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# EFFICACY OF EMERGENCY CONTRACEPTION AND BODY WEIGHT: CURRENT UNDERSTANDING AND RECOMMENDATIONS


## Summary

- **Research has raised the question of whether emergency contraceptive (EC) pills may be less effective for users with higher weight or body mass index.** Some data show that levonorgestrel EC (LNG EC, sold in the U.S. as Plan B One-Step®, Take Action®, and others) may be less effective for individuals weighing over 165 pounds. The effectiveness of ulipristal acetate EC (UPA EC, sold in the U.S. as ella®) may also be reduced for users weighing more than 194 pounds.

- **Regardless of body weight, the most effective form of EC is the copper IUD. The next most effective method is ulipristal acetate.** All patients (but particularly those at higher weights) should be offered the copper IUD or UPA EC if these options are accessible and acceptable. Emerging evidence suggests that the LNG 52 mg IUD is also an effective EC option.

- **No one should be refused or discouraged from using EC based on weight.** LNG EC is usually the most accessible--and sometimes the only--EC option. Patients at higher body weights should be advised that 1.5 mg LNG EC may not work for them and be informed if other, more effective methods are available.

- **Advocates should work to disseminate information about all EC options** and encourage individuals with higher body weights to consult a clinician if they are at risk of pregnancy after unprotected sex.


## Background

### Research

In 2011, an article based on two clinical trials concluded that "the limit of efficacy was reached at a weight of 70 kg [154 lbs] for LNG compared with 88 kg [194 lbs] in women having taken UPA."[1] These findings are of potential clinical significance, yet there are important limitations to the data. These trials were not specifically designed to study the relationship between efficacy and weight, and at one of the study sites, weight and height were self-assessed [as is the case when EC is purchased over the counter (OTC)], not measured. The numbers of participants in the "overweight" and "obese" categories were small, and the number of pregnancies in the highest weight category was extremely small.[2] A pooled analysis of two clinical trials comparing LNG and UPA[1,3] found significantly higher pregnancy rates among participants who took LNG EC with weight ≥165 pounds or BMI ≥ 26kg/$m^2$.[4] An analysis of four World Health Organization (WHO) studies, conducted primarily among populations of African and Asian women, also found an increased risk of pregnancy among those with BMI >30kg/$m^2$, although the results appear to be driven by incongruous findings from one study.[5]

Two pharmacokinetic studies support the theory that clinical obesity reduces the bioavailability of LNG EC. One study (involving 10 women) found that the serum concentration in those who took LNG

1.5 mg was about 50% lower in women with BMI of 30 kg/m$^2$ or greater compared to those with BMI less than 25 kg/m$^2$. In this study, doubling the dose in the higher BMI group brought the serum concentration to a level equaling that of women with lower BMI who had taken the standard dose (1.5 mg).[6] Another pharmacokinetic study (involving 32 women) similarly found that, throughout 24 hours after ingesting LNG EC, serum concentration levels were 50% lower among women with BMI of 30 kg/m$^2$ or greater. Following use of UPA EC, however, blood levels were similar among both BMI groups.[7] Some organizations (including ASEC and the UK Faculty of Sexual and Reproductive Healthcare, part of the Royal College of Obstetricians and Gynecologists[8]) adjusted EC guidelines to include the possibility of a double dose of LNG EC for individuals with higher BMI. However, a recent pharmacodynamic study involving 70 participants with BMI higher than 30 kg/m$^2$ found that taking 3.0 mg LNG did not significantly reduce the chance of follicular rupture within 5 days compared with 1.5 mg LNG.[9]

### Regulatory Decisions

The manufacturer of NorLevo (a 1.5 mg LNG emergency contraceptive pill (ECP)) conducted additional analyses of the data from the 2011 article and requested that European regulatory authorities allow a change to the product label indicating that higher weight may reduce its effectiveness. In November 2013, European authorities granted a label change warning that "in clinical trials, contraceptive efficacy was reduced in women weighing 75 kg [165 lbs] or more and levonorgestrel was not effective in women who weighed more than 80 kg [175 lbs]."[10] Shortly thereafter, Health Canada (the Canadian regulatory authority) authorized the same label change for LNG EC. In July 2014, the European Medicines Agency completed a review of all available data (including data from trials conducted by WHO) and found that "the data were too limited and not robust enough to conclude with certainty that contraceptive effect is reduced with increased bodyweight," and such statements should be removed from product labels.[11] In May 2016, the US Food and Drug Administration (FDA) announced completion of a review of the available data and also concluded that "the data are conflicting and too limited to reach a definitive conclusion as to whether effectiveness is reduced in [women who weigh more than 165 pounds or have a BMI above 25]."[12] It should be noted that all of this regulatory activity took place before the publications of the most recent WHO study and the pharmacokinetic studies showing a reduction of bioavailability of LNG EC in clinically obese individuals.

The UK Faculty of Sexual and Reproductive Healthcare (FRSH) issued guidance recommending that patients with BMI greater than 26 kg/m$^2$ or weighing more than 154 pounds be offered a copper IUD as a first-line EC option and UPA EC as second choice. If these options are not available, FRSH suggested considering 3.0 mg LNG, which may be more effective than a 1.5 mg dose.[8] (As of the time of this publication, this recommendation had not been changed).

## Significance

The U.S. Centers for Disease Control and Prevention reports that the average American woman weighs 170.8 pounds (77.6 kg)[13]; therefore, millions at risk for pregnancy fall into the weight category in which LNG ECPs (and for a smaller subset of users, possibly UPA ECPs) may not work. It is of vital importance that the most effective forms of EC--IUDs and UPA ECPs--be made widely available. However, IUDs and UPA ECPs can only be obtained with the involvement of a healthcare provider in the United States, while LNG EC is available over the counter without age or point-of-sale restrictions.

Many consumers purchase EC directly from stores and pharmacies without consulting a healthcare provider, and many providers do not routinely include counseling about EC in patient interactions. An analysis of the National Survey of Family Growth demonstrated that only 2% of rural and 3% of urban women had received counseling about EC in the last year.[14] Studies of provider practices found that 14% of healthcare providers who treat women of reproductive age and 18% of obstetrician-gynecologists provide or recommend UPA.[15,16]

## Recommendations and Conclusions

Although the evidence is not entirely clear, there appears to be a relationship between the efficacy of EC (particularly LNG) and the weight of the user, and emerging evidence suggests that biological processes may play a determining role. In its May 2016 communication on the subject, the FDA stated that "further research by the manufacturers of [LNG EC] products on the possible impact of weight or BMI on effectiveness should be a priority."[17] It must be noted that the FDA cannot require that manufacturers conduct such studies, and clinical trials with a rare outcome such as pregnancy after use of EC are large and expensive. A clinical trial (NCT03537768) that recently closed enrollment may provide additional information about the ability of a double-dose (3 mg) of LNG EC to prevent pregnancy in individuals with BMI ≥30 kg/m$^2$. Those in need of EC and healthcare providers who serve patients of reproductive age will most likely need to make decisions about EC without complete information about precisely how weight impacts EC efficacy.

Those who serve patients of reproductive age in a clinical setting are in an excellent position to counsel on all options for EC. For everyone, the copper IUD (and possibly the LNG 52 mg IUD[20]) is the most effective EC method. UPA ECPs are the next most effective option, and LNG ECPs are reasonable when these are not available. For patients at higher body weights, special emphasis should be placed on the benefits of an IUD or UPA (although for patients who weigh more than 194 pounds, the efficacy of UPA might be reduced as well). Providers should remind anyone choosing ECPs that the pill should be taken as soon as possible after sex, and all patients should be offered an ongoing contraceptive method if they wish. Hormonal methods can be started simultaneously with use of LNG and no sooner than 5 days after unprotected intercourse with use of UPA (with limited exceptions for regular pill users who miss 3 pills on days 5-7 of the cycle).[18]

However, most individuals do not obtain EC from a clinic. The majority of EC sales take place in retail outlets now that LNG ECPs are available over the counter with no age or point-of-sale restrictions. Thus, advocates should work to spread information about all options for EC and encourage EC users with higher body weights to consult a clinician if they wish to obtain a more effective EC option after unprotected sex. Consumers should also be informed about the possibility of acquiring UPA EC online from a service such as Nurx, Planned Parenthood Direct, or Pandia Health, and they may want to consider acquiring UPA EC prior to needing it, if possible. Health care providers and pharmacists should never deny access to LNG ECPs because of the user's weight.

In several states in the US, ella® can be obtained directly from a pharamist through statewide protocols.

## Options for Emergency Contraception in the U.S.
*(listed in order of effectiveness)*

### Copper IUD*

*Benefits*

- ✓ Nearly 100% effective[19] in preventing pregnancy after sex
- ✓ Provides at least 12 years of excellent ongoing contraceptive protection; maintenance-free
- ✓ Does not contain any hormones
- ✓ Efficacy is not influenced by weight

*Challenges*

- – Must be provided by a clinician; at least one office visit is required
- – Some patients may find the insertion process uncomfortable or invasive; some experience unacceptable changes in menstrual bleeding patterns
- – Not everyone is interested in a long-acting method
- – Though many insurance plans now cover the costs of IUDs through the Affordable Care Act, cost remains a significant barrier for individuals without insurance

**Emerging evidence shows that the LNG 52 mg IUD provided after intercourse may be an effective option[20]*

### Ulipristal Acetate EC Pills (30 mg)

*Benefits*

- ✓ Can work closer to the time of ovulation, after the luteinizing hormone surge has begun, when LNG is not effective.[21]
- ✓ May be more effective than LNG for individuals with heavier body weights.
- ✓ Can be purchased through an online prescription service (such as Nurx, Planned Parenthood Direct, or Pandia Health)

*Challenges*

- – Sold by prescription only in the U.S.
- – Awareness among providers and stocking in pharmacies may be low
- – Efficacy may also be reduced in individuals weighing more than 194 pounds
- – Interactions with progestins may reduce efficacy. Do not start hormonal contraceptives sooner than 5 days after unprotected intercourse if UPA is used or when EC is needed due to missed or late pills, patches or rings, with limited exceptions [18]

### Levonorgestrel EC Pills (1.5 mg)

*Benefits*

- ✓ By far the most widely-available EC option; available for sale at retail outlets to anyone of any age, with no prescription or proof of age requirement.
- ✓ Hormonal contraceptives can be immediately started after use of LNG EC; can be used when EC is needed because of missed or late pills, patches or rings (no interaction with hormonal contraception used prior to EC).

*Challenges*

- – Less effective than other EC methods
- – May be less effective, especially for users with body weight greater than 165 pounds
- – Price may be a significant barrier; the branded product (Plan B One-Step®) costs an average of $48, while the generic products cost about $41[22] (less expensive options are available at sites such as www.afterpill.com)
- – Some health plans may not cover OTC products or will cover them only with a prescription

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