FSRH CEU Statement: Mirena® 52mg LNG-IUD: extension of licence for contraception to 8 years
10th January 2024

The Mirena® 52mg LNG-IUD has now been licensed for 8 years for contraception.[1]

The United Kingdom Medicines Health Regulatory Authority (MHRA) has approved an extension to the Mirena licence from 5 years to 8 years for contraception. There has not been an extension to the licensed duration of use when being used for the management of heavy menstrual bleeding, or for endometrial protection as part of hormone replacement therapy (HRT).

What evidence is available for contraceptive effectiveness in the 7th and 8th years of use?
In 2022, Jensen et al. reported data from the Mirena Extension Trial. Established Mirena users aged 18-35 years were recruited into this multi-centre, single-arm, phase III trial to assess contraceptive effectiveness in years 6 through 8 of Mirena use. One pregnancy (which was ectopic) occurred in year 7 and no pregnancies occurred in year 8. The pooled Pearl Index (PI; pregnancies per 100 woman-years) was 0.40 (95% CI 0.01–2.25) in year 7 and 0.00 (95% CI 0.00–1.90) in year 8; however, numbers were small with only 243 and 223 individuals completing 7 and 8 years of use respectively.[2]

A systematic review[3] from 2020 included four good-to-poor-quality studies of 52 mg LNG-IUDs, with a total of 2098 users extending use beyond 5 years from insertion. The pooled PI was 0.03 (95% CI 0.00–0.71) in year 7. These low failure rates were comparable to those within the licensed duration of use. The authors noted the data were of limited quantity and quality, and often contained scant demographic data (notably age, which would affect background risk of pregnancy).

A review[4] by Wu et al. (2014) reported on much earlier and smaller studies (<100 women). In these studies, no pregnancies were observed in years 6 and 7 of 52mg LNG-IUD use but the review authors stated that the evidence for individuals who are overweight, have obesity or are aged under 25 years was less robust.

The above evidence was considered when the FSRH Clinical Guideline: Intrauterine contraception (March 2023) was developed and led to the recommendation that a Mirena inserted before age 45 years can be used for contraception for 6 years.[5] Whilst the low failure rates in years 7 and 8 were noted, the Guideline Development Group did not determine the evidence to be robust enough, in the context of a 5 year licence, to recommend extending use up to 8 years.

Are there any adverse effects associated with extended use of Mirena?

During years 6-8 of the Jensen study, 31 participants (8.5%) withdrew due to adverse events. The study does not stratify the years in which the events occurred; however, complication rates were low in keeping with studies observing IUC use during licensed durations. Adverse events leading to discontinuation included pain (9, 2.5%), bleeding (11, 3%), expulsion (5, 1.4%), embedded device (1, 0.3%), perforation (3, 0.8%), vaginal infection (1, 0.3%), and other = (8, 2.2%). Bleeding patterns remained similar throughout the 3 years.

Other IUDs are already routinely used for ≥8 years and it is established practice that any 52 mg LNG-IUD inserted at age ≥45 years can be used for contraception until age 55 years. Current clinical experience of extended use does not suggest an increase in adverse events.

How does this affect practice?

- Users of the Mirena 52mg LNG-IUD can now be advised that the device can be used as contraception for 8 years. This also applies to individuals who already have a device in-situ.
- There are no changes to the established FSRH and British Menopause Society recommended duration of use when a Mirena 52mg LNG-IUD is being used for endometrial protection as part of HRT (5 years from time of insertion) or to existing guidance about duration of use of Mirena for heavy menstrual bleeding.

FSRH CEU will be convening an expert group to consider whether this extended use advice can/should be applied to other 52mg LNG-IUD devices, other than Mirena. Currently there is no change to the recommendations for the other LNG-IUDs (see table below for summary). Once a decision has been made, FSRH CEU guidelines and guidance documents will be updated to align with the new recommendation(s).

Type of levonorgestrel-releasing intrauterine device	Mirena	Levosert Benilexa	Kyleena	Jaydess
Total LNG content (mg)	52	52	19.5	13.5
Recommended duration of use for contraception (individuals age <45 years at time of insertion)	8 years	6 years	5 years	3 years
Recommended duration of use for contraception (individuals age ≥45 years at time of insertion)	Until age 55	Until age 55	5 years	3 years
Recommended duration of use for endometrial protection as part of HRT	5 years*	5 years**	Not suitable for this indication	Not suitable for this indication

*Note that the Mirena licensed duration of use for endometrial protection as part of HRT is 4 years, however FSRH supports use of any 52mg LNG IUD for endometrial protection as part of HRT for 5 years.

**Levosert and Benilexa are not licensed for endometrial protection as part of HRT, however FSRH supports use of any 52mg LNG IUD for endometrial protection as part of HRT for 5 years.

References

1. eMC. Bayer plc. Mirena 20 micrograms/24 hours intrauterine delivery system. Last updated on emc: 08 Jan 2024. Available online: https://www.medicines.org.uk/emc/product/1132 (accessed 10/01/2024)
2. Jensen JT, Lukkari-Lax E, Schulze A, Wahdan Y, Serrani M, Kroll R. Contraceptive efficacy and safety of the 52-mg levonorgestrel intrauterine system for up to 8 years: findings from the Mirena Extension Trial. American journal of obstetrics and gynecology. 2022 Dec 1;227(6):873-e1.
3. Ti AJ, Roe AH, Whitehouse KC, Smith RA, Gaffield ME, Curtis KM. Effectiveness and safety of extending intrauterine device duration: a systematic review. American journal of obstetrics and gynecology. 2020 Jul 1;223(1):24-35.
4. Wu JP, Pickle S. Extended use of the intrauterine device: a literature review and recommendations for clinical practice. Contraception. 2014 Jun 1;89(6):495-503.
5. Faculty of Sexual & Reproductive Healthcare. Clinical Guideline *Intrauterine Contraception*. March 2023 (amended July 2023). Available online: https://www.fsrh.org/standards-and-guidance/documents/ceuguidanceintrauterinecontraception/ (accessed 10/01/2024)

The Clinical Effectiveness Unit (CEU) was formed to support the Clinical Effectiveness Committee of the Faculty of Sexual & Reproductive Healthcare (FSRH), the largest UK professional membership organisation working at the heart of sexual and reproductive healthcare. The FSRH CEU promotes evidence based clinical practice and it is fully funded by the FSRH through membership fees. It is based in Edinburgh and it provides a members' enquiry service, evidence-based guidance, new SRH product reviews and clinical audit/research. Find out more here.