

# NEW DRUG EVALUATION

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## ULIPRISTAL (*ellaOne*<sup>®</sup>▼)

Ulipristal is a new prescription-only emergency contraceptive pill licensed for use up to five days after unprotected intercourse. It has been shown to have equivalent efficacy to levonorgestrel in large randomised and single-arm open studies. Its safety profile also appears similar to that of levonorgestrel, with mild gastrointestinal symptoms and disruption of normal menses common. Ulipristal is more than three times as costly as levonorgestrel and therefore recommended as a treatment option only for patients who require contraception between 72 and 120 hours after unprotected intercourse.

### What is it?

Ulipristal (*ellaOne*<sup>®</sup>▼, HRA Pharma) is a new prescription-only emergency contraceptive pill licensed for use up to 120 hours (five days) after unprotected intercourse. <sup>1</sup> As a progesterone receptor modulator it is believed to act via delay of ovulation and inhibition of follicular development. <sup>2</sup> The dose is one 30 mg tablet to be taken as soon as possible and no more than 120 hours following intercourse. Although there is no experience of use in patients aged < 18 years it is not specifically contra-indicated in this group. <sup>1</sup>

### How effective is it?

Initial development of ulipristal for contraception used a 50 mg tablet formulation. Later studies used a 30 mg tablet containing micronised drug, with the two presentations considered bioequivalent. <sup>3</sup>

Efficacy results are reported for 775 patients randomised to contraception with ulipristal 50 mg and 774 with levonorgestrel 2 × 750 micrograms (12 hour dose interval). <sup>4</sup> Most patients were aged between 18 and 34 years and all received treatment between 0 and 72 hours post-coitus. Seven pregnancies were observed in the ulipristal group against an expected number of 47, compared with 13 against an expected 42 with levonorgestrel, yielding an efficacy rate for prevented pregnancies of 85% and 69% respectively ( $p > 0.05$ ).

Efficacy results are also reported for 1,334 patients treated with ulipristal 30 mg as part of a non-comparative open study. <sup>3</sup> Most Patients were aged between 18 and 35 years and were treated 48 to 120 hours following intercourse, although 9% were subsequently found to have received treatment at < 48 hours. Twenty-nine pregnancies were observed against an expected number of 75, yielding an efficacy rate of 61%.

Within a phase III active-comparator study women were randomised to contraception with ulipristal 30 mg ( $n = 939$ ) or levonorgestrel 1.5 mg ( $n = 954$ ) at between 0 and 120 hours post-coitus. There were 15 pregnancies in the ulipristal group and 25 in the levonorgestrel group, yielding pregnancy rates of 1.6% (95% confidence interval [CI] 0.9 to 2.7%) and 2.6% (95%CI 1.8 to 3.9%) respectively. The difference between groups was not significant ( $p > 0.05$ ). <sup>5</sup>

### How safe is it?

At least one adverse event was reported by 61% of patients in the non-comparative phase III study. Adverse effects such as nausea (12%) and abdominal pain (12%) were common although the majority were of mild or moderate intensity. <sup>3</sup> Vomiting affected 2% of patients: <sup>3</sup> If a patient vomits within three hours of taking ulipristal they should take another dose to ensure efficacy is maintained. <sup>1</sup>

In the phase III comparative study ( $n = 2221$ ) the most common adverse effects with ulipristal and levonorgestrel were, respectively; headache (both 19%), dysmenorrhea (13% and 14%), nausea (13% and 11%), abdominal pain (5% and 7%), dizziness (both 5%), fatigue (6% and 4%), and upper abdominal pain (3% and 4%). <sup>5</sup>

Disruption to the normal menstrual cycle (e.g. duration and volume) is common. Ulipristal results in an average increase to the duration of the menstrual cycle of two days. The product data sheet states that the majority of women in the phase III non-comparative study had their next menstrual period at the expected time or within 7 days (81%), while 6% experienced menses > 7 days earlier than expected and 19% had a delay of > 7 days beyond the anticipated onset of menses. Patients are advised to seek a pregnancy test if their period is > 7 days later than expected. <sup>1</sup>

Although there is an absence of long-term follow-up data<sup>3-5</sup> patients are expected to be exposed to only small cumulative life-time doses with long dose intervals.

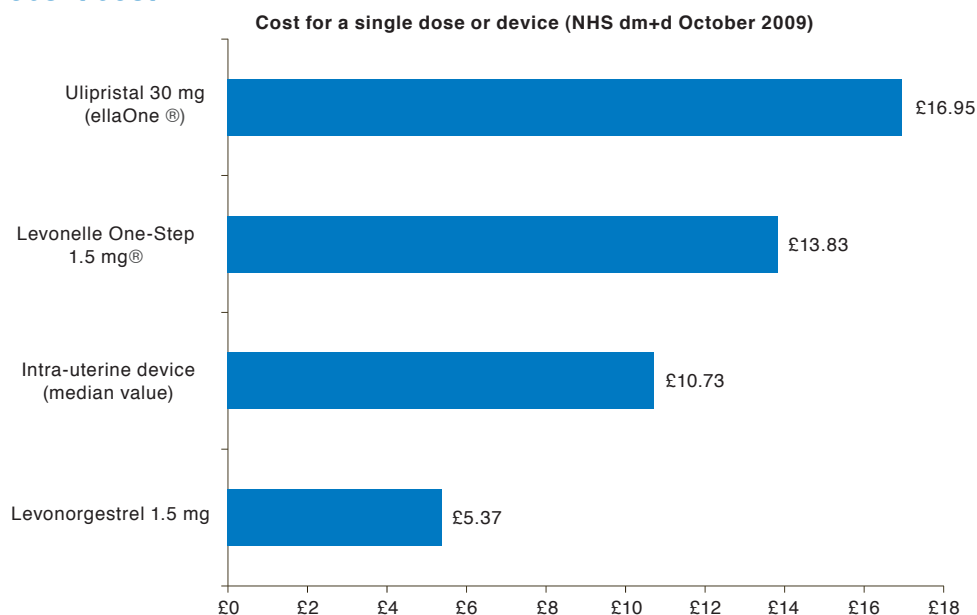
Data regarding pregnancy outcomes following inadvertent or unsuccessful use of ulipristal during gestation are very limited.<sup>3</sup>

All suspected adverse reactions to black triangle drugs such as ulipristal should be reported to the MHRA via the Yellow Card Scheme ([www.yellowcard.gov.uk](http://www.yellowcard.gov.uk)).

### What other options are there?

Levonorgestrel 1.5 mg is licensed for contraception up to 72 hours following unprotected intercourse and is widely accessible via prescription, direct from clinics and community pharmacies, and purchase without prescription. Prior to ulipristal the only licensed post-coital contraceptive option between 72 and 120 hours was the insertion of an intra-uterine device (IUD), although levonorgestrel is sometimes used off-license up to 120 hours too.<sup>6</sup> IUD are regarded as being almost 100% effective and have the advantage of conferring contraception for as long as they remain *in situ*, often up to five years or more.<sup>6</sup> However, they require specially trained healthcare personnel for insertion, which has implications on resource use and availability, and there may be reluctance from patients

### How much does it cost?



towards this comparatively invasive option. Additionally they are associated with rare complications such as pelvic inflammatory disease.<sup>7</sup>

### When should it be used?

Ulipristal has demonstrated equivalent contraceptive efficacy to levonorgestrel in the period up to 72 hours, and up to 120 hours, following unprotected intercourse. It has a similar adverse effect profile to levonorgestrel, however the effects of foetal exposure are not known. Ulipristal is more than three times as costly as generically prescribed levonorgestrel.

Following use of ulipristal within any menstrual cycle, use of barrier contraception (e.g. a condom) is recommended until the next period starts irrespective of, and additional to, use of a regular contraceptive pill.<sup>1</sup>

When oral emergency contraception is required levonorgestrel is recommended in the period up to 72 hours following unprotected intercourse. Ulipristal is a suitable and licensed alternative treatment for the period between 72 and 120 hours although there is no specific evidence that it is more effective than levonorgestrel if used during this interval.

## REFERENCES

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KEY R - review, RCT - randomised controlled trial, U - unpublished

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