NHS
Bath and North East Somerset, Swindon and Wiltshire
Integrated Care Board

MOP UP.

Medicines Optimisation Update
August 2023

To contact NHS BSW ICB Medicines Optimisation Team:
✉ bswicb.prescribing@nhs.net Website: https://bswtogether.org.uk/medicines/

****MOP UP Special Edition – HRT****

This special edition of MopUp newsletter summarises some recent local and national updates for the management of menopause.

Has your practice prescribed unopposed oestrogen to women with a uterus in error? Shared Learning from Medication Safety Events

Locally, several GP practices have identified prescribing errors where women with a uterus have received prescription for oestrogen only HRT without a progestogen. In women with a uterus, progestogen is required alongside oestrogen to adequately protect the endometrium against hyperplasia, a risk factor for endometrial cancer. The increase in this error could be due to numerous factors e.g., increased prescribing of separate oestrogen and progestogen products, increased prescribing of HRT, medicines shortages, patients misunderstanding of the requirements for progestogen to oppose the effects of oestrogen on the endometrium, expired Mirena coil etc.

In the absence of national consensus guidance on how the risk of endometrial hyperplasia from this error should be managed, women with a uterus identified as having received unopposed oestrogen should be discussed on a case-by-case basis with the local specialist team.

Some practices have audited prescribing of oestrogen only HRT to identify women who are receiving it without a progestogen in error. A useful search to support an audit can be found in Arden's here: '*Arden's Ltd - Prescribing | Alerts – Women's Health (20) – On oestrogen | Stop only HRT as has uterus and no LNG-IUS.*' Please note that in addition to the error, this search may identify women who are in fact receiving the correct prescription but coding within the clinical system needs updating e.g., hysterectomy or Mirena coil in situ.

Prescribers are encouraged to use the Arden's template found under 'Auto-Consultation – *Ardens FORMULARY H-N – Menopause*. The template helps prompt prescribers to consider key variables when prescribing and reviewing HRT prescription and ensure that correct clinical system read coding is in place.

The ICB Medicines Optimisation Team will be amending the default directions which appear within SystmOne to '***If you have a womb, you will also need a form of progesterone (could be a pill, patch or coil) to protect against thickening of the womb lining that can be caused by HRT***.' A related Arden's support article is here Note the searches highlighted within this article are similar but not as broad as the suggested search for audit highlighted above, as they assume that a progestogen is on repeat but not being ordered.

British Menopause Society (BMS) Guidance on progestogens and endometrial protection can be found here https://thebms.org.uk/wp-content/uploads/2021/10/14-BMS-TfC-Progestogens-and-endometrial-protection-01H.pdf

A related Joint Safety Alert by the BMS, FSRH, RCGP, RCOG, SfE and RCN Women's Health Forum was published recently Joint BMS FSRH RCGP RCOG SfE and RCN Women's Health Forum safety alert - British Menopause Society (thebms.org.uk)

Please Share Learning from Medication Safety Events you Identify.

Sharing learning from medication safety events and recording events on the national Learn from Patient Safety Events (LFPSE) service helps improve patient safety by raising awareness and prompting local and national actions/alerts to mitigate the risks identified. **If you'd like to share your learning from a medication safety event, get in touch via bswicb.prescribing@nhs.net and mark for the attention of the Medication Safety Team.**

Learn from patient safety events (LFPSE) is the new service replacing the National Reporting and Learning Service (NRLS). Find out about LFPSE for primary care here Register for an account to report safety events here (remember to add the sign in page to your favourites). Or you can report anonymously here.

Appropriate doses of oestrogen and progestogen for treating symptoms of menopause.

If you haven't seen it yet, Joint BMS FSRH RCGP RCOG SfE and RCN Women's Health Forum safety alert - British Menopause Society (thebms.org.uk) raises awareness of the increasing number of women being initiated on high doses of oestrogen which exceed the product licenses, not in line with any clinical guidelines.

We remind clinicians that higher oestrogen doses should only be initiated by a specialist. Good practice in prescribing medicines outside the terms of their licence, must be followed and documented, as per the GMC guide here. In addition, the dose of progestogen should be increased proportionately and it is the responsibility of the specialist to advise on this. Primary care clinicians are under no obligation to take on prescribing outside of product licenses if they do not feel sufficient information has been provided or if they are not in agreement with the treatment pathway.

Levonorgestrel intrauterine devices (LNG-IUDs) as part of HRT

Mirena® is the only LNG-IUD licensed in the UK for progestogenic opposition of oestrogen as part of HRT. Mirena® has a four-year licence for this indication but studies have shown it to be effective and to offer sufficient endometrial protection up to five years within HRT regimens. **The BMS & FSRH support the use of Mirena® or other higher dose (52 mg) LNG-IUD for endometrial protection as part of HRT for 5 YEARS** (outside manufacturer's license).

Practices are reminded to:

- **Check progestogen is adequate** - Low dose LNG-IUDs (Jaydess® 13.5 mg and Kyleena® 19.5 mg) licensed as contraceptives do not give adequate endometrial protection for HRT indication.
- **Ensure robust systems and processes are in place for recalling patients for review/removal of LNG-IUD.** Duration of use will vary depending on the brand of LNG-IUD used and the indication (contraception and/or HRT)
- **Ensure the correct indication is documented within the patient records.** If a patient has a Mirena® or other higher dose (52mg) LNG-IUD sited for contraception which is then transferred to cover provision of progestogen for an HRT regimen, ensure the documented recall date for review/removal of the LNG-IUD is updated accordingly to a maximum of 5 years from the date the LNG-IUD was sited.
- **Check the patient knows the indication for the LNG-IUD and the correct date it is due for review/removal.**

Summary Table below taken from FSRH Clinical Guideline: Intrauterine contraception (March 2023, Amended July 2023)

Table 2 compares the product characteristics of LNG-IUD devices currently available in the UK.

Table 2: Types of levonorgestrel intrauterine device listed in the British National Formulary*

Parameter	Type of LNG-IUD				
	Benilexa®	Levosert®	Mirena®	Kyleena®	Jaydess®
Total LNG content (mg)	52	52	52	19.5	13.5
LNG release rate (mcg/24 h) Initial At end of licensed use	 20.1 8.6	 20.1 8.6	 20 9	 17.5 7.4	 14 5
Frame size (W x L, mm)	32 x 32	32 x 32	32 x 32	28 x 30	28 x 30
Inserter	One-handed inserter	Two-handed inserter	One-handed Evolnserter™	One-handed Evolnserter™	One-handed Evolnserter™
Insertion tube diameter (mm)	4.8	4.8	4.4	3.8	3.8
Silver ring for improved visibility on USS?	No	No	No	Yes	Yes
Colour of threads	Blue	Blue	Brown	Blue	Brown
Recommended duration of use for contraception (years)†	6	6	6	5	3
Licensed duration of use for contraception (years)	6	6	5	5	3
Recommended duration of use for endometrial protection as part of HRT (years)‡	5	5	5	Not recommended	Not recommended
Licensed for endometrial protection?	No	No	Yes	No	No
Licensed for HMB?	Yes	Yes	Yes	No	No
Minimum uterine cavity length (cm)	5.5	5.5	Not indicated in SPC	Not indicated in SPC	Not indicated in SPC

HMB, heavy menstrual bleeding; HRT, hormone replacement therapy; L, length; LNG, levonorgestrel; LNG-IUD, levonorgestrel intrauterine device; SPC, Summary of Product Characteristics; USS, ultrasound scan; W, width.

*See British National Formulary (BNF) (checked on 14/03/2023).
†The FSRH supports use of any 52 mg LNG-IUD for 6 years for contraception.
‡The FSRH supports use of any 52 mg LNG-IUD for 5 years for endometrial protection as part of HRT.

For further guidance on LNG-IUD as part of HRT also see Mirena 20 micrograms/24 hours intrauterine delivery system - Summary of Product Characteristics (SmPC) - (emc) (medicines.org.uk) and https://thebms.org.uk/wp-content/uploads/2021/10/14-BMS-TfC-Progestogens-and-endometrial-protection-01H.pdf

Formulary and Traffic Light Status update for progestogens for HRT

For women using separate oestrogen (e.g. Evorel, Esradot, Oestrogel, Sandrena, Lenzetto, Elleste solo) BSW first line formulary options for progestogenic opposition are:

- Levonorgestrel Intrauterine System (Mirena coil)
- Micronised progesterone (Utrogestan 100mg oral capsules)

But, due to current supply problems with Utrogestan, DHSC recently issued a Medicines Supply Notification and a Serious Shortage Protocol is in place. Read more here.

The BMS have issued a statement regarding progestogen supply. Options include switching women to Evorel Sequi/Conti or FemSeven Conti or to change eligible, otherwise healthy women, to oral HRT. This will allow access to micronised progesterone in Bijuve and dydrogesterone in the Femoston product range, which comes in different doses and both sequential and continuous combined preparations.

The BMS also advise on further alternative options for endometrial protection. **These recommendations may be outside of product licence. Good practice in prescribing medicines outside the terms of their licence, must be followed and documented, as per the GMC guide here**. These include norethisterone, [for women with a BMI less than 30] and medroxygesterone acetate. The exact dose of either drug will depend on the dose of estrogen prescribed and recommendations can be found in the BMS Tools for Clinicians: Progestogens and endometrial protection.

Cyclogest 200 mg, Utrogestan vaginal pessaries 200 mg and Lutigest 100 mg vaginal pessaries are also discussed but the BMS statement notes these formulations "*may not be available from the majority of NHS GPs*". **These are not licensed for endometrial protection** and have historically been assigned RED Traffic Light Status in BSWformulary because they are routinely used in fertility and miscarriage indications by specialists under expert supervision. These vaginal products have now been assigned an **AMBER Traffic Light Status for HRT indications** but may ONLY be considered for prescribing in primary care on the advice of a consultant, and on an exceptional basis to meet the specific needs of an individual patient and for the minimum time necessary. Primary care clinicians are under no obligaton to take on prescribing outside of product licences.

HRT Pre-Payment Certificate (PPC) – Provera (for information)

As per a response to a practice query re branded medroxyprogesterone please see DoHCSC advice :-

I can confirm that generic versions of the listed HRT products are covered by the HRT PPC, providing the prescription is ***written generically****. As it is not possible to determine the indication for a prescription written generically, we have updated the wording in Part XVI (Section X) of the Drug Tariff to make this clearer,* ***from 1 August*** *it will read:*

"Generic versions of the products listed below are also covered by the HRT only PPC, provided the ***prescription is written generically****."*

We are aware that there is not currently a generic medroxyprogesterone product, only Climanor, which is discontinued. We understand that the most commonly used alternative is Utrogestan which is already listed for inclusion. If a prescription is written specifically for **Provera (of any strength) it is not in scope** for the HRT PPC.

For clinicians interested in developing their skills in the management of menopause:

CPPE Learning Gateway – Menopause Menopause (cppe.ac.uk)

British Menopause Society - Education
https://thebms.org.uk/education/overview/

Primary Care Women's Health Forum - Menopause
https://pcwhf.co.uk/resources/?_sft_learning_pathway=menopause

NHS website adds HRT to its Medicines A-Z

Guides to the use of HRT and material to support patients using oral, topical and vaginal oestrogens, micronized progesterone, continuous HRT, sequential HRT and tibolone have been published on the NHS website.