Supporting Pharmacists with HRT decision making

**Dr Nuttan Tanna, IPP, PhD, FFRPS, FRPS.**
Pharmacist Consultant, Women’s Health & Osteoporosis / Bone Health
**London North West University NHS Healthcare Trust, Harrow, Middlesex.**
Clinical Reference Group, NHS England
BMS Menopause Accredited Specialist

Presentation - Specialist Pharmacy Services March 2024.
HRT Prescribing

- Weekly Menopause & Osteoporosis Medication Management Clinics

- Rationale HRT prescribing

- Patient
  - Full medical history
  - Hormone Replacement Therapy Risks and Benefits
    - Individualised for patient
    - Patient’s views
    - Holistic management plan important
  - Alternative options - Prescribed / Non-Pharmacological ..... 

  - Indication, Safety, Efficacy, Compliance & Persistence (Adherence), and Cost effectiveness


Rationale HRT Prescribing

• **Terminology**
  • **Menopause**........Greek language.....
    • Climacteric....the phase
  
  • **Perimenopause**
    • Some endogenous cycling
  
  • **Postmenopause**
    • LNMP one year or more

• **Hormone Replacement Therapy - HRT**
  • **SCT** ......sequential .......mimics menstrual cycle
  • **CCT** ......continuous combined oestrogen + progestogen/progesterone
  • Unopposed oestrogen.........when?
  • Vaginal ERT.......for local relief.....uro-genital syndrome symptomology
The Menopause....

- Average age menopause / UK
  - 50/51 years > Climacteric phase: 45-55

- ~ 1% women > Premature Ovarian Insufficiency [POI]
  - Menopause before age 40 > Young menopause / 40-45 - Early menopause

- With longevity, millions of women - now live 30-40% of their life after menopause

- 8 / 10 women > > > peri-menopausal symptoms
  - Hot flushes and night sweats
  - ~ last about 4 years
  - QoL severely affected

- 25% women with severe menopausal symptoms

- SWAN study arms – symptomatic average 7 years, but up to 12 years....

3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3185240/
Rationale HRT Prescribing

• HRT Risks and benefits
  • NICE NG23 menopause guidance
  • Benefits
    • Vasomotor symptom control
    • Bone protection / osteoporosis and fracture prevention
    • Sleep
    • Low moods / anxiety
    • Sexual health ........role of testosterone [off license; NICE NG23]
  • Risks
    • Breast cancer
    • Strokes / Thrombosis
      • Other ... based on patient’s medical history eg unstable diabetes; thyroid dysfunction; POI.......
  • CHD?
Hormone Replacement Therapy

• HRT Risks and Benefits


• For women between 50-60.....?65
  • Data for added risk calculated over 7.5 years HRT use...
    • Breast cancer
    • CVD – thrombosis and strokes
    • Osteoporosis* [* 3-5 years]

Premature Ovarian Insufficiency [POI]
Measure FSH levels 4-6 weeks apart; if levels over 30 > Premature Ovarian Failure [NICE NG23]

Systemic cyclical circulation
- Estradiol [17b estradiol]
- Natural progesterone

HRT
- physiological replacement
- 17b estradiol / estradiol salts
- Natural progesterone
  - Progestogens
    - C19 testosterone analogues
    - C21 progesterone analogues
    - Natural progesterone
Age Related Changes in Bone Mass

Osteoporosis = loss of bone density?

“Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture.”

The LNWUHT Mid-life Womens Health
- Symptom Assessment Chart

With permission
### Table: Hormone Replacement Therapy (HRT)

MIMS : 1 April 2020  
Last updated 1st April 2020: added Lenzetto

<table>
<thead>
<tr>
<th>Type</th>
<th>Brand</th>
<th>Oestrogen</th>
<th>Progestogen</th>
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<th>Bleed</th>
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**Progestogens:**

- **C19 Testosterone analogues**  
  - Norethisterone  
  - Levonorgestrel

  - Androgenic side effects
  - Libido and energy affect?
  - Bones?
  - Better choice for bleed control

- **C21 Progesterone analogues**  
  - Dydrogesterone
  - Medroxyprogesterone

  - Dydrogesterone – Insulin Resistance; lipid markers?; no affinity for androgen receptors
  - MPA – some affinity for androgen receptors

- **Natural progesterone / UtrogestanRx or GepretixRx**

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**Estrogen throughout month with Progesterone for half the month**

**Initial transient side effects**
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<th>Type</th>
<th>Brand</th>
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LNMP = 1 year or more > Postmenopausal > can be prescribed CCT HRT .......can take upto 4-6 months to settle....
<table>
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<th>Type</th>
<th>Brand</th>
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<th>Progestogen</th>
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<td>Selective oestrogen receptor modulator</td>
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</table>

**Tibolone** > breaks up into 3 isomers – estrogen, progesterone and androgen receptor affinity
- Licensed for PM women ....> alternative ‘no-bleed’ HRT option

**Ospemifene** – new product; licensed for moderate to severe symptomatic vulvar and vaginal atrophy / PM women / ? tried vaginal ERT
<table>
<thead>
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<th>Type</th>
<th>Brand</th>
<th>Oestrogen</th>
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HRT in women with subtotal hysterectomy

• Limited evidence to guide practice.

• Common practice
  • consider sequential progestogens for up to 3 months
  • if no bleeding is noted with this regimen, then it is unlikely that any residual endometrium is present
    • then........oestrogen only HRT can be considered as sufficient.

• Ongoing progestogen intake should be considered
  • With any concerns that the remnant cervical stump may contain residual endometrial tissue in women who experience cyclical bleeding with sequential HRT.

Reference: BMS tools for clinicians: Progestogens and endometrial protection. H Hamoda on behalf of the BMS medical advisory council. Post Reproductive Health 2022(28)1: 40-46
HRT in women with endometriosis:

• CCT should be considered in women following hysterectomy for severe endometriosis
  • to prevent reactivation of residual disease and potentially prevent malignant transformation of residual deposits.

• Limited evidence to guide practice.

Reference: BMS tools for clinicians: Progestogens and endometrial protection. H Hamoda on behalf of the BMS medical advisory council. Post Reproductive Health 2022(28)1: 40-46
HRT in women with endometrial ablation:

• Combined HRT regimens (SCT or CCT as appropriate) in women with endometrial ablation wishing to take HRT

Reference: BMS tools for clinicians: Progestogens and endometrial protection. H Hamoda on behalf of the BMS medical advisory council. Post Reproductive Health 2022(28)1: 40-46
<table>
<thead>
<tr>
<th>Type</th>
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<th>Oestrogen</th>
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Noriday POP 350mcg
(i) 3 daily = 1050 mcg / Norethisterone 1 mg  effective for endometrial protection
(ii) FRSH guidelines > SCT HRT with POP [eg Noriday 350mcg daily] = HRT plus contraception

Mirena IUS – licensed for menorrhagia, contraception and the progestogen component of HRT

Utrogestan – natural progesterone / SPC queries
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**Prasterone pessary** - licensed for vulvar and vaginal atrophy
- biochemically and biologically identical to endogenous DHEA [dehydroepiandrosterone] – converted to oestrogens and androgens....
Prescribing and Supply Issues

• **Serious Shortage Protocols** [Feb 2019 - 2023] > ........................................> Community Pharmacy [nhsbsa.nhs.uk]

• **Oestrogel Rx Plus Utrogestan Rx ........**

• **Transdermal estrogen**
  • Thrombosis risk lower
  • NICE NG23 > with BMI over 30 or some thrombosis risk element ...

• **Natural progesterone**
  • Maybe more breast safe [IMS; BMS guidance]
    • Background ageing related breast cancer risk
      • NHS mammography screening program plus advise self breast exams
      • FH / genetic risk eg with young women with BRCA gene mutation
      • Bleed control issues?

• **Patients need to know**
  1. With use of HRT there is increased exposure to female hormones
  2. We can consider safer options with an individualised risk benefit evaluation
  3. Holistic management plan very important [exercise; weight control; diet; stress relief ....]
- The SOGC Statement on the WHI Report on
- Estrogen & Progestin Use in Post Menopausal Women

- Oct 2002 Volume 24 Number 10 JOGC
Clinical practice paper
Kennedy B et al. Post Reproductive Health 2023;29(3):143-147

- FAQs
  - **Testosterone prescribing [NICE NG23 off-label prescribing]**
    - Clinician Tool – BMS website
    - PIL – Women’s Health Concern Website
  - HRT post-breast cancer diagnosis
  - HRT with FH of breast cancer or cardiovascular risk
  - HRT and Migraine
  - Perimenopausal contraception
  - **Oestradiol approximate equivalent doses**
    - BMS website; NHSE Menopause side effects section
  - HRT and gall bladder disease / and epilepsy
  - Local vaginal oestrogen options
  - Premature Ovarian Insufficiency POI
UtrogestanRx case study

Summary Product Characteristics

• License: For adjunctive use with estrogen in post-menopausal women with intact uterus, as HRT regimen
  • Postmenopausal: 6 months bleed free

• Gestagenic, antiestrogenic, slightly anti-androgenic, anti-aldosterone effects

• Elimination half-life 16.8+/- 2.3 hrs; higher systemic levels if taken with food; Cause drowsiness and dizziness
  • > Take at bedtime, not with food

• Dosage recommendation
  • 200mg at bedtime daily D15-D26 of cycle, bleed expected following week
    • If breakthrough bleed persists [after settling in period of few months]
      • 100mg at bedtime D1-D25, withdrawal bleed less
Utrogestan\textsuperscript{Rx} case study

**Best practice**

- **Perimenopausal**
  - Daily Estradiol with Utrogestan 200mg D15-26 of each cycle
  - …….or with Utrogestan 100mg D1- D25 of cycle?

- **Postmenopausal**
  - LNMP of 1 year ; atrophic static endometrium
    - Daily Estradiol with Utrogestan 100mg daily at bedtime
    - Qs
      - Should we advise Utrogestan 200mg for endometrial protection with higher estradiol dose
      - For h/o menorrhagia – should we advise change to C19 progestogens options / Mirena IUS?
      - Dealing with patient requests for bio-identical hormones [Use BMS consensus leaflet]; wanting same combination being used by a well-known journalist; etc....
Acknowledgement:
My thanks to Miss Joan Pitkin, Consultant Gynaecologist and Lead for the Menopause Service at LNWH [now retired ....]

For
• Academic clinical supervisor
• Superb mentorship whilst we were developing the Menopause MMC service
Practical HRT Prescribing

• Questions?

• Thank you!

Dr Nuttan Tanna
nuttantanna@nhs.net
Case study 1

31 year old patient with LNMP of 2 years; since starting menarche always had infrequent cycling. Has had investigations and had been diagnosed with premature ovarian failure.

For discussion:

• Undertake HRT risk benefit evaluation for this patient and describe your management plan

• What HRT regimens would you recommend to this patient

• List lifestyle interventions for patient
Case study 2

51 year old patient with vasomotor symptoms and erratic bleeding profile. DEXA reports osteopenia at spine site (T score -2.1)

For discussion:
• Undertake HRT risk benefit evaluation for this patient and describe your management plan

• What HRT regimens would you recommend to this patient

• List lifestyle interventions for patient
Clinical risk factors for fragility fracture
Another important Q..................or 2....

• How long can you carry on, on vaginal ERT?
  • GINA 10 mcg? - Product license

• What alternative prescribed options can you recommend for vasomotor symptom control?
  • Is there a non-pharmacological option for patients to consider that is evidence based? – NICE NG23 2015, to be updated 2024