



Heavy menstrual bleeding: levonorgestrel-releasing intrauterine system

The ECLIPSE randomised controlled trial found the levonorgestrel-releasing intrauterine system was more effective than usual medical treatment in reducing the effect of heavy menstrual bleeding on quality of life.



Overview: Heavy menstrual bleeding, or menorrhagia, is defined as excessive menstrual blood loss that interferes with a woman's physical, social, emotional or material quality of life. It should be recognised as having a major impact on a woman's quality of life, and any intervention should aim to improve this rather than focusing on reducing menstrual blood loss. Treatments for heavy menstrual bleeding include drug treatments, non-hysterectomy surgery and hysterectomy.

Current advice: The NICE clinical guideline on [heavy menstrual bleeding](#) recommends that drug treatment should be considered where no structural or histological abnormality is present, or for fibroids less than 3 cm in diameter which are causing no distortion of the uterine cavity. If history and investigations indicate that drug treatment is appropriate and either hormonal or non-hormonal treatments are acceptable, levonorgestrel-releasing intrauterine system (LNG-IUS) should be considered in the following order:

- LNG-IUS provided long-term (at least 12 months) use is anticipated
- tranexamic acid or non-steroidal anti-inflammatory drugs or combined oral contraceptives
- norethisterone (15 mg) daily from days 5 to 26 of the menstrual cycle, or injected long-acting progestogens.

Women offered an LNG-IUS should be advised of anticipated changes in the bleeding pattern, particularly in the first few cycles, which may last longer than 6 months. They should therefore be advised to persevere for at least 6 cycles to see the benefits of the treatment.

The NICE recommendation to consider LNG-IUS as first-line drug treatment for heavy menstrual bleeding, if appropriate, was based on evidence available at the time. However, the Guideline Development Group was aware that the pragmatic, UK-based randomised controlled trial ECLIPSE was underway comparing LNG-IUS with other drug treatments. This trial has now been published.

The LNG-IUS (Mirena), currently costs £88.00 for 1 unit ([MIMS March 2013](#)). In 2012, approximately 135,000 items of Mirena were prescribed in primary care in England, at a cost of about £12 million (NHS Prescription Services, personal communication).

The NICE Pathway on [heavy menstrual bleeding](#) brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.

New evidence: In ECLIPSE ([Gupta et al. 2013](#)), 571 women with menorrhagia were randomised to treatment with LNG-IUS or usual medical treatment (tranexamic acid, mefenamic acid, a combined oral contraceptive, or a progestogen alone), and followed up for 2 years. After randomisation,

treatments could be changed, discontinued, or women could be referred for surgery according to usual practice. The primary outcome was the patient-reported score on the 100-point [Menorrhagia Multi-Attribute Scale](#) (MMAS). This measures the effect of heavy menstrual bleeding on 6 domains of daily life: practical difficulties; social life; psychological health; physical health; work and daily routine; and family life and relationships.

In both groups, the MMAS score improved from baseline at 6 months, 1 year and 2 years, but improvements were greater in the LNG-IUS group compared with usual treatment (mean difference in scores over 2 years=13.4 points, 95% CI 9.9 to 16.9, $p<0.001$). The authors suggested that this difference was both statistically and clinically significant, noting that it was more than 0.5 standard deviations, which has been [identified](#) as the minimum clinically important difference for health-related quality of life measures. The difference of 13.4 points represented a change in 2 or 3 MMAS domains from substantially affected by heavy menstrual bleeding to minimally affected, or from minimally affected to unaffected.

Secondary outcomes included surgical intervention. Hysterectomy was performed in 6% of the women in both groups, and endometrial ablation was performed in 4% of the LNG-IUS group and 6% of the usual treatment group ($p=0.44$). At 2 years, more women were still using LNG-IUS than usual treatment (64% versus 38%, $p<0.001$). There was no significant difference between the groups in the frequency of serious adverse events ($p=0.59$).

The authors noted the limitation that LNG-IUS could not be compared with individual medical treatments, and there was substantial switching between treatments throughout the study. As the accompanying [editorial](#) discusses, no patient-based outcome measure for heavy menstrual bleeding has gained universal acceptance. However, the MMAS has been widely used and [validated](#).

Commentary: "In 2007, when the NICE clinical guideline on heavy menstrual bleeding was published, studies in UK primary care were lacking so recommendations were based on studies from other countries or in secondary care. The ECLIPSE trial addresses this issue.

"The results essentially confirm NICE guidance that LNG-IUS should be considered before other drug treatments for heavy menstrual bleeding. The study design and characteristics of the participants favour generalisability of the findings, and the authors used patient-centred end points as recommended by the NICE guideline. The follow-up period of 2 years is longer than most studies, but is still less than ideal. However, additional analyses at 5 years and 10 years are planned.

"The LNG-IUS is not perfect. It did not lower the rate of surgical intervention compared with usual medical treatment, and about a third of women discontinued the device by 2 years. The challenge is now for commissioners to ensure that all eligible women can access this treatment in primary care." – **Dr Mark Shapley, General Practitioner, Newcastle-under-Lyme, Staffordshire**

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