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Providing Ongoing Hormonal Contraception after Use of Emergency Contraceptive Pills

Background

In March 2015, the United States (US) Food and Drug Administration (FDA) authorized a change to the label for ulipristal acetate (UPA) emergency contraception (EC), sold in the US as ella[®], to recommend that patients who use ella[®] wait five days before starting a hormonal contraceptive method. This change was prompted by new research showing that starting a specific progestin-only pill (a formulation that is not available in the US) the day after taking UPA EC may compromise the efficacy of UPA. Implications of this change for clinical practice may be significant; until recently, clinical guidelines recommended immediate initiation of ongoing contraception following use of oral EC.^{1,2} This recommendation was intended to increase uptake of more effective ongoing contraception for EC users, and thus reduce the subsequent risk of pregnancy. This fact sheet describes what is known about this issue, discusses outstanding questions, and offers some recommendations for providers.

New Evidence

The US ella[®] label now includes the following statement: “After using ella[®], if a woman wishes to use hormonal contraception, she should do so no sooner than 5 days after the intake of ella[®], and she should use a reliable barrier method until the next menstrual period.”³ The concern is that immediately following UPA EC (which is an anti-progestin) with a progestin-containing hormonal contraceptive could interfere with the ability of UPA EC to delay ovulation. A recent pharmacodynamic study by Brache and colleagues showed that starting a desogestrel progestin-only pill (DSG POP) the day after UPA intake significantly increased the chance of ovulation within five days.⁴ (The five-day timeframe is important for users of EC because this is the window in which sperm are believed to remain viable in the female genital tract.⁵) In this crossover study, women with imminent ovulation (with a lead follicle measuring between 14mm and 16mm) took UPA or a placebo and then started either a placebo pill or a DSG POP the next day. Among cycles in which women started a placebo pill the day after taking UPA EC, ovulation occurred within 5 days in one (3%) of 29 cycles; when women started a DSG POP, ovulation occurred within 5 days in 13 (45%) of 29 cycles. These results indicate that immediate start of a DSG POP can indeed counteract the effects of UPA EC and expose the individual to the same risk of pregnancy faced without use of UPA EC. This is a small study of one type of hormonal contraception (a pill formulation that is not available in the US), but it is biologically plausible that this effect may apply more broadly.

Outstanding Questions

These results are compelling, and may have substantial clinical significance. However, some important outstanding questions remain, many of which are described by Dr. Anna Glasier in her 2015 commentary⁶:

1. Do these results apply to other oral contraceptive pills?

The pill formulation studied by Brache *et al* is widely-used in Europe, but is not available in the US. This distinction may be relevant because DSG POPs, unlike other POPs, are effective at inhibiting ovulation (albeit through different biological mechanisms than UPA), while other POPs function primarily through cervical mucus changes. Combined oral contraceptive pills (which contain an estrogen as well as a progestin) also work by inhibiting ovulation and may or may not have the same effect on UPA EC.

2. Do these results apply to other forms of hormonal contraception?

The impact of immediate initiation of other forms of hormonal contraception on UPA EC has not been studied; the FDA's recommendation in the ella[®] label is extrapolated to all hormonal contraceptives based on Brache's pharmacodynamic study of the DSG POP. Implants, injections, and intrauterine systems require direct involvement of a healthcare provider, so a patient cannot simply go home and self-administer the method after a waiting period. Although the evidence is very limited, until more studies are completed, a prudent and conservative approach is to assume that these effects apply broadly to other hormonal contraceptives.

3. Do these results apply to other forms of emergency contraception?

No similar studies have assessed whether immediate start of hormonal contraceptives might impact the ability of levonorgestrel (LNG) EC to delay ovulation. However, the theoretical concern is far greater in the case of UPA EC due to the potential interactions between progestins and anti-progestins.

4. Five days after UPA, or five days after unprotected sex?

The outcome of interest in the study by Brache and colleagues was ovulation within five days of UPA intake; however, since sperm are thought to remain viable for five days after sex occurs, any additional days beyond sperm viability are likely not relevant to pregnancy risk. It is important, however, to remind patients that this applies to acts of intercourse that occur before UPA EC is taken. Changing the start of the five-day waiting period from the day that UPA EC was taken to the day that unprotected sex occurred could offer more flexibility for patients to schedule their follow-up contraception appointment.

5. Given what is known, and not known, how do we weigh the potential risks and benefits of waiting to start ongoing contraception following use of UPA?

Until more studies are available that include a broader range of hormonal contraceptives, including the levonorgestrel intrauterine system (LNG IUS), the implant, the injection, and the oral contraceptive pills available in the United States, providers and patients will have to make the best decisions that they can with the information that is available now. And given the expense and complexity of conducting such studies for each hormonal method, it is possible that such studies will never be done. For provider-dependent methods, an important outstanding issue is how to weigh competing risks: the risk of pregnancy from the act of intercourse that already occurred (and the potential to increase that risk by initiating a method that could compromise the efficacy of UPA) versus the future risk of pregnancy if a patient is not able to return for a follow-up contraception visit.

Recommendations and Counseling Points

As a result of this new evidence, some recommendations suggest waiting to start any hormonal contraception for five^{3,6,7} or six⁸ days after UPA is taken. This is a very reasonable, albeit conservative, recommendation that would mitigate any risk that the effectiveness of UPA might be compromised. However, delaying ongoing contraception may increase the future risk of pregnancy, as the complex circumstances of people's lives may prevent some from returning for the follow-up contraception visit for provider-dependent methods. Until (and, indeed, if) future research clarifies interactions between UPA EC and other hormonal contraceptives, providers may want to reconsider their protocols for starting ongoing contraception following use of UPA EC.

Keep in mind:

- **The copper IUD is the most effective EC option.** Here, we focus on EC pills given the recent changes to the ella[®] label. However, the copper IUD is by far the most effective EC method. When inserted after unprotected sex, the copper IUD prevents nearly 100% of pregnancies from the act of intercourse that already occurred⁹ and is highly effective as an ongoing contraceptive method. Preliminary data show that LNG EC provided simultaneously with the LNG IUS may be an excellent option for EC¹⁰, but data are still too limited to universally recommend this approach. For patients who want to start the LNG IUS, we recommend following the Selected Practice Recommendations for Contraceptive Use² guidelines to rule out pregnancy before providing the LNG IUS (*see Box 1*).
- **UPA EC is more effective than LNG EC** because it works closer to the time of ovulation and is typically the preferred option for EC. Data from one analysis suggest that UPA EC may be more effective than LNG EC for those who are obese and overweight¹¹, although another study did not show this effect.¹² UPA EC is more effective than LNG EC for all users, regardless of weight, but if UPA EC is not available and EC is needed, no one should be denied LNG EC because of weight.
- **UPA EC is not always available in the US.** Although UPA EC was approved by the FDA in 2010, access to this form of EC is far from universal in the US. Many providers outside of family planning and public health clinics may not be familiar with UPA¹³, and pharmacies predominantly stock LNG EC products, which are OTC.¹⁴ LNG EC is less effective, but as it is approved for OTC sale, generally more available.
- **Count 5 days from intercourse.** For patients using UPA EC and starting a hormonal contraceptive, we recommend starting the five-day period of delay when unprotected sex occurred (before use of UPA EC), rather than when UPA EC is taken. This approach may maximize scheduling flexibility while minimizing potential compromise of UPA efficacy. However, if it is difficult to accurately determine the date of intercourse, it may be best to start the delay period at EC intake.
- **Consider pregnancy risk.** For someone who is likely within the fertile period (based on cycle day), it is particularly important to prioritize the efficacy of EC over concerns about ongoing contraception and emphasize UPA as a first-line option for oral EC.
- **For patients who need EC because of missed or late pills, patch or ring,** LNG EC, rather than UPA EC, is recommended due to potential interactions between progestins and anti-progestins.

Box 1: Ruling out pregnancy

The US Centers for Disease Control's Selected Practice Recommendations for Contraceptive Use² includes a checklist that providers can use to be reasonably certain that a patient is not pregnant. Many of these criteria (listed below) may not apply to EC clients. Providers are urged to proceed with caution before providing the LNG IUS if pregnancy cannot be excluded; this may mean asking the patient to return after pregnancy can be ruled out.

You can be reasonably certain a patient isn't pregnant if there are no signs of pregnancy and one of the following applies. The patient is:

- ≤ 7 days after the start of normal menses
- ≤ 7 days after spontaneous or induced abortion
- ≤ 4 weeks postpartum
- Fully/nearly fully breastfeeding, amenorrheic, and < 6 months postpartum
- No sexual intercourse since the start of last normal menses
- Correctly and consistently using a reliable method of contraception

Choosing a Method

Note: The copper IUD is by far the most effective EC method. If the copper IUD is not acceptable to the patient or cannot be provided immediately, offer oral EC followed by the ongoing contraceptive method of the patient's choice.

Points to Consider With Patients

1. Is UPA EC available?
2. Is the patient at high risk for pregnancy from the act of intercourse that just occurred, based on cycle day and the timing of unprotected sex?
3. Is the patient more concerned about pregnancy risk from previous or future sex?
4. Is the patient likely to return for a contraception visit?
5. Is the patient presenting for EC because of missed or late pills, patch or ring?

APPROACH 1: UPA EC plus ongoing contraception

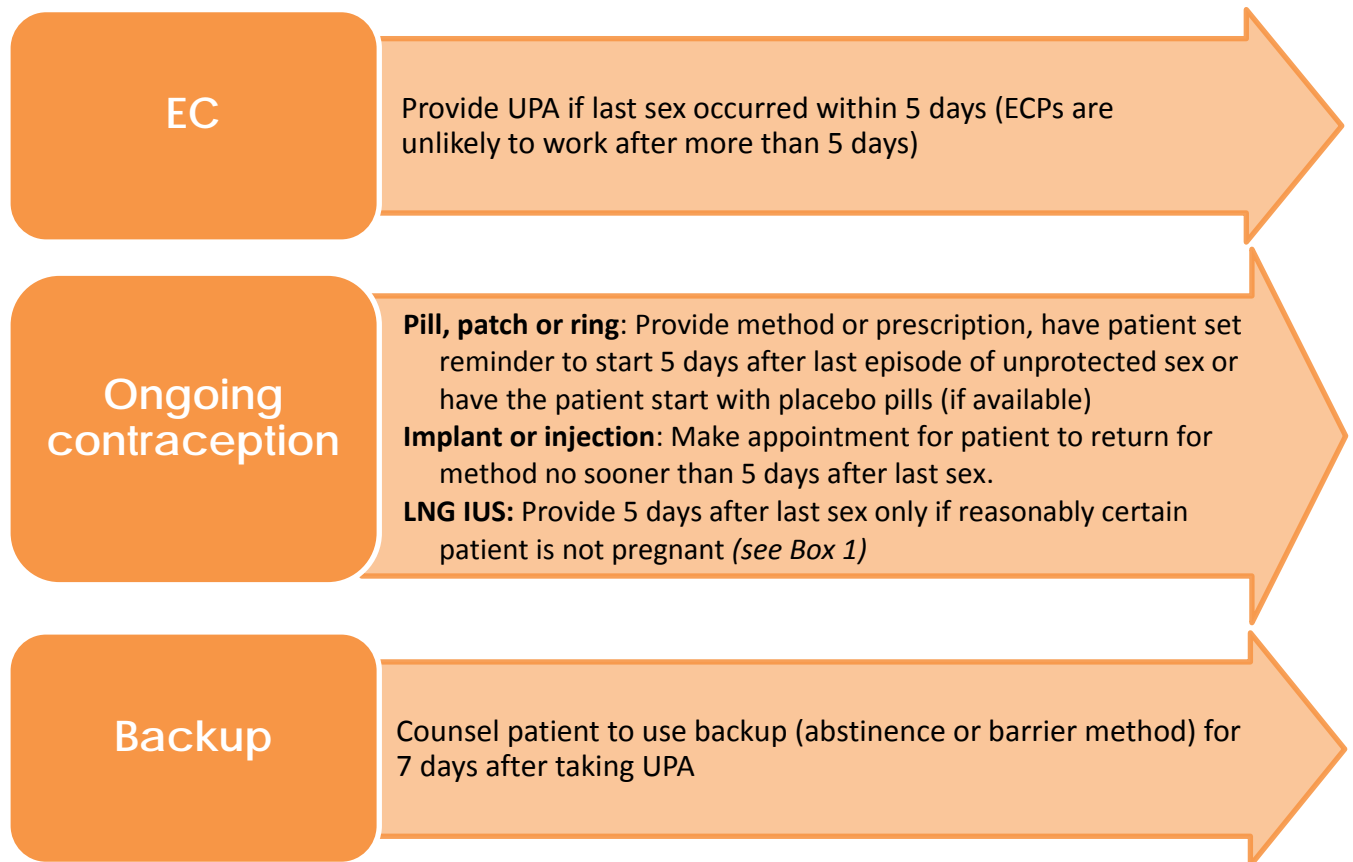
This is a first-choice option when:

- UPA EC is available

The patient is:

- at high risk for pregnancy from the previous act of intercourse, based on cycle day and timing of sex
- more concerned about pregnancy risk from previous sex than future sex
- interested in ongoing contraception and likely to return for a follow-up visit

Clinical quick reference for providing UPA EC + ongoing contraception:



APPROACH 2: LNG EC plus ongoing contraception

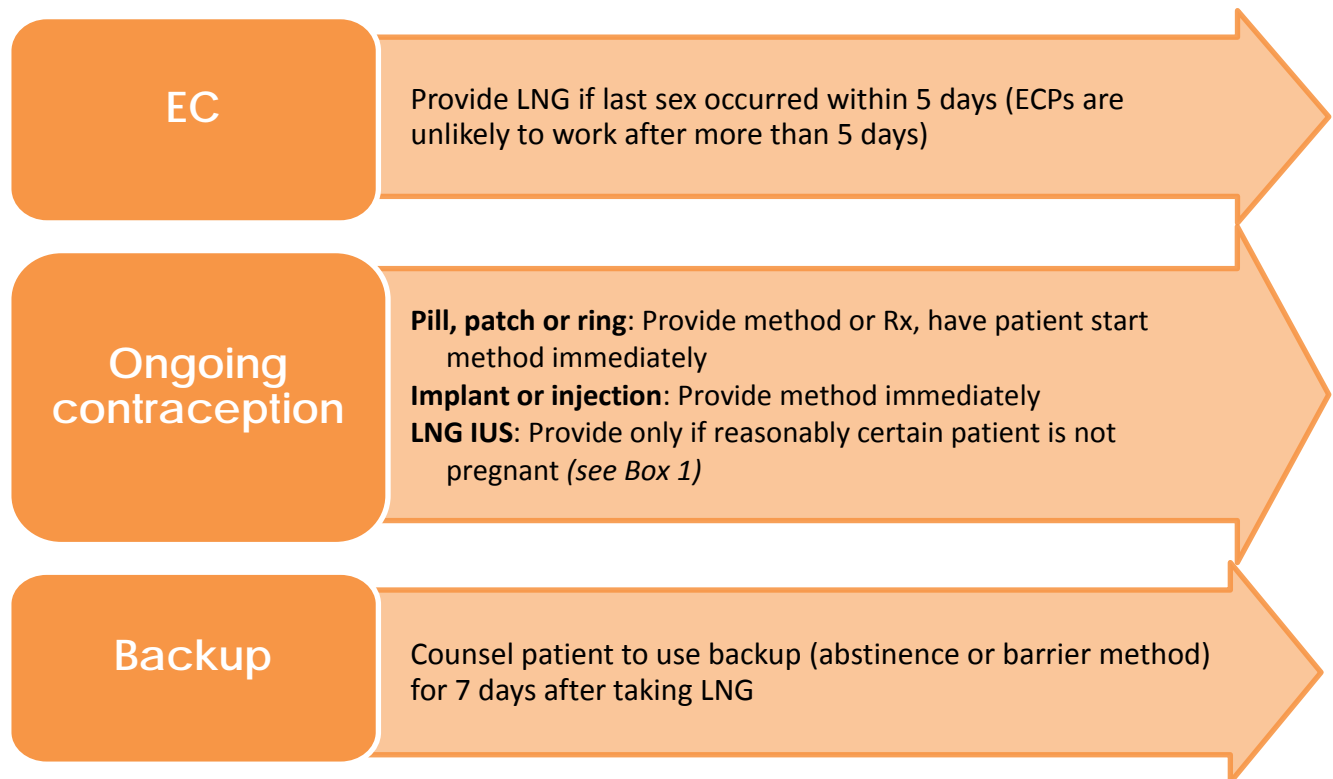
This is a first-choice option when:

- UPA EC is not available

The patient is:

- at relatively low risk for pregnancy from the recent act of intercourse, based on cycle day and timing of sex
- more concerned about pregnancy risk from future sex than previous sex
- interested in ongoing contraception and is not likely to return for a follow-up visit
- seeking EC due to missed or late pills, patch or ring

Clinical quick reference for providing LNG EC + ongoing contraception:



Summary and Conclusion

Uncertainty is inherent in scientific progress; new research may provide important suggestive findings on which to build but leave other key questions unanswered. In this case, compelling research indicates that starting a DSG POP the day after taking UPA EC may significantly reduce the efficacy of UPA, thereby increasing pregnancy risk. But important questions remain, particularly about how broadly these findings apply to other hormonal contraceptive methods. This is of critical importance: EC clients may be at substantial future risk of pregnancy, and providers want to support those who would like to start a new ongoing contraceptive method as quickly and easily as possible. Ideally, new research will become available to clarify the effects of all ongoing hormonal contraceptives on UPA EC. In the meantime, providers and patients must use the evidence that is available today to weigh competing risks and find the best method for each patient.

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