New Medicine Policy Recommendation

Levonorgestrel 13.5 mg intrauterine delivery system (Jaydess®) ▼

Contraception for up to 3 years

Recommendation: Green (restricted)

Levonorgestrel intrauterine delivery system (IUS) (Jaydess®) is recommended as a contraceptive for up to 3 years, second line to Mirena, only for women who want periods or if there are problems inserting a Mirena.

Summary of supporting evidence:

The levonorgestrel 13.5 mg IUS is a progestogen-only LARC which is inserted into the uterine cavity within seven days of the onset of menstruation to provide contraception for up to three years. An average of 6 micrograms of levonorgestrel per 24 hours is released over this time.

Evidence:

- A phase III, open-label, randomised parallel-group study evaluated the safety and efficacy of levonorgestrel 13.5 mg IUS (n=1432) or levonorgestrel 19.5 mg IUS (n=1453) for three years.
- The primary outcome was the pregnancy rate, calculated as the Pearl Index (the number of pregnancies per 100 woman-years).
- A total of ten pregnancies occurred in the levonorgestrel 13.5 mg IUS group over the 3-year study (Pearl Index of 0.33 pregnancies per 100-woman years; [95% CI: 0.16 to 0.60]), four of which were as a result of expulsion of the system.
- The 3-year cumulative failure rate was calculated as 0.9% for the 13.5 mg levonorgestrel IUS. There were no major differences in pregnancy rates for each individual year of the three year study.
- Of the 74% (1053/1432) participants in the 13.5 mg levonorgestrel group surveyed either at the end of the study or at final study visit (for those who discontinued early), 95% were “very satisfied” or “somewhat satisfied” with treatment and 77% indicated they would have continued using the levonorgestrel IUS after the study. However, 27% of women did not complete the questionnaire and those who discontinued prior to the introduction of the survey were not captured by the results, therefore limiting how the results can be generalised.
- The measurement of pain and ease of placement of the IUS were both subjective measures of efficacy.
- Investigators were not blinded to treatment allocation due to the visible differences in hormone reservoir in the IUS.

Safety:

- There was a high drop-out rate from the study – study completion was 57% (819/1432) of patients in the 13.5 mg levonorgestrel group.
- 84% (n=1194/1432) of women reported adverse events (AE)s in the levonorgestrel 13.5 mg group. Most common were: acne (10%), ovarian cysts (7.7%), dysmenorrhoea (6.8%), pelvic pain (4.7%) and vaginal haemorrhage (4.5%).
- Discontinuation of treatment due to any AE over the three years occurred in 22% (n=313/1,432) of women in 13.5 mg levonorgestrel group. The most common AEs resulting in discontinuation were bleeding disturbances including amenorrhea (4.7%).
- 0.6% (n=8/1,432) patients reported a serious AE related to treatment; defined as uterine perforations, ectopic pregnancy and pelvic inflammatory disease.
- Treatment was discontinued as a result of serious AEs by 1.0% of women in the levonorgestrel

13.5 mg group. Three ectopic pregnancies and two pelvic inflammatory diseases were reported in 13.5 mg levonorgestrel group.

- The MHRA issued a drug safety update in June 2015 regarding risk factors for uterine perforation during insertion of IUDs – see link for further information https://www.gov.uk/drug-safety-update/intrauterine-contraception-uterine-perforation-updated-information-on-risk-factors

Guidance:

- NICE Clinical Guideline 30 "Long-acting reversible contraception (September '14 update)" recommends that women requiring contraception should be given information about, and offered a choice of, all available methods of contraception including LARC.
- In addition, it recommends that contraceptive service providers should be aware that all currently available LARC methods (intrauterine devices, the IUS, injectable contraceptives and implants) are more cost effective than the combined oral contraceptive pill even at 1 year of use. The intrauterine devices, IUS and implants are more cost effective than the injectable contraceptives. The guidance also states that increasing the uptake of LARC methods will reduce the numbers of unintended pregnancies.
- The Summary of Product Characteristics for levonorgestrel 13.5 mg IUS states that healthcare professionals experienced in the insertion of other intrauterine systems can fit the levonorgestrel 13.5 mg IUS and do not necessarily require further training.
- Levonorgestrel 13.5 mg IUS has a smaller IUS T-frame, drug reservoir and a narrower insertion tube compared to Mirena® however the SMC summary states that it is unclear if the levonorgestrel 13.5 mg IUS would be more suitable for women with a narrower cervical canal and/or smaller uterine cavity. Of note it is not recommended as a first-line contraceptive in nulliparous women due to a lack of clinical experience in this group.
- There is a lack of comparative data of the levonorgesterel 13.5 mg IUS with other licensed contraceptives. The phase II dose finding studies included Mirena® as a comparator but was insufficiently powered to establish non-inferiority. The trial compared the levonorgestrel 13.5 mg preparation to the alternative strength 19.5 mg product; however this is currently unavailable in the UK. Therefore the failure rate can only be compared naively to failure rates in other studies or clinical practice.

Cost:

- Mirena® is currently the only other levonorgestrel-releasing intrauterine system available in the UK, releasing 20 micrograms of levonorgestrel over 24 hours. It is effective for a five year period and at a cost of £88 is less costly than Jaydess® (£69.22), if used for the full five year period.* However, this does not take the rate of unintended pregnancies or discontinuation of a preparation into consideration.

*Please note a full new medicine review has not been carried out for the production of the above recommendation. A national body has performed a full assessment of the evidence, safety and cost effectiveness of this medicine and this document has been used in the preparation of the local policy recommendation.**Prices taken from MIMS online (August 2015).

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