least 2 years after the LMP in women < 50years and at least one year if 50 years or older *(see appendix 1 for advice on stopping specific methods)*
- In women who are amenorrhoeic on contraception and in women > 50 years an FSH may be helpful
- Contraception can be stopped aged 55 even if the patient is still having bleeds as the chance of pregnancy is negligible

Sexual Health

- The prevalence of STI's has risen in those over 50 years and new relationships are common at this stage
- Offer STI screening where appropriate

Urogenital atrophy

- Women should be asked about symptoms at every consultation
- Low dose vaginal oestrogen can be continued as long as needed, systemic absorption is minimal, so no progestogen or endometrial monitoring is needed
- Advise the use of vaginal moisturisers and lubricants *(see page on treatment)*

Libido – see section below on Testosterone

HORMONAL TREATMENT OF THE SYMPTOMS OF MENOPAUSE

Hormone Replacement Therapy (HRT)

- The type of HRT suitable for each woman is variable and depends on factors such as her symptoms, her stage in the menopausal transition and whether she has an intact uterus
- HRT consists of an oestrogen alone for women who have had a hysterectomy or a combination of oestrogen and progestogen if the uterus is present to offer endometrial protection
- It is the **oestrogen component which provides symptomatic relief**, the progestogenic component purely acts to protect the endometrium
- Progestogens can be given cyclically or continuously depending on the menopausal status of the woman
- Different routes of administration are available including oral, transdermal, subcutaneous and vaginal

Components of HRT – oestrogens and progestogens

- There are two types of oestrogen - natural and synthetic.
- Synthetic oestrogen e.g. ethinylestradiol is used in CHC
- Natural oestrogens e.g. estradiol is the mainstay of HRT
- Progestogens used in HRT are largely synthetic e.g. LNG/NET but can also be micronised e.g utrogestan
- Tibolone – synthetic steroid with mild estrogenic, progestogenic and androgenic actions. It is used in postmenopausal women who want to maintain amenorrhoea and has a role in preventing osteoporosis.

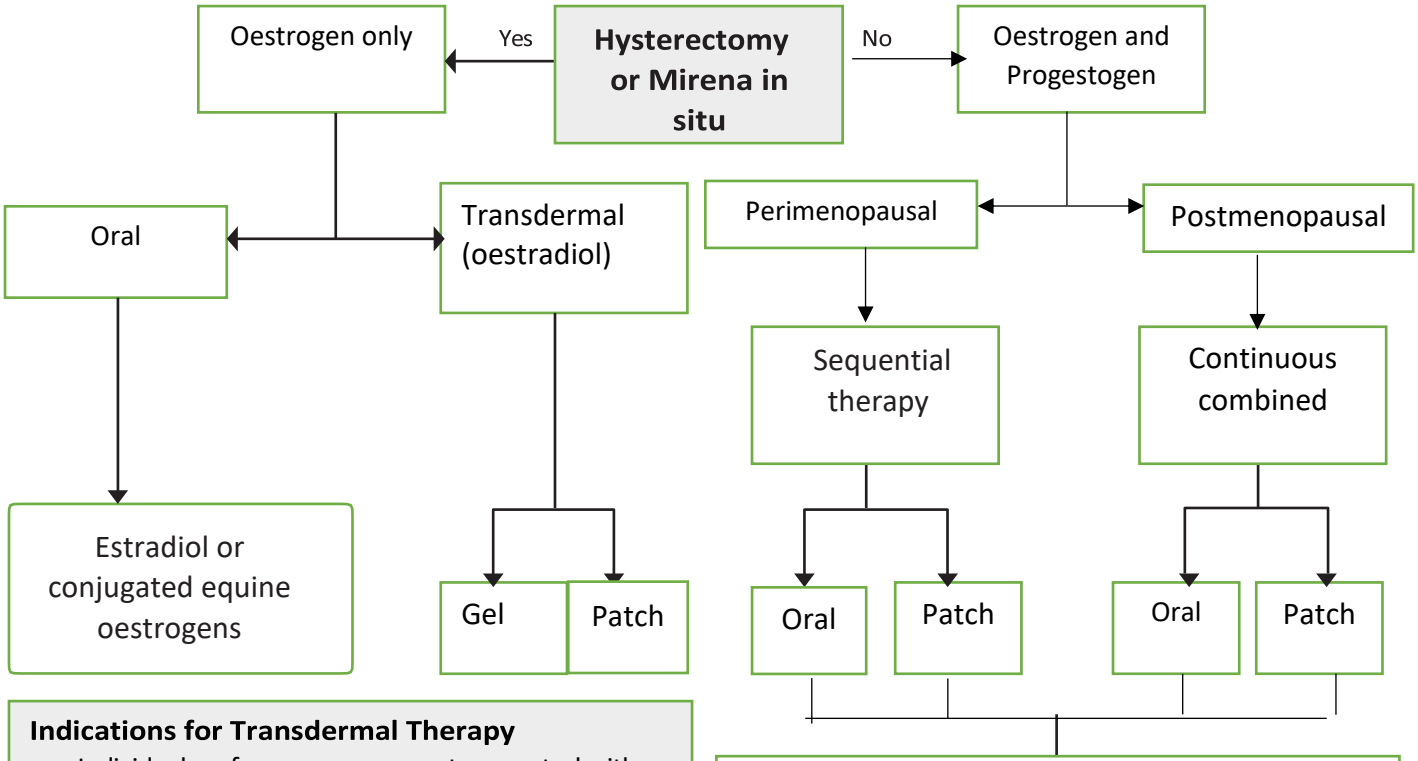
HRT REGIMES

HRT regime	Uses	How to take	Bleeding pattern
Unopposed oestrogen	Women without a uterus	daily oestrogen via suitable route	n/a
Sequential combined cyclical HRT	Perimenopause and in first year or two after menopause	oestrogen daily plus progestogen for 10-14 days every 28-30 day cycle	Cyclical withdrawal bleeding, mimics normal menstrual cycle
Sequential long cycle HRT	Women with significant progestogenic side effects or infrequent periods but not yet PM	oestrogen daily for 12 weeks and progestogen for last 14 days	Bleeding 3 monthly **Only use short term due to risk of endometrial cancer. Specialist only.**
Continuous combined HRT	Postmenopausal women	oestrogen + progestogen daily	No bleeding
Tibolone	Postmenopausal women	2.5mg daily	No bleeding

PRESCRIBING PRINCIPLES

- Individualised approach and involve women in decision making
- Start cyclical HRT at the start of natural menstrual cycle to reduce irregular bleeding or at any time if she has not any recent bleeding
- Use the lowest effective doses to minimise hormonal side effects
- **Progestogens should always be given in conjunction with oestrogen in non-hysterectomised women**
- Allow 3 months of treatment before changing due to side effects as things may settle, if not consider changing the dose, route or type of estrogen (see table on managing side effects)
- Explain the expected bleeding pattern of method and that irregular bleeding is common in first 3-6 months (needs investigating thereafter)

HRT TREATMENT FLOWCHART SUMMARY (adapted from BMS HRT guide)



Indications for Transdermal Therapy

- Individual preference, poor symptom control with oral
- GI disorder affecting oral absorption
- Previous or family history of VTE BMI >30
- HTN + Migraine
- Use of hepatic inducing enzymes medication
- Gall bladder disease

- Start with low dose preparation that provides adequate symptom control
- In POI higher doses tend to be needed
- Consider addition of testosterone therapy after bilateral oophorectomy

OESTROGENS	
Oestradiol	• 0.5mg (combined only)/ 1mg / 2mg oral • 25mcg / 37.5mcg / 40mcg / 50mcg / 75mcg / 80mcg/ 100 mcg patches • 0.06% Oestrogel 0.75mg • 500mcg / 1mg Sandrena gel • 10mcg vaginal tablets • 7.5mcg vaginal ring
Oestriol	0.1% / 0.01% vaginal creams or pessary, 50mcg/g vaginal gel
Conjugated oestrogens	0.3mg / 0.625mg / 1.25mg
PROGESTOGENS	
Micronised progesterone (utrogestan)	100mg, 200mg or 300mg oral at night
Dydrogesterone, norethisterone	Combined only
Levonorgestrel	Combined and IUS
Medroxyprogesterone acetate	

Estradiol – Equivalent doses (adapted from the BMS practical prescribing)				
	Very low	**Low**	**Medium**	**High**
Oral	0.5mg	1mg	2mg	3mg
Patch	Half 25	25	50	75-100
Gel-pump	½ pump	1 pump	2 pumps	3-4 pumps
Gel-sachet	½ x 0.5mg sachet – 0/25	0.5mg	1mg	1.5-2mg

Progestogen dose per licensed estrogen dose (adapted from BMS Unscheduled Bleeding 2024)							
Estrogen dose	**Micronised progesterone**		**Medoxy progrogesterone**		**Norethisterone**		**LNG-IUD 52mg**
	Continuous	Sequential	Continuous	Sequential	Continuous	Sequential	One -for up to 5 years of use
Ultra/Low	100mg	200mg	2.5mg	10mg	5mg*	5mg*	
Standard	100mg	200mg	2.5-5mg	10mg	5mg*	5mg*	
Moderate	100mg	200mg	5mg	10mg	5mg	5mg	
High	200mg	300mg	10mgˆ	20mgˆ	5mg	5mg	

*1mg provides endometrial protection for ultralow to standard dose estrogen but the lowest stand-alone dose currently available in the UK is 5mg (off license use of 3 noriday POP i.e. 1.05mg, could be considered if 5mg is not tolerated).
ˆThere is limited evidence in relation to optimal MPA dose with high dose oestrogen, the advised dose is based on studies reporting 10mg providing protection with up to moderate dose estrogen.

TREATMENT OF UROGENITAL SYMPTOMS

- Vaginal oestrogens are used for those with urogenital symptoms who do not want or are unable to take systemic HRT or for those with ongoing urogenital symptoms despite taking HRT (which is common as systemic HRT does not penetrate the urogenital tract well).
- The systemic absorption from vaginal oestrogens is low and hormone levels remain in the postmenopausal range
- If the vaginal preparations are used in standard doses, there is no need to add a progestogen for endometrial protection and they can be used long term
- Vaginal oestrogens can be used alongside systemic HRT if symptoms are not adequately controlled by systemic treatment

VAGINAL OESTROGEN PREPERATIONS	
Estradiol	**Estriol**
Vagifem/Vagirux (tablet)	Ovestin (0.1%) (cream)
Estring (ring) changed 3 monthly	Gynest (0.01%) (cream)
Tablets and cream should be used nightly for 2 weeks and then twice weekly maintenance can be used long term. Estring may give better symptom control than other preparations.	

ANDROGEN REPLACEMENT - TESTOSTERONE

- All women have decreasing levels of testosterone but those who have had a bilateral oophorectomy have even lower levels as around 50% of circulating testosterone is lost (rest by adrenals)
- There are no licenced testosterone products for women in the UK available
- NICE/BMS recommend a trial of conventional HRT before testosterone use -transdermal preparations may be more effective than oral for libido due to the reduced effect on SHBG.
- NICE/BMS reference off-label use of testosterone in low doses, but risks and benefits need to be carefully explained
- Side effects of testosterone are generally rare if levels are maintained within female physiological levels – commonest side effects are excess hair growth, acne and weight gain which are all reversible upon stopping, rare side effects include voice deepening, alopecia and clitoral enlargement.
- NICE/BMS advise that testosterone can be prescribed off licence in well oestrogenised women with low testosterone and symptoms of low libido, it cannot currently be recommended for cognition, mood, energy or musculoskeletal health due to a lack of evidence.
- Libido and other psychosexual issues are often multifactorial and a bio-psycho-social approach should be taken e.g. psychosexual counselling and lubricants/moisturisers should be tried before giving testosterone replacement. All can also be used alongside testosterone replacement.

TESTOSTERONE PREPARATIONS (adapted from BMS Testosterone, 2022)	
Testim gel [Endo Ventures Ltd] 1% testosterone gel in 5ml tubes	Starting dose 0.5ml (5mg) per day making each tube last for 10 days
Tostran [Kyowa Kirin Ltd] (2% testosterone gel in a canister containing 60g	Starting dose 1 metered pump of 0.5g = 10mg on alternate days – each canister should last 240 days
Testogel [Besins Healthcare UK] (2.5g sachets containing 40.5mg testosterone)	Starting dose 1/8 of a sachet/day = approx. 5mg/day i.e. each sachet should last 8 days
AndroFeme cream [Lawley Pharma] (1% testosterone cream in 50ml tubes with screw cap	Starting dose 0.5ml/day = 5mg /day i.e. each tube should last 100 days
Testosterone Implants [Smartway Pharma] (100mg implanted pellets) – imported from USA	

PRESCRIBING TESTOSTERONE

- Women should already be on HRT
- Check oestradiol levels to ensure the patient is well oestrogenised (>400nmol/L) (titrate up if low and monitor response before commencing testosterone)
- Check total testosterone is in the low or normal range (different labs have different reference ranges) but this will provide a baseline
- Prescribe as per the table above
- The gel should be applied to lower abdomen/ upper thighs and left to dry before dressing.
    - Wash hands and avoid contact with partners/children
    - The application areas should not be washed for 2-3hours
- Avoid/express caution in pregnancy, breastfeeding, active liver disease, hormone sensitive breast cancers, competitive athletes
- Monitoring: Review symptoms and check total testosterone levels after 2-3 months to ensure they're within female physiological levels and there has been a response to treatment (it may take 6/12).

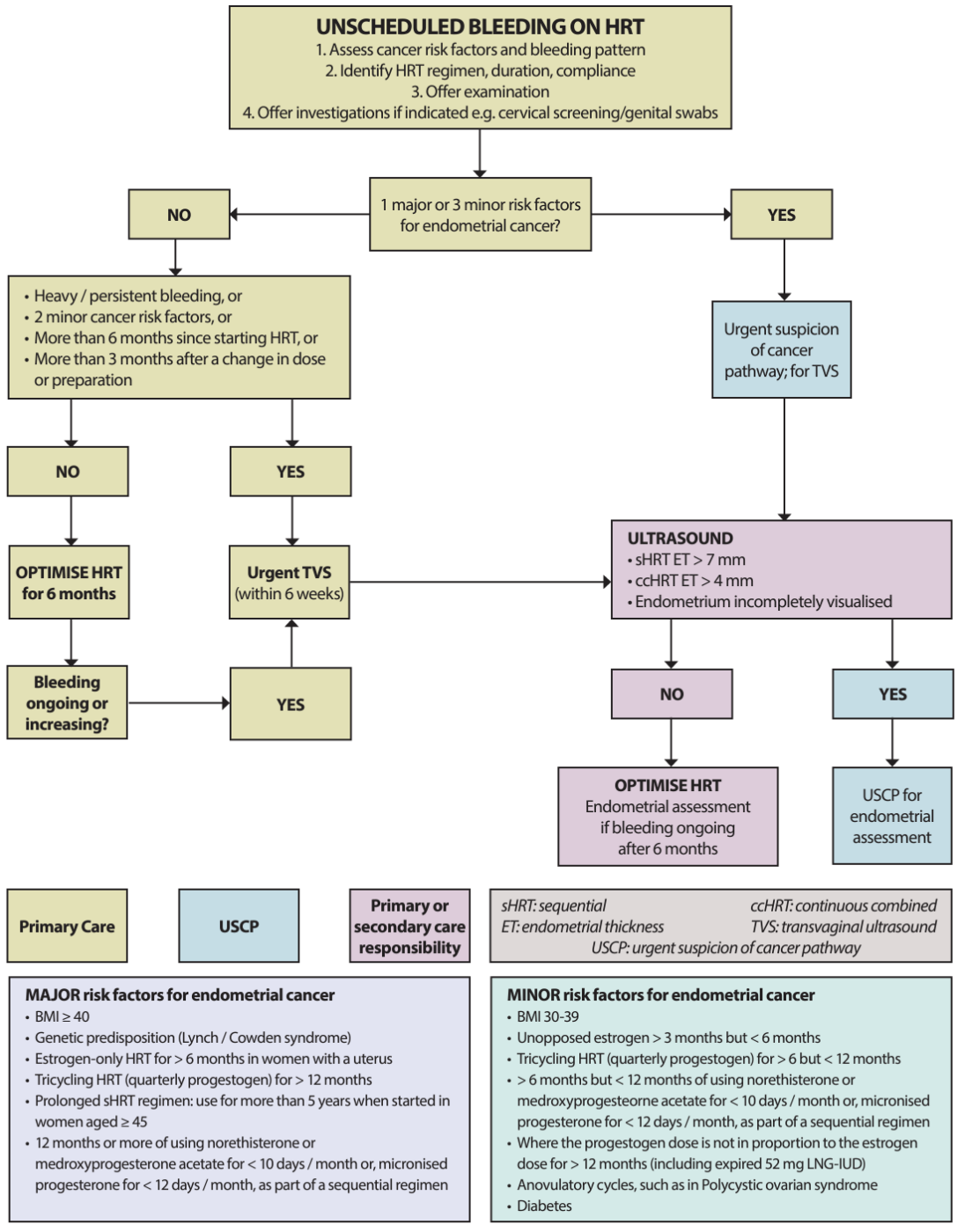
FOLLOW-UP

After initiating HRT or after changing HRT preparations review progress at 3 months. Once established on HRT patients should be reviewed annually.
At each review asses the following:

- Check the effectiveness of the HRT and enquire about side effects and bleeding patterns
- If there are side effects consider changing dose, preparation, route of administration (see appendix)
- Discuss the pros and cons of continuing HRT and decide to continue, reduce dose or stop as appropriate
- Discuss health promotion including blood pressure, weight, screening, and breast awareness

MANAGEMENT OF BLEEDING

In women on cyclical HRT monthly withdrawal bleeds are expected and in those taking continuous combined HRT irregular bleeding is common over the first 3-6 months but should be investigated thereafter.
See flow chart below, reproduced from the BMS Unscheduled bleeding on HRT 2024



BENEFITS AND RISKS OF HRT

GENERAL PRINCIPLES

- The risk/benefit balance of HRT varies for each woman and from year to year depending on symptoms, medical history, and number of years that HRT has been taken
- HRT dosage, regimen and duration should be individualised with annual evaluation of advantages and disadvantages
- **Prescribing HRT for 5 years in women less then 60 does not increase risks**
- For most symptomatic women (especially if < 60yrs) the benefits of short-term HRT outweigh the risks
- The risks can be lowered by choosing appropriate regimes (see below)
- There is no upper age limit or duration of use for HRT if benefits continue to outweigh potential risks

BENEFITS

Improvement in quality of life and symptoms inc:

- Vasomotor symptoms
- Sexual dysfunction
- Urogenital symptoms

Osteoporosis

- Decreased risk of fragility fractures

Musculoskeletal

- May increase muscle mass and strength

Cardiovascular disease

- For women with POI or early menopause – decreased risk of CVD

Women with comorbidities

Women with or at high risk of breast cancer

- Avoid fluoxetine and paroxetine if on tamoxifen
- refer to specialist

Women with a history of, or at high risk of VTE

- Consider transdermal rather than oral HRT e.g. BMI over 30 kg/m^2
- Refer to haematology prior to starting if high risk (e.g FH of VTE or hereditary thrombophilia)

Women with HTN or risk factors for CVD

- Transdermal HRT not contraindicated
- Optimise medical management of HTN etc

Migraine with aura

- Not a contraindication to HRT
- Transdermal route may trigger less migraines as oestrogen levels more stable

Other - Refer to specialist as appropriate

RISKS

VTE

- Increased risk with oral oestrogen (2-4x)
- No increased risk with transdermal oestrogen
- Lower risk with micronised progesterone

CHD and stroke

- HRT does not increase risk when started < 60yrs
- Increased risk when started > 60 years (TD oestrogen does not increase stroke risk)

Endometrial cancer

- Risk if unopposed oestrogen given to those with a uterus
- Reduced with addition of progestogen
- Continuous progestogen better long-term protection

Breast cancer (see appendix for infographic)

- HRT with oestrogen alone - little or no increase in risk
- Combined HRT - slight increase in risk after minimum 5 years use in those > 50yrs (extra 3-4/1000 women)
- Any increase in risk of breast cancer is related to treatment duration and reduces after stopping HRT

Ovarian cancer

- Small increased risk

Contraindications to HRT

- Acute liver disease with abnormal LFTs
- Pregnancy
- Undiagnosed abnormal PVB
- Active or recent MI
- Suspected or active breast or endometrial cancer
- Porphyria cutanea tarda

NON-HORMONAL TREATMENT OF THE MENOPAUSE

For women who do not want to take HRT or are unsuitable, consider the following as treatment strategies

Lifestyle modifications

- exercise (aerobic, sustained, regular exercise such as swimming or running),
- lighter clothing, sleeping in a cooler room, and
- reducing stress may be sufficient to manage hot flushes for many women. Mindfulness/yoga/ CBT
- Avoidance of possible triggers such as spicy foods, caffeine, smoking, and alcohol may help.

Offer tailored treatment based on individual symptoms

Vasomotor Symptoms

- Consider 2-week trial of fluoxetine 20mg OD, citalopram 20mg OD, or venlafaxine (37.5 mg BD)

NB: use of SSRIs is unlicensed **paroxetine and fluoxetine must not be used in women on tamoxifen**

Vaginal dryness

- Vaginal moisturisers e.g. Replens MD
- Vaginal lubricants e.g. Sylk, YES

NB: will help with dryness but will not treat vaginal atrophy

Psychological symptoms

- Refer for CBT
- Consider antidepressants if patient also has a diagnosis of depression

NB: no evidence for antidepressants if no diagnosis of depression

PHARMACOLOGICAL ALTERNATIVES TO HRT (only to be started following specialist advice)

1. Clonidine – centrally acting alpha adrenoreceptor agonist – may be useful for tamoxifen induced flushes. Side effects dry mouth, sedation, dizziness, insomnia.
2. Gabapentin – can reduce hot flushes by 50% at 900mg OD – can be an option for women with breast cancer
3. Progestogens – e.g NET, megestrol acetate and medroxyprogesterone acetate – increased risk of VTE and breast cancer
4. Fezolinetant – NK3 receptor antagonist – for moderate/severe hot flushes (only on private prescription)

COMPLEMENTARY AND ALTERNATIVE THERAPIES

Complementary therapies are used as they are perceived to be a safe alternative to traditional HRT. There is a lack of evidence surrounding the efficacy and safety of these products and this should be explained to women. Need to mention CBT and evidence support efficacy

Phytoestrogens e.g. isoflavones found in soy, chickpeas etc may help vasomotor symptoms but their safety is unknown and different preparations may vary.

Herbal remedies - not subject to the strict regulations that apply to drugs and there is little control or regulation of the quality and contaminants. Interaction with conventional therapies is a major concern.

- black cohosh may possibly help with vasomotor symptoms but quality varies between preparations
- Evening primrose oil and dong qaui – no evidence for treatment of menopause NOTE: NICE includes St John's wort as showing some benefit

Complementary therapies – reflexology, acupressure, reiki – no evidence

Bioidentical hormones - technically means having the same molecular structure as found in body so estradiol and progesterone are technically bioidentical HRT. This term is often misused to refer to unregulated products. There is no evidence to support these compounds and no safety regulations in the UK. All regulatory bodies advise against them.

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APPENDICES:

Appendix 1: Table on when to stop contraception adapted from FSRH guideline; Contraception for Women aged more than 40 years

Contraceptive Method	Age 40-50 years	Age > 50 years
Non-hormonal	Stop contraception after 2 years of amenorrhoea	Stop contraception after 1 year of amenorrhoea
Combined hormonal contraception	Can be continued	Stop at age 50 and switch to a non-hormonal method or IMP/POP/LNG-IUS, then follow appropriate advice.
Progestogen-only injectable	Can be continued	Women ≥50 should be counselled regarding switching to alternative methods, then follow appropriate advice
Progestogen-only implant Progestogen-only pill Levonorgestrel intrauterine system	Can be continued to age 50 and beyond	Stop at age 55 when natural loss of fertility can be assumed for most women. • If a woman over 50 with amenorrhoea wishes to stop before age 55, FSH level can be checked. • If FSH level is >30 IU/L the IMP/POP/LNG-IUS can be discontinued after 1 more year. • If FSH level is in premenopausal range then method should be continued and FSH level checked again 1 year later • A Mirena inserted ≥45 can remain in situ until age 55 if used for contraception or heavy menstrual bleeding

Appendix 2 – Managing side effects of HRT (adapted from menopause matters)

Managing side effects of HRT (adapted from menopause matters)

Estrogenic side effects – often transient wait 3 months before switching	
Symptoms	**Management**
Breast tenderness, enlargement	Reduce dose of oestrogen. OTC evening primrose oil may help
Gastrointestinal symptoms: bloating, nausea	Take with food or consider an alternative route.
Other symptoms: leg cramps, headache	Change type or route of oestrogen

Progestogenic side effects	
Symptoms	**Management**
• Headache • Depressed mood • PMS type symptoms • Breast tenderness • Acne/greasy skin	**1. Change to a different progestogen** Testosterone derived – Norethisterone, Norgestrol or Levonogestrel Progesterone derived – Dydrogesterone, Medroxyprogesterone Micronised progesterone - Utrogestan **2. Change route** Progestogen by Mirena® may reduce side effects **3. Change drug class or regime** • If postmenopausal and on sequential regime, change to continuous combined with a lower dose progestogen • Consider tibolone