



Levonorgestrel or ulipristal: Is one a better emergency contraceptive than the other?

➡ Comparison of these two FDA-approved agents should take more into account than just efficacy measured by the crude pregnancy rate

One of the best-kept secrets in women's health is the availability of effective emergency contraceptives that have few side effects and are inexpensive. Who are candidates for emergency contraception? They include women in whom another method of contraception recently failed; those who recently had unprotected intercourse; and those who have been sexually assaulted.

What are the three most commonly used emergency contraceptive options? They are:

- levonorgestrel, 1.5 mg
- insertion of a copper intrauterine device (IUD)
- ulipristal, 30 mg.

You are likely familiar with protocols for emergency contraceptives using levonorgestrel (Plan B One-Step) (see the **FIGURE**, panel A) and the copper IUD (ParaGard). You may not be as familiar with ulipristal (sold under the name Ella) (**FIGURE**, panel B), approved recently by the Food and Drug Administration for use as long as 120 hours after intercourse.

Ulipristal is a selective progesterone-receptor modulator that has predominantly antiprogesterin activity. The drug blocks or delays ovulation and suppresses endometrial growth.¹ Interestingly, ulipristal can block ovulation for as long as 5 days, even

if administered after the onset of the luteinizing hormone (LH) surge.²

All have relative advantages, disadvantages

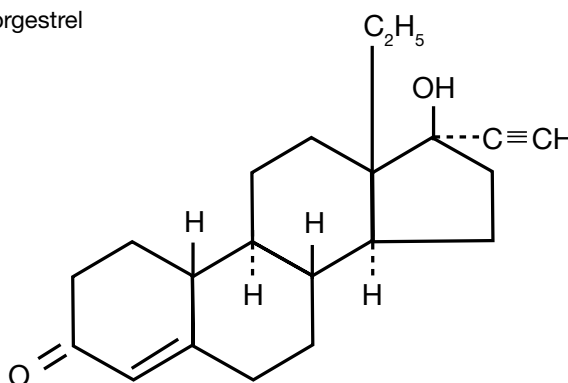
It's difficult to conclude, with confidence, that any one of the options for emergency contraception is "best" in

every circumstance. For example, although generic levonorgestrel is the least expensive of the three options, a copper IUD provides the most cost-effective "emergency" contraception, viewed across a multi-year time frame.

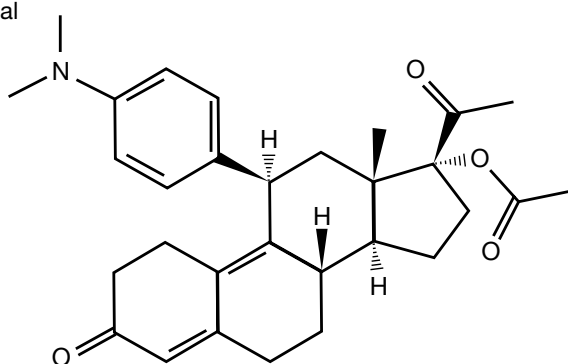
A copper IUD is seldom inserted as emergency contraception, however.

Chemical structure of two emergency contraceptives

A Levonorgestrel



B Ulipristal



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TABLE 1 Scorecard from 2 trials of levonorgestrel and ulipristal for emergency contraception

Trial	Levonorgestrel				Ulipristal			
	Dosage	Subjects	Pregnancies	Pregnancy rate	Dosage	Subjects	Pregnancies	Pregnancy rate
Creinin ⁴	Two doses, 0.75 mg each	774	13	1.68%	50 mg	775	7	0.90%
Glasier ⁵	One dose, 1.5 mg	958	25	2.61%	30 mg, micronized*	941	15	1.59%
Combined data	—	1732	38	2.19%	—	1716	22	1.28%

Note: In the Creinin study, 4 women were enrolled as long as 72 h after intercourse. In the Glasier study, 5 women were enrolled as long as 120 hours after intercourse.

*The 30-mg micronized formulation of ulipristal used in the Glasier study and the 50-mg formulation of ulipristal used in the Creinin study are thought to have similar drug potency.

In one report, from England, only 3% of 158,000 women who requested emergency contraception received a copper IUD.³

Because levonorgestrel and ulipristal are the most commonly used options for emergency contraception, how do we select which agent to recommend?

Levonorgestrel vs. ulipristal

Fortunately, ulipristal and levonorgestrel have been tested, head to head, in two superbly designed and executed large clinical trials.^{4,5} In both trials, investigators reported that ulipristal, when used for emergency contraception, resulted in fewer pregnancies than levonorgestrel (TABLE 1).

By combining the results from both studies, crude pregnancy rates for ulipristal and levonorgestrel users were, respectively, 1.28% and 2.19%. Formal meta-analysis of the two studies concluded that ulipristal was, to a degree of statistical significance, more effective than levonorgestrel when taken at 24 hours, 72 hours, or 120 hours after sexual intercourse.⁵

Ulipristal and levonorgestrel had similar side effect profiles in the two trials. The most commonly reported

side effects were headache, nausea, fatigue, and abdominal pain.

The matter of cost-effectiveness

One dose of ulipristal is more expensive than generic levonorgestrel. In the health system in which I work, the cost to the patient of one dose of ulipristal is approximately \$45; one dose of brand-name levonorgestrel, 1.5 mg (Plan B One-Step), is priced similarly. A generic prescription for two 0.75-mg levonorgestrel pills (sold under the name Next Choice), however, costs the patient approximately \$30.

In an era of cost-conscious health care, some authorities have questioned whether ulipristal is cost-effective because it is more expensive than generic levonorgestrel.⁶ Investigators who conducted a formal cost-benefit analysis in the United Kingdom, reported that ulipristal was more cost-effective than levonorgestrel.⁷ In their analysis, one dose of ulipristal was assumed to be 3 times more expensive than generic levonorgestrel. But because ulipristal was more effective than levonorgestrel at reducing the rate of unintended pregnancy, it was more cost effective because it reduced the burden of the costly care associated with unintended pregnancy.

Availability of levonorgestrel and ulipristal

For women who are 17 years or older, levonorgestrel is widely available without a prescription. Such access avoids the cost and delay inherent in a visit to a clinician to obtain a prescription.

Ulipristal is available only with a prescription (TABLE 2). The FDA recommends that

...pregnancy should be excluded before prescribing Ella (ulipristal). If pregnancy cannot be excluded on the basis of history and/or physical examination, pregnancy testing should be performed.

Some physicians interpret this recommendation to mean that a visit to a physician and a pregnancy test are required before they can prescribe ulipristal. Possible alternatives to an office visit before prescribing ulipristal as emergency contraception would be for you to:

- ask the patient to call the office with her menstrual cycle information, and to ensure that office staff reviews that information before you prescribe the drug
- ask the patient to perform a home pregnancy test before you prescribe ulipristal.

For women who lack access to

TABLE 2 What FDA says about emergency contraception with levonorgestrel and ulipristal

Labeling	Levonorgestrel	Ulipristal
Approved indication	Emergency contraception, as long as 72 h after intercourse	Emergency contraception, as long as 120 h after intercourse
Women 17 y and older	Available without a prescription	Prescription required
Women younger than 17 y	Prescription required	

regular health care, levonorgestrel is clearly the best option for emergency contraception. Years of clinical data show that levonorgestrel, if taken accidentally by a pregnant woman, is unlikely to harm the pregnancy.

Unlike what we know about levonorgestrel, few data exist about the safety of a 30-mg dose of ulipristal in a woman who is pregnant. Some clinicians clearly view safety data as favoring continued use of levonorgestrel for emergency contraception.

A swift and reliable agent of change for women

The stunningly sudden and irrevocable failure of a barrier contraceptive is

quickly followed by dismay and fear. A woman who both knows how to use an emergency contraceptive and has access to highly effective medication can transform a nightmare into calm and successful rescue from the possibility of unintended pregnancy. 

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