STATEMENT FROM THE CLINICAL EFFECTIVENESS UNIT
September 2015

Faculty of Sexual and Reproductive Healthcare (FSRH) response to new data on quick-starting hormonal contraception after use of ulipristal acetate 30mg (ellaOne®) for emergency contraception.

In 2010, the FSRH introduced guidelines supporting immediate commencement ("quick-start") of hormonal contraception after administration of oral emergency contraception (EC).[1] There is evidence that after oral EC, further episodes of unprotected intercourse in the same cycle put women at risk of pregnancy.[2] The advice applied to both levonorgestrel (LNG) and ulipristal acetate (UPA) given as EC.

UPA is a selective progesterone-receptor modulator. Its primary mechanism of action as EC is to delay ovulation until sperm from an act of unprotected intercourse are no longer viable. In contrast to LNG, UPA can delay ovulation even after the start of the luteinising hormone (LH) surge,[3] and meta-analysis of the available data concludes that UPA prevents significantly more pregnancies than LNG.[4]

It has, however been postulated that:

1. The effectiveness of a progestogen-containing contraceptive method that is quick started immediately after administration of UPA might be reduced by UPA due to competition at the progesterone receptor site.
2. The effect of UPA in delaying ovulation might be reduced by quick-starting a progestogen-containing contraceptive.

Regarding 1: Two recent studies suggest that UPA may not reduce the effectiveness of quick-started hormonal contraception.[5,6] In their double-blind, randomised, placebo-controlled trial, Cameron *et al*. found no difference between the time taken for a combined oral contraceptive (COC) to induce ovarian quiescence when started immediately after UPA (*n*=39) and when the COC was taken after placebo (*n*=37). Brache *et al.* studied use of a desogestrel progestogen-only pill (POP) quick-started after UPA 30mg or after placebo. The crossover, placebo-controlled trial randomised 58 women at mid cycle to receive either UPA or placebo, both followed immediately by 20 days of desogestrel 75mcg. No significant differences were demonstrated with respect to time to ovarian quiescence or cervical mucus penetrability.

The studies are small, and the endpoints are ovulation and cervical mucus permeability rather than pregnancy. They do not provide evidence relating to quick-starting the traditional POP, subdermal implant, combined contraceptive ring or combined transdermal patch. However, the findings are generally reassuring in that they do not suggest any likely reduction in effectiveness of hormonal contraception following UPA.

Regarding 2: Brache *et al.* also considered the effect of a quick-started desogestrel POP on the ability of UPA to delay ovulation. After UPA alone, ovulation occurred within five days of administration in only one out of 29 cycles studied. In contrast, when desogestrel 75mcg was quick-started immediately after UPA administration, ovulation occurred within five days (when sperm would remain potentially viable) in 13 out of 29 cycles. The difference in ovulation rate is significant (p= 0.0054).[6]

In the absence of evidence regarding other POP formulations and other hormonal contraceptive methods, the CEU would recommend that after taking UPA for EC, a woman should not start a hormonal contraceptive method for at least 5 days and be advised to use barrier methods or to abstain from sex until effective hormonal contraceptive cover has been achieved.

Since UPA does not appear to affect the mechanism of action of hormonal contraception, women should be advised that when hormonal methods of contraception are started (after at least 5 days) then the usual recommended contraceptive precautions should be taken (barrier or abstinence) for a number of days, depending of the method used: [1]

UPA = day 0	**Methods (day UPA+5)**	**Requirement for additional contraception**
UPA then wait at least 5 days	Combined oral contraceptive pill (except Qlaira®)	7 days
	Qlaira®) Combined oral contraceptive pill	9 days
	Combined vaginal ring/ transdermal patch	7 days
	Progestogen-only pill (traditional/ desogestrel)	2 days
	Progestogen-only implant or injectable	7 days

References:

1. Faculty of Sexual and Reproductive Healthcare. Quick Starting Contraception. 2010 http://www.fsrh.org/pdfs/CEUGuidanceQuickStartingContraception.pdf [Accessed 25 September 2015]
2. Cheng L, Che Y, Gülmezoglu AM. Interventions for emergency contraception. *Cochrane Database Syst Rev 2012;* **8**: CD001324.

3. Glasier AF, Cameron ST, Fine PM, *et al*. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomised non-inferiority trial and meta-analysis. *Lancet 2010;* **375**: 555-562.
4. Brache V, Cochon L, Deniaud M, *et al*. Ulipristal acetate prevents ovulation more effectively than levonorgestrel: analysis of pooled data from three randomized trials of emergency contraception regimens. *Contraception 2013*; **88**: 611-618.
5. Cameron ST, Berger C, Michie L, *et al.* The effects on ovarian activity of ulipristal acetate when 'quickstarting' a combined oral contraceptive pill: a prospective, randomized, double-blind parallel-arm, placebo-controlled study. *Hum Reprod 2015*; **30**: 1566-1572.
6. Brache V, Cochon L, Duijkers IJM, *et al.* A prospective, randomised pharmacodynamic study of quick-starting desogestrel progestin-only pill following ulipristal acetate for emergency contraception. *Hum Repro 2015*. doi:10.1093/humrep/dev241 [Advance Access published September 23, 2015]