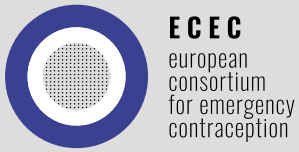
New uses for ulipristal acetate (UPA)

Embracing scientific progress and sustaining access to emergency contraception



US edition - January 2025

Outline

Introduction 3
01. New research studied UPA in an abortion regimen. What do we know? 5
02. Challenges and opportunities 6
03. Key takeaways 7
04. Background information 15

- Types of emergency contraceptive (EC) pills 15
- Availability of EC pills worldwide 19
- Tools and references 23

This resource was developed by the European Consortium for Emergency Contraception (ECEC) and the American Society for Emergency Contraception (ASEC) to support individuals and organizations working to protect and advance access to emergency contraceptive (EC) pills, at a time when this contraceptive may come under unusual scrutiny. EC pills are used to prevent pregnancy after unprotected sex, contraceptive failure, and/or sexual assault.

ASEC's and ECEC's ultimate goal is to ensure that everyone has equitable, affordable access to safe products that meet their reproductive health needs, including both EC and medication abortion, and that multiple options to meet the needs of people throughout their reproductive cycles and reproductive life remain available to all.

Two main types of EC pills are widely available: one containing 30 mg of ulipristal acetate (UPA) and one containing 1.5 mg of levonorgestrel (LNG). EC pills with a low dose of mifepristone (10 to 25 mg) are also available in a few countries. This variety of EC pills has made messaging about EC more complex, and recent research on the use of UPA for other indications will make it even more so.

This resource provides basic information about oral EC methods, medication abortion methods and new research developments.

Key Takeaways

1.As science progresses, we need accurate communication about how medicines can be used for different reproductive health conditions.

2. Emergency contraceptive (EC) pills are essential for reproductive health and autonomy.

3. Ulipristal acetate (UPA) has been studied for a range of other indications.

4. Studying UPA for other indications does not change what we know about use of UPA as EC.

5. EC pills (with UPA, levonorgestrel or mifepristone) are different from medication abortion.

6. Misoprostol alone is safe and effective for early abortion.

7. A safe and effective regimen for medication abortion using misoprostol and mifepristone is already very well established.

8. The new study of UPA and misoprostol for medication abortion is small and preliminary; its aim is to explore the feasibility of this regimen.

01

New research studied UPA in an abortion regimen. What do we know?

- A recent study explored a new combination of medications and their effectiveness at terminating an early pregnancy. This study registry is available here↗.
- The study was conducted in Mexico from 2019-2022 among approximately 133 patients, exploring whether using ulipristal acetate (UPA) with misoprostol can terminate a pregnancy up to 63 days (or nine weeks). UPA is the active ingredient in the newer generation of EC pills.
- The study investigated 60 mg and 90 milligrams (mg) of UPA followed by 800 micrograms (µg) of misoprostol, similar to the companion dosage used in medication abortion regimens with mifepristone.
- The dose of UPA used in the study is double (or triple) the current dose for EC (30 mg). ASEC and ECEC are not involved nor have participated in this study in any way.

02

Challenges and opportunities

Publication of this study may put a spotlight on EC pills, since UPA is currently marketed and indicated for EC use. This creates renewed opportunities to educate about the importance of EC and its role in preventing pregnancy; dispel myths around EC pill use, safety, and mechanism of action; and uplift the importance of both EC and medication abortion while clarifying the differences. However, it could also be used to launch new attacks on EC access and/or to conflate EC and medication abortion.

This study and others under way may open a discussion about the development of new indications for well-established reproductive health products, and the importance of understanding and communicating about the use of different products across the reproductive health spectrum.

03

Key takeaways

01. As science develops, we need accurate communication about how medicines can be used for different reproductive health conditions.

- This study opens a discussion about new indications for well established reproductive health products.
- Misoprostol, for instance, is already used for a variety of other medical indications such as prevention of gastric ulcers, postpartum hemorrhage, and for cervical ripening and labor induction. Mifepristone is used for EC in some countries, and is being studied for use as a regular contraceptive.
- Understanding why and how different products can be used across the reproductive health spectrum is important for supporting reproductive health and autonomy across a person's life course.

02. EC pills are essential for reproductive health and autonomy.

- EC pills are made with levonorgestrel (LNG, the most common around the world), ulipristal acetate (UPA), or mifepristone (in a small number of countries)
- EC is the only contraceptive method that can be used after sex to reduce the risk of pregnancy. EC pills are an important method and the available data suggests a significant increase in use over the past decade in many parts of the world.
- EC pills offer privacy, confidentiality and control to users.
- EC pills are especially important for people in vulnerable or marginalized situations, i.e.: those who have experienced forced or unwanted sex, or people who may not be able to access clinic-based contraceptive services easily (due to young age, displacement or other factors).
- EC pills are more likely to work the sooner they are taken; this makes timely access to EC pills particularly critical.

03. Ulipristal acetate (UPA) has also been studied for a range of other indications.

- UPA is a relatively new compound; other valuable indications for UPA in gynecologic care beyond EC are being investigated.
- UPA has already been marketed to treat uterine fibroids, and is being researched for endometriosis, bleeding in IUD users, and breast cancer prevention.
- This recent study investigates whether UPA can be used as part of an abortion regimen.

04. Studying UPA for other indications does not change what we know about UPA as EC.

- UPA EC pills delay or suppress ovulation. They are not 100% effective in preventing pregnancy: they have not been shown to prevent pregnancy if ovulation has already occurred.
- People who have used UPA as indicated for EC (30 mg of UPA taken within 5 days after unprotected sex), or providers who have prescribed or dispensed this regimen, have not experienced or provided an abortion.
- UPA EC pills are very effective in preventing pregnancy and are the most effective quality-assured* oral EC available:
  - UPA EC pills are labelled for use up to 120 hours (5 days) after unprotected sex, while LNG EC pills are labelled for use up to 72 hours (3 days) after sex.
  - UPA EC pills have a wider window of action and are more effective than LNG EC pills because they can work closer to the time of ovulation. UPA EC can still inhibit ovulation when the luteinizing hormone (LH) surge has begun, a point at which LNG EC pills are no longer effective.
  - UPA EC pills may be more effective than LNG EC pills for those who weigh more than 165 lbs.
- UPA EC is a well-established product that has been safely used by over 58 million worldwide. It was first approved by the European Medicines Agency (EMA) in 2009, and has since been approved by the US Food and Drug Administration (FDA) in 2010 and by numerous other medicines agencies globally.

*Quality assured means that a product meets global standards for pharmaceutical ingredients, good manufacturing practices (GMP), testing of products, regulatory guidelines for authorization of marketing, and correct storage and distribution practices.

05. EC pills (with UPA, LNG or mifepristone) are different from medication abortion.

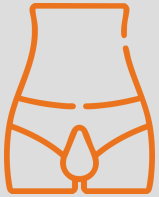
- EC pills and medication abortion are necessary for reproductive health and autonomy. Confusion between the two can present a barrier to broader access and could cause uncertainty about which regimen is needed at which part of the reproductive cycle.
- Emergency contraception prevents pregnancy from starting, while medication abortion terminates an existing pregnancy.
- Access to safe, effective abortion care and contraception is essential to ensure everyone has the freedom to make decisions about their bodies and lives.
- There is no evidence that LNG↗ or UPA↗ EC pills on their own would cause an abortion. It would be incorrect and misleading for people seeking to end a pregnancy, to be told that "using the *morning after pill* and misoprostol can induce abortion".

06. Misoprostol alone is safe and effective for early abortion.

- Misoprostol is used alone (usually in repeated doses) to safely and effectively end a pregnancy; this study does not indicate that UPA on its own is an abortifacient.
- Misoprostol alone is well-studied and is recommended when mifepristone is not available.
  - 37 brands of misoprostol are currently found in 104 countries medab.org↗
- Misoprostol's wide range of indications (including for non-gynecological uses such as gastric ulcers) means that it is widely available in many settings.

07. A safe and effective regimen for medication abortion using misoprostol and mifepristone is already very well established.

- This two-medication regimen (mifepristone followed by misoprostol) was FDA-approved 25 years ago for early abortion care.
- While access to mifepristone remains challenging in some settings, access to this abortion regimen has expanded in the past decade. Today, mifepristone is approved for medication abortion in at least 105 countries. gynuity.org
  - About 36 brands of mifepristone for medication abortion are currently sold in 57 countries
  - 20 brands of dedicated two-medicine products ("combipacks" with mifepristone and misoprostol) are currently available in 46 countries medab.org.
- The World Health Organization (WHO) provides detailed and evidence-based recommendations on the use of these regimens in its 2022 Abortion care guideline, and the global health community encourages countries to align national clinical guidelines and practice to this standard. According to these recommendations, the combination regimen is more effective than misoprostol alone for early abortion.



08. The new study on UPA and misoprostol for medication abortion is small and preliminary; its aim is to explore the feasibility of this regimen.

- In many settings, cost, policy, and bureaucratic barriers make mifepristone registration, import, and/or access very difficult. Given these challenges, researchers are seeking more options for safe, effective abortion care, including testing new combinations of medications.
- Given that the study did not include a comparison group, the UPA and misoprostol combination cannot be directly compared to established medication abortion regimens (mifepristone + misoprostol or misoprostol alone).

04

Background information

The term emergency contraception (EC) is used to describe methods of contraception that can be used to prevent pregnancy after unprotected sex, contraceptive failure, or sexual assault. The most common forms of EC pills contain levonorgestrel (LNG) or ulipristal acetate (UPA). A third type with a low dose of mifepristone is also marketed in a handful of countries. The WHO strongly recommends making UPA and LNG EC pills available without a prescription (*WHO recommendations on self-care interventions: making over-the-counter emergency contraceptive pills available without a prescription. WHO, 2024*). When assessing effectiveness of each type of EC, it is important to note that, for each individual and for each use of EC pills, effectiveness will vary depending on the timing of unprotected intercourse in relation to ovulation.

Types of emergency contraceptive (EC) pills

EC pills with levonorgestrel (LNG)

- Active ingredient: 1.5 mg of levonorgestrel (a second-generation synthetic progestin)
- Marketed since the 1990s
- Indication according to label: use as soon as possible up to 72 hours after unprotected sex
- Efficacy: high from 0-72 hours after sex; moderate from 72 to 96 hours; and low or null beyond 96 hours
- US brands: Aftera, AfterPill, EContra One-Step, Julie, Morning After Pill, My Way, New Day, Plan B One-Step, PostDay One-Step and many others
- Main mechanism of action: inhibits or delays ovulation
- Availability: registered or imported in at least 147 countries. Available without prescription in at least 88 countries.

EC pills with ulipristal acetate (UPA)

- Active ingredient: 30 mg of ulipristal acetate (a selective progesterone receptor modulator)
- Marketed since 2009 in Europe and 2010 in the USA. Available without prescription in most of Europe since 2014
- Indication according to label: use as soon as possible up to 120 hours after unprotected sex
- Efficacy: high from 0 to 120 hours after sex
- US brands: ella
- Main mechanism of action: delays ovulation
- Availability: registered or imported in at least 75 countries. Available without prescription in at least 56 countries.

EC pills with mifepristone

- Active ingredient: 10 to 25 mg of mifepristone (a selective progesterone receptor modulator)
- Marketed for EC in six countries; to date, none of the mifepristone EC products are quality-assured
- Indication according to label: use up to 120 hours after unprotected sex
- Efficacy: high from 0 to 120 hours
- Brands: Ciel EC, Fivedays, Gynepriston, Mifestad 10, Mifepriston 10mg, Sky EC25 and others
- Main mechanism of action: inhibits or delays ovulation. Depending on the phase of the menstrual cycle, may interfere with implantation
- Availability: registered or imported in Armenia, China, Moldova, Russian Federation, Vietnam and Ukraine.

Availability of EC pills worldwide

ECEC european consortium for emergency contraception

american society for emergency contraception asec

LNG EC pills are registered or available in at least 147 countries worldwide

As of July 2024

Registered or available as **non-prescription** *88 countries*

Registered or available as **prescription-only** *35 countries**

Available but registration **status unknown** *24 countries*

*though in some places, ECPs are often sold without a prescription

ECEC european consortium for emergency contraception

american society for emergency contraception asec

UPA EC pills are registered or available in at least 75 countries worldwide

As of July 2024

Registered or available as **non-prescription** *56 countries*

Registered or available as **prescription-only** *19 countries**

* and Départements d'outre-mer, Territoires d'outre-mer

ECEC european consortium for emergency contraception

american society for emergency contraception asec

Mifepristone EC pills are registered or available in 6 countries

As of July 2024

Registered or available as **non-prescription** 1 *country*

Registered or available as **prescription-only** 5 *countries*

Tools and references

World Health Organization (WHO). (2021). Emergency contraception [fact sheet]. *Available at* ***www.who.int***

WHO (2024). WHO recommendations on self-care interventions: Making over-the-counter emergency contraceptive pills available without a prescription [technical document]. *Available at* ***www.who.int***

American Society for Emergency Contraception. (2023). Mechanism of Action of Levonorgestrel Emergency Contraceptive Pills. *Available at* ***www.americansocietyforec.org***

International Consortium for Emergency Contraception, WHO, International Federation of Obstetrics and Gynecology, and International Planned Parenthood Federation. (2010). Fact sheet on the safety of levonorgestrel-alone emergency contraceptive pills (LNG ECPs). *Available in* ***English***, ***French***, *and* ***Spanish*** *at* ***www.ec-ec.org***

International Consortium for Emergency Contraception. (2013). Emergency contraception and Medical Abortion: What's the Difference? *Available in* ***English***, ***Spanish***, *and* ***French*** *at* ***www.ec-ec.org***

WHO (2022). Family Planning – A Global Handbook for Providers, Chapter 3: Emergency Contraceptive Pills. *Available at* ***fphandbook.org***

UNFPA, USAID and WHO. (2021). Training Resource Package for Family Planning. Emergency Contraceptive Pills. *Available at* ***www.fptraining.org***

Faculty of Sexual and Reproductive Healthcare of the United Kingdom. (2023). Emergency Contraception [guidelines and statements]. *Available in* ***www.fsrh.org***

European Consortium for Emergency Contraception. (2016). Emergency Contraception Wheel. *Available in* ***English*** *and* ***French*** at ***www.ec-ec.org***

This document was prepared by Cristina Puig Borràs and Kelly Cleland. It is based in part on a toolkit developed by ConwayStrategic for use in the United States (US). ASEC and ECEC thank Catherine Kilfedder, Angela Dawson, Nathalie Kapp, Milka Dinev, Safia Ahsan, Sarah Webb, Andrea Fearneyhough and the Concept Foundation for their review of earlier versions of this brief.

Correspondence to: ecec [at] eeirh [dot] org and kelly [at] americansocietyforec [dot] org
January 2025
Permission granted to reproduce and translate for personal and educational use.
Commercial copying, hiring and lending are prohibited.
Design and layout: laclaracomunicacio.coop↗

The American Society for Emergency Contraception (ASEC) and the European Consortium for Emergency Contraception (ECEC) are communities of practice that work together to increase knowledge of and access to emergency contraception globally.

With support of Children's Investment Fund Foundation (CIFF),
In partnership with Population Services International (PSI).

CIFF CHILDREN'S INVESTMENT FUND FOUNDATION

psi Europe

ASEC is hosted by Ipas; ECEC is hosted by the East European Institute for Reproductive Health.
Visit our websites to learn more and contact us to join our online communities:
www.americansocietyforec.org↗ and www.ec-ec.org↗