Ulipristal acetate: emergency contraception for up to five days

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KEY POINTS

- ulipristal acetate (EllaOne) is a progesterone receptor modulator
- licensed for use as emergency contraception by adults for up to 5 days after unprotected intercourse
- available as a 30mg tablet; recommended dose is 1 tablet (£16.95)
- it is the first oral contraceptive for emergency use up to 120 hours following unprotected intercourse; it is available only on prescription and not currently at pharmacies
- clinical trials of ulipristal acetate have not been published in full; the available data suggest it prevents approximately 60 per cent of pregnancies, with no diminution of efficacy up to 5 days after intercourse
- it appears to be comparable in efficacy with levonorgestrel (Levonelle 1500)
- the commonest adverse events in clinical trials were headache, nausea and abdominal pain; altered cycle length is common
- an oral emergency contraceptive that can be taken up to 5 days after unprotected sex could help prevent more unwanted pregnancies

Ulipristal acetate (EllaOne) is a new oral emergency contraceptive licensed for up to 120 hours following unprotected intercourse. In our New products review, Steve Chaplin presents the data relating to its efficacy and adverse effects and Dr Sharon Cameron discusses its role as an emergency contraceptive.

Guidance on the provision of emergency contraception states that a single dose of 1.5mg levonorgestrel (Levonelle 1500) should be taken within 72 hours of unprotected intercourse or a copper intrauterine device (IUD) may be inserted within five days.[1] Levonorgestrel may be obtained as a prescription-only medicine or from pharmacies without a prescription.[2]

In 2008/09, 7 per cent of UK women aged 16-49 used emergency hormonal contraception within the previous year and fewer than 0.5 per cent used an emergency IUD.[3] Most women obtain emergency hormonal contraception from community pharmacists (approximately 40 per cent), the GP or practice nurse (approximately 30 per cent) or a community contraception clinic (16 per cent).[3]

The technology

Ulipristal acetate (EllaOne) is a selective progesterone receptor modulator licensed as emergency contraception within 120 hours (five days) of unprotected sexual intercourse or contraceptive failure. It is believed to act principally by inhibiting ovulation.

The recommended dose is a single 30mg tablet, repeated once if vomiting occurs within three hours of administration. Ulipristal acetate is contraindicated in pregnancy. Efficacy and safety in women with impaired renal or hepatic function, and in girls aged under 18, is unknown.

The efficacy of ulipristal acetate may be reduced by drugs that induce CYP3A4 enzymes such as carbamazepine and St John's wort, and by drugs that reduce gastric acidity such as proton-pump inhibitors. Ulipristal acetate may reduce the efficacy of concurrent combined hormonal contraception, and barrier contraception is recommended after use.

Clinical trials

The efficacy of 30mg ulipristal acetate has been evaluated in women over 18 years old in an uncontrolled trial (available as an abstract[4] and in more detail in the European Public Assessment

Time window	mITT (n)	Observed pregnancies (n)	Expected pregnancies (n)	Observed pregnancy rate (95% CI)	Expected pregnancy rate	Prevented fraction (95% CI)	RR (95% CI)
48-72h (day 3)	693 (56%)	16	42	2.31% (1.4-3.75%)	6.01%	61.9% (36.3-77.2%)	2.62 (1.57; 4.39)
72-96h (day 4)	390 (31%)	8	19	2.05% (0.97%-4.07%)	4.95%	57.9% (14.6-79.2%)	2.38 (1.17; 4.81)
96-120h (day 5)	158 (13%)	2	8	1.27% (0.05-4.79%)	4.90%	75.0 % (6.2-93.3%)	4.00 (1.07; 14.9)
mITT = modified intent to treat population; RR = relative risk							

Table 1. Observed and expected pregnancies in the test population[5]

Report[5]) and in a comparative trial with levonorgestrel (also in abstract form).[6]

The uncontrolled trial was a single-arm study in which women presenting 48-120 hours after unprotected intercourse received a single dose of ulipristal acetate 30mg.[4,5] The primary end-point was the incidence of pregnancy compared with the expected incidence in this population, based on conception probabilities by cycle day.

In 1241 women, the pregnancy rate after treatment was 2.10 per cent; this was significantly lower than the expected rate of 5.53 per cent. Pregnancy rates declined with time since intercourse from 2.31 per cent on day 3 to 2.05 and

1.27 per cent on days 4 and 5 respectively (see Table 1). The estimated proportion of pregnancies prevented was 61 per cent.

The comparative trial randomised 1899 women presenting within 120 hours of unprotected intercourse to a single dose of 30mg ulipristal acetate or levonorgestrel 1.5mg[6] (though levonorgestrel is licensed only for use up to 72 hours after intercourse).

Pregnancy rates were not significantly different (1.6 per cent with ulipristal acetate and 2.6 per cent with levonorgestrel; odds ratio 0.59, CI 95% 0.39-1.14).

Adverse effects

In the uncontrolled trial, 61 per cent of women reported at least one adverse event.[5] The most frequent events were headache (18 per cent), nausea (12 per cent) and abdominal pain (12 per cent).[5]

Post-treatment cycle length was increased by an average of 2.9 days, though 6 per cent of women reported the onset of menses a week earlier than expected; overall, cycle length changed by more than seven days in 19 per cent of women.[5]

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Place in therapy

The introduction of ulipristal acetate, an orally active emergency contraceptive that can be taken up to five days after unprotected sex, could help prevent more unwanted pregnancies.[1,2]

Studies have shown that when given just before ovulation (when the risk of pregnancy is greatest), ulipristal acetate is a more potent inhibitor of ovulation than levonorgestrel, suggesting that it should be a more effective emergency contraceptive.[3,4]

An IUD is a more effective form of emergency contraception and can be used beyond 72 hours, but it requires a skilled health professional to insert and may not be acceptable to all women in view of its invasiveness.[7]

Since the availability of emergency contraception at pharmacies, increasing numbers of women are choosing to access emergency contraception in this way.[8] While ulipristal acetate may eventually become available from pharmacies and on patient group direction (PGD), this cannot occur until there are more safety data.

Ulipristal acetate thus raises challenges for service delivery on whether to use this more effective but less accessible emergency contraception, and could lead to a reversal of the flow of patients requesting emergency contraception at the pharmacy back to the contraceptive services provider.

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