## New uses for ulipristal acetate (UPA)

Embracing scientific progress and sustaining access to emergency contraception





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This brief was developed by the European Consortium for Emergency Contraception (ECEC) and the American Society for Emergency Contraception (ASEC) to support individuals and organisations 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 reproductive health products that meet their reproductive health needs, inclusive of both EC and medical abortion, and that multiple options to meet the needs of women\* throughout their reproductive cycles and reproductive life remain available to all.

Two main types of EC pills have been widely available since 2009: 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 brief aims to support the reproductive health, rights, and justice communities in managing this complexity and to strengthen advocates' knowledge and understanding of EC. It provides basic information about oral EC methods, medical 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 an essential reproductive health medicine and tool for women's autonomy.
- 3. Ulipristal acetate (UPA) is the active ingredient in the most effective EC pill available in much of the world.
- 4. Studying UPA for other indications does not change what we know about UPA as EC.

- 5. EC pills (with UPA, levonorgestrel or mifepristone) are different from medical abortion.
- 6. Misoprostol alone is safe and effective for early abortion.
- 7. A safe and effective regimen for medical abortion using misoprostol and mifepristone is already very well established.
- 8. The study of UPA and misoprostol for medical abortion is small and preliminary; its aim is to explore the feasibility of this regimen.





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

- A recent study explored a new combination of medications and their effectiveness at terminating an early pregnancy.
   This study registry is available <a href="here">here</a>.
- 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 the medical 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.





# 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 the media, the general public and policy makers 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 medical abortion while clarifying the differences. However, it could also be used to launch new attacks on EC access and/or to conflate EC and medical 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.





#### Key messages

### O1. As science develops, accurate communication about how medicines can be used for different reproductive health needs is critical.

- This study opens a discussion about how new indications for well established reproductive health products are introduced in the reproductive health supplies markets and explained to the general public.
- Misoprostol, for instance, is already used for a variety of other medical indications such as prevention of gastric ulcers, postpartum haemorrhage, and for cervical ripening and labour 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 are or can be used across the reproductive health spectrum is an important pathway to supporting reproductive health and autonomy across a woman's life course.





### 02. EC pills are an essential reproductive health medicine and tool for women's autonomy.

- EC is the only contraceptive method that can be used after sex to reduce the risk of pregnancy. EC pills are highly valued and an important method for women; the available data suggests a significant increase in their 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 women in vulnerable or marginalised situations, i.e.: those who have experienced forced or unwanted sex, or women 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. UPA is the active ingredient in the most effective EC pill available in much of the world:

- UPA is a relatively new molecule that has other valuable indications in gynaecologic care, beyond EC, that are being investigated.
- UPA has already been marketed to treat uterine fibroids, and is being researched for endometriosis, bleeding in IUD users, breast cancer prevention and other conditions.







#### 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 (that is, EC pills with 30 mg of UPA, taken within 5 days after unprotected sex), or providers who have prescribed or dispensed this regimen, have not caused nor induced 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 unprotected 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: they 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 75 kg.
- UPA EC pills are a well-established product and have been safely used by over 58 million women worldwide. They were first approved by the European Medicines Agency (EMA) in 2009, and have since been approved by the US Food and Drug Administration (FDA) in 2010 and 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 medical abortion.

- Both EC pills and medical abortion are of critical importance for reproductive health and autonomy. Confusion between the two can lead to medical risks, and present a barrier to broader access; it could cause uncertainty about which regimen is needed at which part of the reproductive cycle.
- Emergency contraception prevents pregnancy from starting, while medical 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.
- EC pills containing LNG have not been used nor studied for in this
  research. A higher dose of ulipristal acetate (the active ingredient of the
  newer generation of EC pills) in combination with misoprostol, has been
  studied. It would be incorrect and misleading for women seeking to end
  a pregnancy, to be told that "using the morning after pill + misoprostol
  can induce abortion".
- There is no evidence that <u>LNG</u> or <u>UPA</u> EC pills on their own would cause an 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 a well-studied method for abortion that 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 medical abortion using misoprostol and mifepristone is already very well established.

- This two-medication regimen (mifepristone followed by misoprostol) was first approved more than 35 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 medical abortion in at least 105 countries (see <u>gynuity.org</u>?):
  - About 36 brands of mifepristone for medical 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 medical 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 the established medical abortion regimens (mifepristone + misoprostol or misoprostol alone).







### 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 to individuals who wish to use EC (WHO recommendations on self-care interventions: making over-the-counter emergency contraceptive pills available without a prescription. WHO, 2024.

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 secondgeneration synthetic progestin)
- Marketed since the 1990s
- Indication according to label: emergency contraception to be used 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
- Brands: Cumbran, Escapelle, Levodia, Levonelle, Lydia, Monbell, Norlevo, Pilem, PiDaNa, Plan B, Postday, Postinor, PostPill, Securite 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.





#### 2. 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: emergency contraception to be used as soon as possible up to 120 hours after unprotected sex
- Efficacy: high from 0 to 120 hours after sex
- Brands: ella, ellaOne, Dvella, FemelleOne, Femke, Lencya, Prevent One, ulip, Ulipristal Stada, Ulipristal Mylan, Ulipristal acetate Sandoz and others
- Main mechanism of action: inhibits or delays ovulation
- Availability: registered or imported in at least 75 countries. Available without prescription in at least 56 countries.





#### 3. 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: emergency contraception 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







#### 1.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, ECPs are often sold without a prescription

New Zealand





### 2. 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





#### 3. 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



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Correspondence to: ecec [at] eeirh [dot] org and kelly [at] americansocietyforec [dot] org 1st edition - January 2025

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Design and layout: <a href="mailto:laclaracomunicacio.coop">laclaracomunicacio.coop</a>

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ASEC is hosted by Ipas; ECEC is hosted by the East European Institute for Reproductive Health.

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