FSRH CEU Statement: Extended use of all 52mg LNG-IUDs for up to eight years for contraception

Following the change in licence of Mirena® to eight years[1], the CEU have reconvened the Intrauterine Contraception (IUC) Guideline Development Group (GDG) to consider the extended use of all 52mg LNG-IUDs to eight years for contraception. Overall, whilst the evidence is limited, the GDG felt there was sufficient evidence to make the following recommendations.

Recommendations

The FSRH IUC GDG support extended use of any 52mg LNG-IUD for up to eight years for contraception if the user is under 45 years old at the time of insertion.

There is insufficient evidence to support use of any 52mg LNG-IUD beyond eight years for contraception. If an individual presents for replacement of the device after eight years, criteria for reasonably excluding pregnancy must be met, as per FSRH guidance[2].

Key points

- The available evidence has shown a low pregnancy rate (Pearl Index <0.4) in individuals using a 52mg LNG-IUD between years six and eight for contraception.
- The limited evidence does not show an increase in bleeding in women who continue to use the 52mg LNG-IUD beyond six years.
- There is **no change** to existing guidelines regarding use of the 52mg LNG-IUD for heavy menstrual bleeding or endometrial protection.
- As per existing guidelines, if a 52mg LNG-IUD is inserted over the age of 45, it can be used for contraception until the age of 55.
- It must be noted that use of Benilexa® and Levosert® for eight years is off-label and prescribers should follow recommendations as set out in MHRA[3]/GMC[4] guidance and the recently updated FSRH Service Standards for Medicines Management[5].

The evidence

A systematic search of the literature identified two key studies (the Mirena Extension Trial [MET][6,7] and ACCESS IUS[8,9]), a systematic review[10] and two small observational studies[11,12] describing extended use of the LNG-IUD beyond six years.

The MET study enrolled 362 existing users of Mirena®, with a mean age of 29.4 (SD 3.1). Of these, 305 continued into year seven, 243 into year eight and 223 completed year eight. The mean age of those 223 participants who completed eight years was 29.6 (SD 2.9) at the start of the study, i.e. very similar to the mean age of the overall cohort at the start of year six.

The ACCESS IUS trial[8,9] enrolled 1,714 women using Liletta® (known as Benilexa® in the UK). Of the original cohort, 576 entered year seven, 477 entered year eight and 339 entered year nine,

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83 participants completed nine years and 77 participants completed ten years. The mean age of the 1,714 women at enrolment was 27.3 (SD 5.7) years.

A systematic review[10] (four studies, n = 82 to 601 at year seven) and two small observational studies[11,12] (n=46 to 67 at seven years) reported pregnancy rates, LNG levels and adverse events in women using the 52mg LNG IUD[a] for up to eight and a half years. Although numbers were small in the observational studies, they support findings from the MET[6] and ACCESS IUS[8,9] trials.

Effectiveness

The Pearl Index (pregnancies per 100 women years) was found to be consistently low across all studies, ranging from 0.03 (95% CI 0.00 to 0.71)[10] to 0.40 (0.01 to 2.25)[5] at seven years and 0 at eight years[6,8]. No pregnancies were reported after year six in the two observational studies[11,12].

Jensen et al 2023[7], estimated *in vivo* LNG release rates for the Mirena® of 21.6µg/d at insertion, reducing to 10.7µg/d at five years' use and 7.04µg/d at eight years' use. This is comparable to an estimated release rate of 7.4µg/d at five years for the Kyleena® (19.5mg LNG-IUD) and higher that the estimated release rate of 5µg/d at three years for the Jaydess® (13.5mg LNG-IUD)[13].

Safety and adverse events

One ectopic pregnancy was reported at six and a half years in the MET[6] trial and one ectopic pregnancy was reported in year seven of the ACCESS IUS[8] study.

There were no perforations reported during years seven to ten in ACCESS IUS[8,9], and a perforation rate of 1.1% was reported during years seven and eight of the MET[6]. Perforations were not reported by the other studies[10,11,12].

The expulsion rate was very low between years six to eight, ranging between 0 to 1.4% in the majority of studies and 0.3% across years nine and ten in the ACCESS IUS[9] study.

Rates of pelvic infection were low after year six, with two pelvic infections (0.3%) in the ACCESS IUS[8] study in years seven and eight. No pelvic infections were reported in the MET study[6], or in years nine and ten of the ACCESS IUS study[9].

Infection rates were variable in the other studies, with 0 to 3.2% (Ti et al[10]; type of infection not specified) 1.9% (MET[6]; treatment-emergent events classes as 'infections and infestations') to 14.1% (ACCESS IUS[8]; vulvovaginal mycotic infection or vaginal bacterial infection).

[a]The Hidalgo et al[12] study and one of the studies included within the Ti et al[10] systematic review (McNicholas et al[16]) used unspecified 52mg LNG IUDs. All other studies used the Mirena.

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Bleeding profiles

Overall, amenorrhoea rates remained consistent beyond six years of use, ranging from 18.3% (start of year six) to 33.6% (end of year eight) in the MET[6] trial and around 40% in years six to ten in the ACCESS IUS study[8,9]. Similar rates were reported by Hidalgo et al[12].

It should be noted that women continuing beyond the initial five-year period of use were likely to have been satisfied with their devices and bleeding patterns, so the data from these longer studies do not include those who discontinued due to problematic bleeding earlier on.

Overall, there was a very low rate of discontinuation due to bleeding in the years of extended use, with 0-3% discontinuing due to bleeding in most studies (MET[6], ACCESS IUS[8,9], Faúndes et al, Brazilian cohort[11], one study in the systematic review: Bahamondes et al[14]). Higher numbers (approximately 8.5%) discontinued due to bleeding in two of the smaller studies (Faúndes et al, Dominican Republic cohort[11]; one study in the systematic review: Rowe et al[15])

Return to fertility

In the MET study, it is stated that the 12-month return-to-fertility rate was 77.4%[6]. Return-to-fertility rates were not reported for any of the other studies.

Generalisability of evidence

The study findings relate mainly to individuals over 18 years old. There is no indication that any participants were under 18 in the ACCESS IUS study[8,9]. In the MET[6] trial eight of the 362 women were under 18, with a minimum age of 14. Approximately 10% of participants in the Faúndes et al study were under 20 years of age[11].

The MET[6] and ACCESS IUS[8,9] studies were large single-arm extension trials that provided non-comparative evidence. The MET[6] trial only included women who had already used a Mirena® for four and a half to five years and were happy to continue for up to eight years. The ACCESS IUS[8,9] study followed women from device insertion for up to 10 years, although only approximately 34% continued beyond six years. Therefore, generalisability to the wider population of LNG-IUD users may be limited.

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