

QUICK GUIDE

Simplifying HRT for menopause.

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Introduction

HRT prescribing can seem bewildering with a vast variety of preparations and modes of delivery available.

Here we try to simplify the process of prescribing HRT with a basic guide. Treatment should be individualised to suit the likes and preferences of the patient whilst balancing the benefits and risks of HRT, as well as considering underlying risk factors and any other medical conditions.^{1,2}

STEP 1: Oestrogen

- Women who are postmenopausal are lacking oestrogen, so it is given to raise blood oestradiol level and help symptoms.³
- Women who are perimenopausal have fluctuating levels of oestrogen.⁴

Mode of delivery:

- Oestrogen can be given as a tablet or as a patch, gel, or spray.⁵
- Most oestrogen therapy is now 'body-identical' estradiol rather than conjugated equine oestrogens' (e.g., Premarin⁶, Premique⁷).
- Transdermal estradiol is unlikely to increase the risk of VTE or stroke above that of nonusers of HRT and should be considered first line especially in women with risk factors for these conditions.^{1,8}
- Oestrogen can be given combined with a progestogen in a patch or tablet, or alone with a separate progestogen.⁵
- The preparation used depends on patient choice:
 - Oestradiol gel:
 - Easy for patient to adjust dose.^{9,10}
 - Some women find it messy and inconvenient.⁹
 - Oestradiol patch
 - Fixed dose so not as easy to adjust as gel or spray.^{9,10}
 - Can be given combined with a transdermal progestogen⁵ (e.g., Evorel Conti/Sequi¹¹).
 - Some women find patches more convenient than daily application.⁹
 - Can cause skin irritation or fall off.^{9,10}
 - Vary widely in size: Estraderm > Evorel > Estradot.¹²

– Oestradiol spray

- Less messy than gel, absorbed quickly, and dose can be easily adjusted.⁹
- Maximum licensed dose often not enough for some women, as noted by O. Hum, Dr (email correspondence, April 2024), and may not be as suitable for those who may need a higher dose.¹³

– Oral oestradiol

- Some people do not absorb transdermal preparations well so may find this more effective.¹⁴
- Avoid in women at high risk of VTE or stroke¹, or with migraine with aura.¹⁵

STEP 2: Progestogen

Terminology:

- A progestin is an artificial progesterone¹⁶ (e.g., desogestrel¹⁷, norethisterone¹⁸).
- Micronised progesterone is 'body-identical' and identical in structure to the 'natural' progesterone produced by menstruating women¹⁹ (e.g., Utrogestan²⁰, Gepretlix²⁰)

Purpose:

- Progestogens are needed to protect against endometrial stimulation from unopposed oestrogen.²¹
- Giving oestrogen to a woman with a womb without adequate progestogen will increase their risk of endometrial hyperplasia and endometrial cancer.²¹

Mode of delivery:

- Progestogens can be given combined with oestradiol in tablets or patches OR given separately alongside oestradiol.
- Stand-alone progestogens:
 - 52 mg LNG-IUD:
 - The Mirena coil is the only licensed 52 mg LNG-IUD for endometrial protection.²¹
 - It is licensed up to 4 years, but analysis of current evidence has led to both the BMS and FSRH advising that it can safely be used up to 5 years.²²
 - The FSRH have agreed that any 52 mg LNG-IUD can be used for endometrial protection.²²
 - Provides contraception, treats menorrhagia, good at controlling unscheduled bleeding but unacceptable to some women.²²
 - Kyleena and Jaydess cannot be used alone for endometrial protection.²²

Continued overleaf →

- **Micronised progesterone:**
 - Often better tolerated with fewer side effects than artificial progestogens^{23,24}
 - Can be used vaginally (off license) at the same dose as oral: this often eliminates any side effects although there is limited evidence assessing the efficacy.²¹
 - Thought to give a lower breast cancer risk compared with synthetic progestins.²⁴
- **Artificial progestogens**
 - Other progestins can be used for endometrial protection either combined with oestradiol or separately
 - Dydrogesterone may have a lower risk of breast cancer than the other progestins.
 - Single dose desogestrel (75 mg), depot contraception or implant should not be used as endometrial protection alongside oestrogen.²²
- **Sequential or continuous?**
 - If a woman has had a period within the last year, then the progestogen is given **sequentially (cyclically)** for 12-14 days a month.²¹
 - If a woman has not had a period in the last year (either because she is postmenopausal or because she is on hormonal contraception that stops her periods) then the progestogen is given **continuously (every day)**.²¹
- The dose of progestogen **must** be proportional to the dose of oestrogen to achieve adequate endometrial protection.
- When to switch to continuous from sequential:
 - When you think that the woman might be postmenopausal
 - If over 50 years old and has been on HRT for over a year
 - If withdrawal bleeds cease on sequential HRT
 - If over 55
 - If under 50 but periods were very sparse before starting HRT

STEP 3: Always ask about

- 1) Contraception:**
 - HRT preparations are not contraceptive.²²
 - If a woman, over 50 years of age, who is not taking hormonal contraception has been amenorrhoeic for over a year then contraception can be safely stopped.²²
 - If a woman is on HRT, it is difficult to tell when to stop contraception, so it is recommended to continue until aged 55.²²
- 2) Vulvo-vaginal and urinary symptoms**
 - About 50% of postmenopausal women will have symptoms of genitourinary syndrome of menopause (GSM): vaginal dryness or burning, painful intercourse, dysuria, urinary urgency, or incontinence, recurrent urinary tract infections (UTIs).^{1,24}
 - Vaginal oestrogen preparations can be prescribed alongside systemic preparations.⁸
 - If vaginal oestrogen is used **alone** no progestogen is needed for endometrial protection.⁸
 - Available as gels, creams, pessaries, and rings.⁸
 - GSM is chronic and progressive²⁵; treatment needs to be adequate in dosing and can be continued lifelong.^{8,24}

STEP 4: Review

- 3 months after starting, then annually.²
- At each review: assess effectiveness and side effects, review type and dose, discuss risk/benefit balance of continuing, check concordance with treatment, ask about bleeding, ask about GSM symptoms.⁸

Duration of use:

- Arbitrary limits should not be placed on the duration of usage of HRT.⁸
- Risk/benefit balance of continuing should be discussed each year and a shared decision made with respect to whether to continue or stop HRT.⁸

For more guidance about when to stop contraception use the FSRH guidance on contraception for women aged over 40 years



References

- 1 BMS, WHC. Recommendations on HRT. 2023. Accessed April 15, 2024. <https://tinyurl.com/4ahd5tuf>
- 2 NICE. Menopause: Diagnosis and Management NG23. 2023. www.nice.org.uk/guidance/ng23
- 3 NHS. Menopause treatment. Published 2022. Accessed April 15, 2024. <https://tinyurl.com/47ze5tuj>
- 4 NHS. Symptoms: Menopause. Published 2022. Accessed April 12, 2023. <https://tinyurl.com/4mecdtaj>
- 5 BMS. HRT – Practical Prescribing. 2022. Accessed April 15, 2024. <https://tinyurl.com/42h98j73>
- 6 NICE, BNF. Conjugated estrogens. Published 2024. Accessed April 15, 2024. <https://tinyurl.com/2p8rsdpa>
- 7 NICE, BNF. Conjugated oestrogens with medroxyprogesterone. Published 2024. Accessed April 15, 2024. <https://tinyurl.com/mr3s245y>
- 8 BMS. HRT Guide. 2022. Accessed April 15, 2024. <https://tinyurl.com/77ks5u5r>
- 9 Kopper NW, Gudeman J, Thompson DJ. *Drug Design, Development and Therapy*. 2008;2:193–202
- 10 NHS. Types: Hormone replacement therapy. Published 2019. Accessed April 15, 2024. <https://tinyurl.com/4sfbzw8p>
- 11 NICE, BNF. Estradiol with norethisterone. Published 2024. Accessed April 15, 2024. <https://tinyurl.com/2dha9vs4>
- 12 NICE, BNF. Estradiol. Published 2024. Accessed April 15, 2024. <https://tinyurl.com/ms4juewa>
- 13 BMS. Unscheduled Bleeding. 2024. Accessed April 22, 2024. <https://tinyurl.com/3kkrec8z>
- 14 Bird D, Ravindra NM. *Med Devices Sens*. 2020;3(6). doi:10.1002/mds3.10069
- 15 WHC. Migraine and HRT. 2023. Accessed April 15, 2024. <https://tinyurl.com/5262zkaw>
- 16 Garcia-Sáenz M, Ibarra-Salce R, Pozos-Varela FJ, et al. *J Clin Med*. 2023;12(10). doi:10.3390/jcm12103388
- 17 BNF. Desogestrel. Published 2024. Accessed April 15, 2024. <https://tinyurl.com/y2fm2pe7>
- 18 BNF. Norethisterone. Published 2024. Accessed April 15, 2024. <https://tinyurl.com/y8f783kx>
- 19 Asi N, Mohammed K, Haydour Q, et al. *Syst Rev*. 2016;5(1):121. doi:10.1186/s13643-016-0294-5
- 20 BNF. Progesterone. Published 2024. Accessed April 15, 2024. <https://tinyurl.com/37wrat3r>
- 21 BMS. Progestogens and Endometrial Protection. 2021. Accessed April 15, 2024. <https://tinyurl.com/33u2a5pw>
- 22 FSRH. Contraception for Women Aged over 40 Years. 2023. Accessed April 15, 2024. <https://tinyurl.com/y7m7jbnw>
- 23 Regidor PA. *Geburtshilfe Frauenheilkd*. 2014;74(11):995–1002. doi:10.1055/s-0034-1383297
- 24 Hamoda H, Panay N, Pedder H, et al. *Post Reprod Health*. 2020;26(4):181–209. doi:10.1177/2053369120957514
- 25 Angelou K, Grigoriadis T, Diakosavvas M, et al. *Cureus*. 2020;12(4):e7586. doi:10.7759/cureus.7586