

IMAP Statement on advances in emergency contraception

Introduction

This statement has been prepared by the International Medical Advisory Panel (IMAP) and was approved in April 2025.

Emergency contraception (EC) refers to any contraceptive method that can be used after having unprotected or inadequately protected sexual intercourse but before pregnancy occurs, providing women and anyone who can become pregnant with the opportunity to prevent an unwanted pregnancy.¹ EC is a safe and effective method for preventing unwanted pregnancy and can reduce the risk of pregnancy by up to 99%. Recommended EC methods include pills (levonorgestrel 1.5 mg or ulipristal acetate 30 mg) or copper intrauterine device (IUD) insertion (1, 2). Access to EC is a critical component of comprehensive sexual and reproductive health services and should be considered an essential right for all individuals (3).

Despite its effectiveness, EC is not frequently used after unprotected intercourse (4-6). In many settings, people face barriers to accessing EC, and most women are unaware of EC as a way to protect against pregnancy after intercourse has happened. However, in almost every country, the most educated people are the most likely to be aware of and use EC. Some providers lack knowledge about EC, favour adding restrictions to EC access, and have negative attitudes toward providing EC to those who may need it, including unmarried women, survivors of sexual and gender-based violence, and adolescent girls (7).

One of the common reasons for denying women access to EC is that it is misperceived or purposefully mis-defined as causing an abortion. Consequently, it is essential to emphasize that EC prevents pregnancy and does not end it (2). Education of the public, providers and policymakers should stress that EC does not cause an abortion, unlike medical abortion pills taken during pregnancy. EC pills are safe to use for women of all ages with few side effects which are similar to those of oral contraceptive pills, such as nausea and vomiting, irregular vaginal bleeding, and fatigue (8, 9). There are no known long-term negative impacts on health or fertility (9).

Dedicated EC products are available in most countries and are included in the World Health Organization (WHO) Model List of Essential Medicines (10). EC is included in the list of 13 essential commodities in the Framework for Action of the UN Commission on Life-Saving

¹ NOTE: This document is inclusive of women, girls and all people who can become pregnant, including intersex, transgender and gender diverse. References to women include all with the capacity to become pregnant.

Commodities for Women and Children (11). EC is also a component of the Minimum Initial Service Package for reproductive health in emergencies and part of the Inter-Agency Reproductive Health Kits for clinical management of rape and short-acting methods of family planning (Kits 3 and 4) (11). For a more detailed overview of EC, refer to IPPF Client-Centred Clinical Guidelines for Sexual and Reproductive Healthcare (9).

Purpose of the statement

The purpose of this statement is to review newly published data on 1) increasing the effectiveness of levonorgestrel emergency contraceptive pills (LNG-ECP) by using pre-coital administration or combined with a non-steroidal anti-inflammatory drug; 2) the potential use of LNG-ECP as a regular contraceptive method for infrequent sex; 3) ulipristal acetate (UPA) which is an established EC method and is now being studied combined with misoprostol (an effective method of abortion in itself) for termination of early pregnancy; and 4) the underutilization of low dose mifepristone as an EC method.

Intended audience and stakeholders

This statement is aimed primarily at IPPF Member Associations to review recently published data on EC products and inform related health care. Other sexual reproductive health organizations, policymakers, researchers, and activists may also benefit from the guidance.

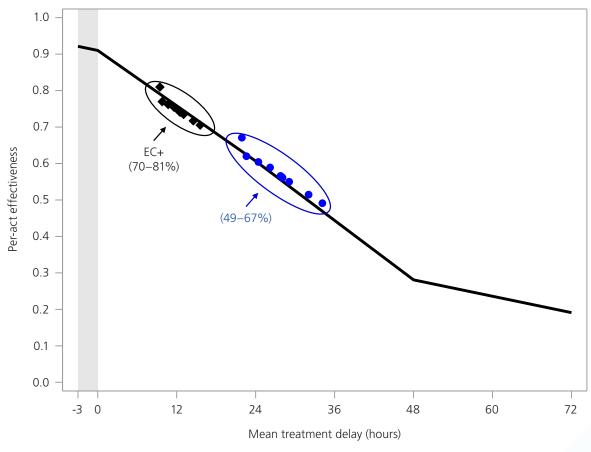
The need to take LNG-EC before ovulation means, on average, its effectiveness decreases as the delay between sex and ingestion of the drug increases.

Increasing the effectiveness of LNG emergency contraception: new evidence

Current product labels state a 1.5 mg oral dose of LNG is a safe and effective EC when ingested before ovulation; it has no apparent impact on the risk of pregnancy when taken after ovulation (12). The need to take LNG-EC before ovulation means, on average, its effectiveness decreases as the delay between sex and ingestion of the drug increases – hence the recommendation it be taken as soon as possible following unprotected sex (13, 14). Based on mathematical modelling of existing data, the effectiveness of LNG-ECP could exceed 90% for individuals taking the drugs with no post-coital delay (15). In nine published studies of subjects taking medications within 72 hours after sex, however, the maximum attainable effectiveness ranged from just 49% to 67% when accounting for the distribution of treatment delays among study subjects (Fig. 1, blue circles). From the same modelling, these effectiveness rates would have increased to between 70% and 81% if half of the study subjects had an advanced supply of LNG-ECP and took it just a few hours (up to three hours) before sex (15).

The WHO Selected Practice Recommendations for Contraceptive Use recommends an advanced supply of EC pills to decrease delay to intake and thus increase the methods' effectiveness (1, 13). Despite clear evidence that reducing treatment delay will increase LNG-EC's per-act effectiveness, a systematic review of 11 randomized intervention studies evaluating the advance provision of EC found none could demonstrate decreased cumulative rates of pregnancy over time in the advanced provision groups (odds ratio (OR) 0.98, 95% confidence interval (CI) 0.76 to 1.25 in studies with twelve-month follow-up data) despite more frequent reported EC use (single use: OR 2.47, 95% CI 1.80 to 3.40; multiple use: OR 4.13, 95% CI 1.77 to 9.63) as well as faster intake in the populations studied (weighted mean difference (WMD) -12.98 hours, 95% CI -16.66 to -9.31 hours) (5). Importantly, advanced provision did not lead to increased rates of sexually

Figure 1: Increase in population-average, maximum attainable effectiveness if 50% of each cohort had advanced provision of LNG-EC and took it 3 hours before sex (black squares) compared to the effectiveness of original nine studies (blue circles)



Adapted from Taylor, Kapp and Steiner 2024

transmitted infections (OR 1.01, 95% CI 0.75 to 1.37) or higher frequency of unprotected intercourse across the studies. A closer analysis of one randomized trial with detailed information on method use suggested that some participants substituted LNG-EC for other contraceptive methods, which may explain why advanced provision did not translate to a decrease in cumulative pregnancy rates (16). Additionally, authors from another study hypothesized that even with advanced provision, women were not taking the LNG-EC quickly enough, as the mean delay to ingestion was 17 hours (15).

Adding a non-steroidal anti-inflammatory drug such as meloxicam or piroxicam to LNG may also

increase the effectiveness of EC. These drugs block the enzyme COX-2, which synthesizes ovarian prostaglandins that play a critical role in ovulation (17–20). Existing evidence on the combined use of LNG and non-steroidal medicine indicates that the combination may be more effective as a contraceptive than either component alone (18, 20). A recent randomized controlled trial in China found that levonorgestrel plus piroxicam prevented 94.7% of expected pregnancies compared with 63.4% for levonorgestrel plus placebo (20). No differences were noted between the two groups in the proportion of women with a change in the timing of their next period or the adverse event profile (20).

Promising research on a new use for LNG as an on-demand contraceptive

Infrequent sex is an important reason for not using contraception among women of reproductive age. On average, 34% of women in Latin America and the Caribbean, 31% in Asia, and 19% in Africa said they were not using a method because they have sex infrequently or not at all (21). Women not currently having sex or having infrequent sex may not choose contraceptives which require daily action (such as taking a pill) or longer-acting methods which require insertion or injection, in part due to not wanting to use a method with possible side effects for a benefit (preventing pregnancy) that is needed rarely. Pericoital methods may, therefore, have more appeal; in fact, research has shown that in some settings, women have adopted LNG-EC use as a regular contraceptive (21). A systematic review of 30 peer-reviewed papers published between 2014–2023, which included research

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from six countries across five world regions, suggested widespread appeal for on-demand oral contraceptives to be used just before or after sex. A proof-of-concept study of 1.5 mg LNG as a pericoital on-demand contraceptive method among more than 300 women for six months, conducted by the WHO, suggested that 1.5 mg LNG is safe when used within 24 hours before or after sex for contraception (22). Still, it was only modestly effective (incidence rate between 7–11 pregnancies per 100 woman-years) compared to other hormonal contraceptive methods. Additionally, feasibility studies in Ghana and Kenya have demonstrated both demand and acceptability for a levonorgestrel pericoital pill available from pharmacies for users reporting infrequent sex (23, 24). Pericoital use of the LNG pill had high levels of satisfaction and was popular with new users. Research is ongoing to improve the efficacy of a pericoital pill method such as LNG, better understand the side effect profile (particularly disordered bleeding) and establish a product that can be registered for such use.

New potential uses for ulipristal (UPA) do not change what we know about its ability to delay/disrupt ovulation to prevent pregnancy as an emergency contraceptive

Although UPA at 30 mg is an established and marketed emergency contraceptive pill, it has also been studied and used for other indications at different doses, including treatment of fibroids, endometriosis, treatment of bleeding in IUD users, and breast cancer prevention. UPA is a selective progesterone receptor modulator, meaning that it interferes with naturally-occurring progesterone - a hormone necessary for the maintenance and growth of the conditions listed above, as well as pregnancy. One recent study explored the use of 60mg of UPA in combination with misoprostol for early pregnancy termination, which is the first time UPA in combination with misoprostol had been used for inducing abortion (25). Studying UPA for other indications, including for abortion, does not change what is known about emergency contraception: UPA in a non-pregnant person can delay or suppress ovulation. It is not known to prevent pregnancy once ovulation has occurred. Like LNG, UPA is not 100% effective. Still, there are advantages over LNG-EC: UPA has a longer window of effectiveness to prevent ovulation than LNG and is likely more effective for those with a higher body weight. Overall, the recent study indicates that UPA deserves more research about how useful and effective it may be compared to other medical abortion regimens. However, there are already well-established, safe

and effective medical abortion regimens with mifepristone and misoprostol, or misoprostol alone. It is unclear whether UPA with misoprostol would offer any benefits over existing regimens, which indicates the need for further study. There is a risk, however, that politicians could inappropriately apply the findings of this study to restrict UPA availability for EC. Any efforts to limit access would be detrimental to those seeking EC, given the advantages over LNG when available (better efficacy among those with higher body mass indices and up to 5 days after unprotected sex) (<u>26</u>).

Mifepristone is a safe, effective affordable EC method whose availability should be expanded

Mifepristone is also a progesterone antagonist with many possible uses in gynecology. A 2019 systematic review of interventions for EC included more than 40 studies of low-dose (25–50 mg) mifepristone used for EC (27). Compared to LNG, mifepristone was 40% more effective according to the review's analysis at preventing pregnancy. Although mifepristone is a safe, effective, and generally affordable medicine, it is not widely available in the low-dose used for EC. In fact, in 2020, only 6 countries had a registered mifepristone product available for EC despite studies demonstrating both safety and effectiveness (28). The limited availability of mifepristone has impeded global recommendations for EC use, which has been worsened by concerns about the conflation of EC and medical abortion. Work is ongoing to develop and register a dedicated mifepristone EC product to attain stringent-regulatory approval, thereby increasing product availability and global recommendations for use.

Recommendations

Widely include EC in sexual and reproductive health services and programming.

- Programs should include all locally available methods: both LNG-ECP and UPA pills and the copper IUD. The methods should be available to all ages of clients who report or expect to have unprotected intercourse and desire to avoid pregnancy. IUDs are the most effective emergency contraceptive and can remain in place as an ongoing, highly effective method for those who prefer adopting a long-acting method. Emergency contraception is a critical service to offer in humanitarian settings and sexual and gender-based violence programming for post-exposure prophylaxis after rape or sexual violence.
- Comprehensive sexual education programs should include information about the indications for use and availability of EC, including where it may be accessed (generally available from pharmacies in addition to health clinics).
- Health providers and pharmacists should be trained to facilitate access to EC for those who need it, including providing appropriate counselling, promoting advance provision for back-up to other contraceptive methods or during times when other contraceptive methods are not being used.

Advocate to reduce barriers to EC access.

- Promote over-the-counter availability of EC pills with no age or marital status restrictions and lift any other regulatory or policy limitations that maintain medically unnecessary restrictions.
- Ensure EC is integrated into national policies and essential services packages, including in humanitarian settings.

Comprehensive sexual education programs should include information about the indications for use and availability of EC.

Advocate for advance provision of emergency contraceptive pills.

 Advanced provision of EC pills that can be kept on hand makes it more likely that a client will use the pills after unprotected intercourse as well as to use them earlier after sex, which increases their effectiveness. Advanced provision can avoid unintentional delays to treatment. Adolescents may particularly benefit from advanced provision as they may be more likely to have unplanned sex and face barriers when accessing emergency contraception.

Promote use up to 3 hours prior to sex for those who otherwise anticipate having unprotected intercourse.

Modelling of published data of LNG-ECPs demonstrates effectiveness increases substantially with use up to 3 hours before sex and is as safe as taking the pills after sex. This manner of administrating LNG-ECPs could be appropriate and prevent more pregnancies for those who anticipate unprotected sex; it has shown to be acceptable in various populations (18–21). Research is needed to establish whether counselling on this option leads to improved and timely use.

De-stigmatize repeated or planned use of emergency contraception.

Emergency contraception should not be perceived as only to be used in an emergency. Pharmacists and healthcare providers should not impose barriers to repeated or planned use. Although EC has not been approved as a routine method with an established and available product, limited clinical data supports its safety and modest efficacy. However, more effective methods of contraception are available for ongoing use: a wide range of existing hormonal methods, as well as the copper IUD, have all been shown to be more effective in preventing pregnancy, but they may not be preferred by women having infrequent sex.

Support/ advocate for future and ongoing research to advance effective on-demand pericoital methods.

 A coitally-dependent contraceptive, which is discrete and does not require the cooperation of a sexual partner, may be attractive to many women, particularly those who have infrequent sex. A dedicated product should be developed and marketed to meet these needs, building on the safety and efficacy data already existing for pericoital use of levonorgestrel. Advocacy for the development of a dedicated product and further international clinical trials to support regulatory approval should be supported by the field of sexual and reproductive health researchers and activists.

Include mifepristone 25–50mg in global guidance for emergency contraception.

 Ensuring that mifepristone 25–50mg is included in global guidelines for contraceptive use will increase awareness and demand for additional effective options for EC.
 Highlighting the need for more effective, safe, post-coital methods will build the case for investment from manufactures to develop and make a dedicated mifepristone EC product widely available.

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Who we are

The International Planned Parenthood Federation (IPPF) is a global service provider and a leading advocate of sexual and reproductive health and rights for all. We are a worldwide movement of national organizations working with and for communities and individuals.

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