

A New Drug for Emergency Contraception: But Not in Catholic Hospitals?

Over the past few months, various media outlets have announced a new medication for emergency contraception. The drug is ulipristal acetate or CDB-2914. Unlike levonorgestrel (Plan B) which is a synthetic progestin, ulipristal acetate is a selective progesterone-receptor modulator. As such, it is in the same class of drugs as mifepristone (RU486, the abortifacient drug).

Ulipristal is being promoted because it seems to be effective for longer than levonorgestrel. It is approved for use beyond 72 hours after unprotected sexual intercourse and up to 120 hours, whereas levonorgestrel's effectiveness diminishes with time and is approved for use within 72 hours of sexual intercourse. For the first 72 hours, ulipristal appears to be as effective as levonorgestrel and seems to be as well tolerated. Drug promoters say that it provides women and health care providers with an alternative choice for emergency contraception that can be used up to five days after unprotected sexual intercourse.

May ulipristal acetate be considered as a morally licit alternative to Plan B in Catholic hospitals? The answer to this question depends on the mechanism of action of the medication. Because the drug is relatively new, there has not been

the same extent of research on the mechanism of action of ulipristal as there has been on levonorgestrel. However, there are initial indications that the medication, at least in higher doses, affects the endometrium and, hence, could be abortifacient.

In a Feb. 13, 2010 article in *The Lancet* ("Ulipristal acetate versus levonorgestrel for emergency contraception: a randomized non-inferiority trial and meta-analysis"), Anna Glasier et al. state that "progesterone-receptor modulators, including ulipristal acetate, given at higher doses have an effect on endometrial histology and histochemistry that could theoretically impair implantation of a fertilized oocyte. Although an endometrial effect, and therefore an additional postovulatory mechanism of action, cannot be excluded, the dose of ulipristal acetate used in this trial was specifically titrated for emergency contraception on the basis of inhibition of ovulation and might be too low to inhibit implantation" Vol. 375, p. 560).

Describing the mechanism of action of ulipristal (in the dose in which it was given in their trials), the authors go on to say: "By contrast, when ulipristal acetate is given in the presence of a follicle measuring 18-20 mm, it prevents ovulation in 60% of cycles, therefore potentially preventing pregnancy in substantially more women than does levonorgestrel. The ability of ulipristal

acetate to inhibit ovulation is particularly important because at this time in the cycle the probability of conception is at its peak and the frequency of sexual intercourse is at its highest” (p. 560).

An article published in the February 2010 issue of *Obstetrics and Gynecology* (Paul Fine, et. al., “Ulipristal Acetate Taken 48-120 Hours after Intercourse for Emergency Contraception,” Vol. 115, no. 2, pp. 257-263) supports this particular mechanism of action: “Levonorgestrel acts by interfering with the luteinizing hormone peak but does not seem to interfere with the ovulatory process when taken close to ovulation, a time when intercourse is most likely to lead to fertilization. Ulipristal acetate, on the other hand, has been shown to prevent ovulation and thus fertilization even after the luteinizing hormone surge has begun” (p. 257). Later in the article, the authors explain that ulipristal acetate “inhibits or delays ovulation in a dose-dependent fashion” (p. 258).

Other contributions to the literature on this drug, however, raise red flags. In a “Comment” in the same issue of *The Lancet* cited above, the authors raise the possible abortifacient effect of ulipristal: “Ulipristal has similar biological effects to mifepristone, the antiprogestin used in medical abortion and marketed for emergency contraception in China and Russia. ... The mechanism of action of mifepristone has been extensively studied and the striking similarity with ulipristal suggests a similar mechanism of action for both. Indeed, administration of ulipristal

in mid-follicular phase suppresses lead follicle growth, causing a dose-dependent delay in folliculogenesis and suppression of plasma oestradiol with, at higher doses, a new lead follicle often recruited. A delay in endometrium maturation was seen after ulipristal at 10, 50, and 100 mg. ... The results are similar to those described after mifepristone” (p. 527). And later, they state: “Levonorgestrel and mifepristone ... have different mechanisms of action, because levonorgestrel has no effect on implantation whereas mifepristone can prevent it, which might also apply to ulipristal. ... This finding suggests that in women receiving ulipristal 72-120 h after an unprotected intercourse, an anti-implantation effect cannot be excluded, as Glasier and colleagues acknowledge” (p.528).

A more recent article provides even more evidence of endometrial effects of ulipristal (Pamela Stratton, et al., “Endometrial effects of a single early luteal dose of the selective progesterone receptor modulator CDB-2914,” *Fertility and Sterility* 93, no. 6 [April 2010]: 2035-2041). The authors report that “CDB-2914 appeared to inhibit endometrial development while sparing menstrual rhythm. The current study was the first dose-ranging study to document significant endometrial effects with low doses of CDB-2914 given in the early luteal phase. Similar endometrial effects have been observed among those receiving mifepristone (200 mg); however, these endometrial effects were present at lower doses (10 mg). ... Either effect of CDB-2914, endometrial atrophy or continued

proliferation, however, may hamper implantation” (p. 2039, 2040). While these early studies may not be conclusive, the fact that ulipristal is a cousin of mifepristone and that early studies on its mechanism of action indicate changes in the endometrium that can interfere with implantation, there seems to be sufficient reason for Catholic hospitals *not* to employ this medication for emergency contraception. And it is precisely this type of development that make it so important to ensure some type of conscience provision in legislation requiring hospitals to administer emergency contraception.

its surface. In addition, it has been shown that mifepristone inhibits blastocyst attachment, whereas levonorgestrel does not have any effect on its attachment in this model. Thus, this study may partially explain the reason for embryos to attach on levonorgestrel exposed endometrial construct” (p. 263). Recent studies continue to suggest that levonorgestrel does not prevent implantation.
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A footnote. Interestingly, several of the articles consulted with regard to the mechanism of action of ulipristal also discuss levonorgestrel (Plan B). They are consistent in describing the mechanism of action of levonorgestrel as “interfering with ovulation.” One such study (Chun-Xiz Meng et al., “Effect of levonorgestrel and mifepristone on endometrial receptivity markers in a three-dimensional human endometrial cell culture model,” *Fertility and Sterility*, 91, no. 1 [January 2009]: 256-264) reports the following: “The present study shows that the molecular profile of this three dimensional endometrial construct is similar to the receptive endometrium, and exposure to Mifepristone leads to a significant change in its molecular expression, whereas levonorgestrel has no effect. In a recently published study from our laboratory, we have shown that this model allows the preimplantation stage embryo to attach on