

FSRH Guideline

Emergency Contraception

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Details of changes to original guidance document

Subsequent to the publication of this guideline in March 2017 the following revision has been made.

Date	Revision
29 May 2017	<p>Table 1(page 6). <i>Indication for EC for the method Intrauterine contraception (Cu-IUD and LNG-IUS) has been revised to:</i></p> <p><i>If UPSI has taken place in the 7 days prior to removal, perforation, partial or complete expulsion. Oral EC is indicated if there has been UPSI in the last 5 days. Depending on the timing of UPSI and time since IUD known to be correctly placed, it may be appropriate to fit another Cu-IUD for EC.</i></p>
04 December 2017	<p>Table 1(page 6). <i>Indication for EC for the method Combined hormonal contraception, progestogen-only pill and progestogen-only implant has been revised to:</i></p> <p><i>EC is indicated if there is UPSI or barrier failure during, or in the 28 days following, use of liver enzyme-inducing drugs. Offer a Cu-IUD (unaffected by liver enzyme-inducing drugs) or a double dose (3 mg) of LNG-EC. UPA-EC is not recommended in this situation.</i></p> <p>Resource 1 (page 48). Examples of antiretrovirals drugs have been removed.</p>

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NICE has accredited the process used by the Faculty of Sexual & Reproductive Healthcare to produce this guideline. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

Abbreviations Used

BMI	body mass index
CEU	Clinical Effectiveness Unit
CHC	combined hormonal contraception/contraceptive
CI	confidence interval
COC	combined oral contraception/contraceptive
Cu-IUD	copper intrauterine device
CYP450	cytochrome P450 hepatic enzymes
DMPA	depot medroxyprogesterone acetate
EC	emergency contraception
EMA	European Medicines Agency
FSRH	Faculty of Sexual & Reproductive Healthcare
GDG	guideline development group
GTD	gestational trophoblastic disease
hCG	human chorionic gonadotrophin
HFI	hormone-free interval
HRT	hormone replacement therapy
IMP	progestogen-only implant
IUC	intrauterine contraception
LAM	lactational amenorrhoea method
LARC	long-acting reversible contraception/contraceptive
LH	luteinising hormone
LMP	last menstrual period
LNG	levonorgestrel
LNG-EC	levonorgestrel (for emergency contraception)
LNG-IUS	levonorgestrel-releasing intrauterine system
MHRA	Medicines and Healthcare products Regulatory Agency
OR	odds ratio
PEPSE	post-exposure HIV prophylaxis after sexual exposure
PGD	patient group direction
POP	progestogen-only pill
RCT	randomised control trial
SPC	Summary of Product Characteristics
SRH	sexual and reproductive healthcare
STI	sexually transmitted infection
UKMEC	UK Medical Eligibility for Contraceptive Use
UPA	ulipristal acetate
UPA-EC	ulipristal acetate (for emergency contraception)
UPSI	unprotected sexual intercourse (no contraception used or contraception used incorrectly)

Grading of Recommendations

Please refer to [Appendix 1](#) for a full explanation of the classification of evidence level and grading of recommendations.

- A** At least one meta-analysis, systematic review or randomised controlled trial (RCT) rated as 1++, and directly applicable to the target population;
or
A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results.
- B** A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results;
or
Extrapolated evidence from studies rated as 1++ or 1+.
- C** A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; *or*
Extrapolated evidence from studies rated as 2++.
- D** Evidence level 3 or 4;
or
Extrapolated evidence from studies rated as 2+.
- ✓ Good Practice Point based on the clinical experience of the guideline development group.

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Executive Summary of Recommendations

When is emergency contraception (EC) indicated?

D	Women who do not wish to conceive should be offered EC after unprotected sexual intercourse (UPSI) that has taken place on any day of a natural menstrual cycle.
✓	Women who do not wish to conceive should be offered EC after: <ul style="list-style-type: none"> • UPSI from Day 21 after childbirth (unless the criteria for lactational amenorrhoea are met). • UPSI from Day 5 after abortion, miscarriage, ectopic pregnancy or uterine evacuation for gestational trophoblastic disease (GTD).
✓	Women who do not wish to conceive should be offered EC after UPSI if their regular contraception has been compromised or has been used incorrectly.

Provision of EC

What are the responsibilities of EC providers?

✓	EC providers who cannot offer all EC methods should give women information regarding the other methods and signpost them to services that can provide them. If a woman is referred on for a copper intrauterine device (Cu-IUD), oral EC should be given at the time of referral in case the Cu-IUD cannot be inserted or the woman changes her mind.
✓	Providers of oral EC should advise women that oral EC methods do not provide contraceptive cover for subsequent UPSI and that they will need to use contraception or abstain from sex to avoid further risk of pregnancy.
✓	Women requesting EC should be given information regarding all methods of ongoing contraception and how to access these.

How effective are the different methods of EC?

C	EC providers should advise women that the Cu-IUD is the most effective method of EC.
B	EC providers should advise women that ulipristal acetate EC (UPA-EC) has been demonstrated to be effective for EC up to 120 hours after UPSI.
B	EC providers should advise women that levonorgestrel EC (LNG-EC) is licensed for EC up to 72 hours after UPSI. The evidence suggests that LNG-EC is ineffective if taken more than 96 hours after UPSI.
B	EC providers should advise women that UPA-EC has been demonstrated to be more effective than LNG-EC.
B	EC providers should advise women that the available evidence suggests that oral EC administered after ovulation is ineffective.

What is the effect of weight/body mass index (BMI) on the effectiveness of EC?

✓	Women should be informed that the effectiveness of the Cu-IUD is not known to be affected by weight or BMI.
C	Women should be informed that it is possible that higher weight or BMI could reduce the effectiveness of oral EC, particularly LNG-EC.

What drug interactions are relevant to use of EC?

D	EC providers should advise women using enzyme-inducing drugs that the effectiveness of UPA-EC and LNG-EC could be reduced.
✓	Women requiring EC who are using enzyme-inducing drugs should be offered a Cu-IUD if appropriate. A 3 mg dose of LNG can be considered but women should be informed that the effectiveness of this regimen is unknown. A double-dose of UPA-EC is not recommended.
✓	EC providers should be aware that the effectiveness of UPA-EC could be reduced if a woman takes progestogen in the 5 days after taking UPA-EC.
✓	EC providers should be aware that the effectiveness of UPA-EC could theoretically be reduced if a woman has taken progestogen in the 7 days prior to taking UPA-EC.

Are there any contraindications/restrictions to use of EC?

D	EC providers should be aware that the contraindications to insertion of a Cu-IUD for EC are the same as those for routine IUD insertion.
D	EC providers should be aware that UPA-EC is not suitable for use by women who have severe asthma controlled by oral glucocorticoids.

Are there any specific considerations for women who are breastfeeding and require EC?

B	EC providers should be aware that breastfeeding women have a higher relative risk of uterine perforation during insertion of intrauterine contraception than non-breastfeeding women. However, the absolute risk of perforation is low.
D	Breastfeeding women should be advised not to breastfeed and to express and discard milk for a week after they have taken UPA-EC.
C	Women who breastfeed should be informed that available limited evidence indicates that LNG-EC has no adverse effects on breastfeeding or on their infants.

What methods of EC should be offered to a woman who has had UPSI and wishes to avoid pregnancy? (See decision-making algorithms to facilitate choice of EC)

✓	All women requiring EC should be offered a Cu-IUD if appropriate as it is the most effective method of EC.
✓	EC providers should be aware that a Cu-IUD can be inserted up to 5 days after the first UPSI in a natural menstrual cycle, or up to 5 days after the earliest likely date of ovulation (whichever is later).
✓	If a Cu-IUD is not appropriate or not acceptable, women should be advised that oral EC should be taken as soon as possible if there has been UPSI within the last 5 days.
✓	EC providers should consider UPA-EC as the first-line oral EC for a woman who has had UPSI 96–120 hours ago (even if she has also had UPSI within the last 96 hours).
✓	EC providers should consider UPA-EC as the first-line oral EC for a woman who has had UPSI within the last 5 days if the UPSI is likely to have taken place during the 5 days prior to the estimated day of ovulation.

B	EC providers should advise women that the available evidence suggests that oral EC administered after ovulation is ineffective.
✓	Adolescents who need EC should be offered all methods of EC including the Cu-IUD.
✓	Women requiring EC after sexual assault should be offered all methods of EC including the Cu-IUD.

Can oral EC be used if there has also been UPSI earlier in the cycle?

D	EC providers can offer a woman UPA-EC or LNG-EC if she has had UPSI earlier in the same cycle as well as within the last 5 days, as evidence suggests that UPA-EC and LNG-EC do not disrupt an existing pregnancy and are not associated with fetal abnormality.
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Can oral EC be used more than once in a cycle?

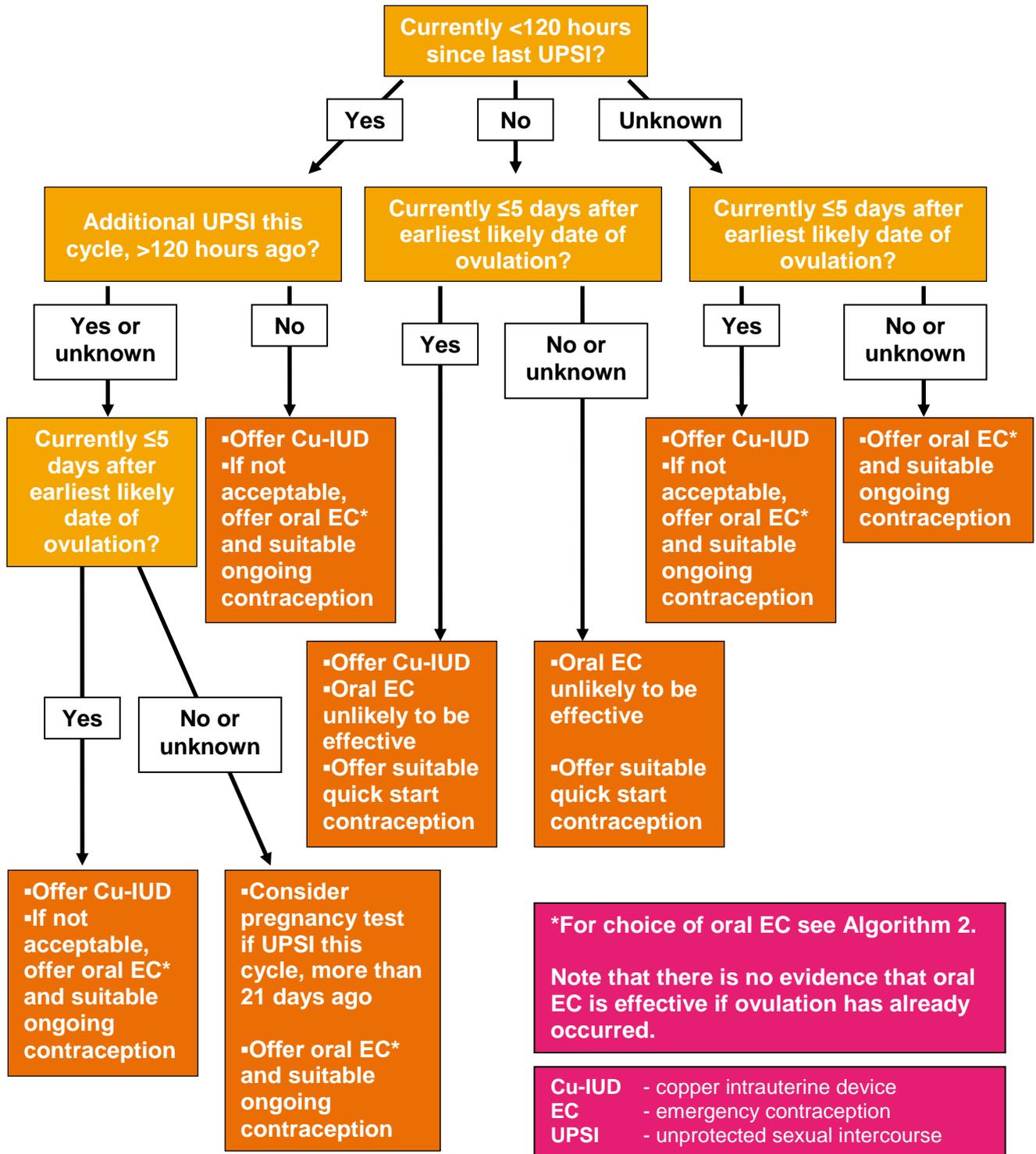
D	If a woman has already taken UPA-EC once or more in a cycle, EC providers can offer her UPA-EC again after further UPSI in the same cycle.
D	If a woman has already taken LNG-EC once or more in a cycle, EC providers can offer her LNG-EC again after further UPSI in the same cycle.
✓	EC providers should be aware that if a woman has already taken UPA-EC, LNG-EC should not be taken in the following 5 days.
✓	EC providers should be aware that if a woman has already taken LNG-EC, UPA-EC could theoretically be less effective if taken in the following 7 days.

What should women be advised regarding future contraception?

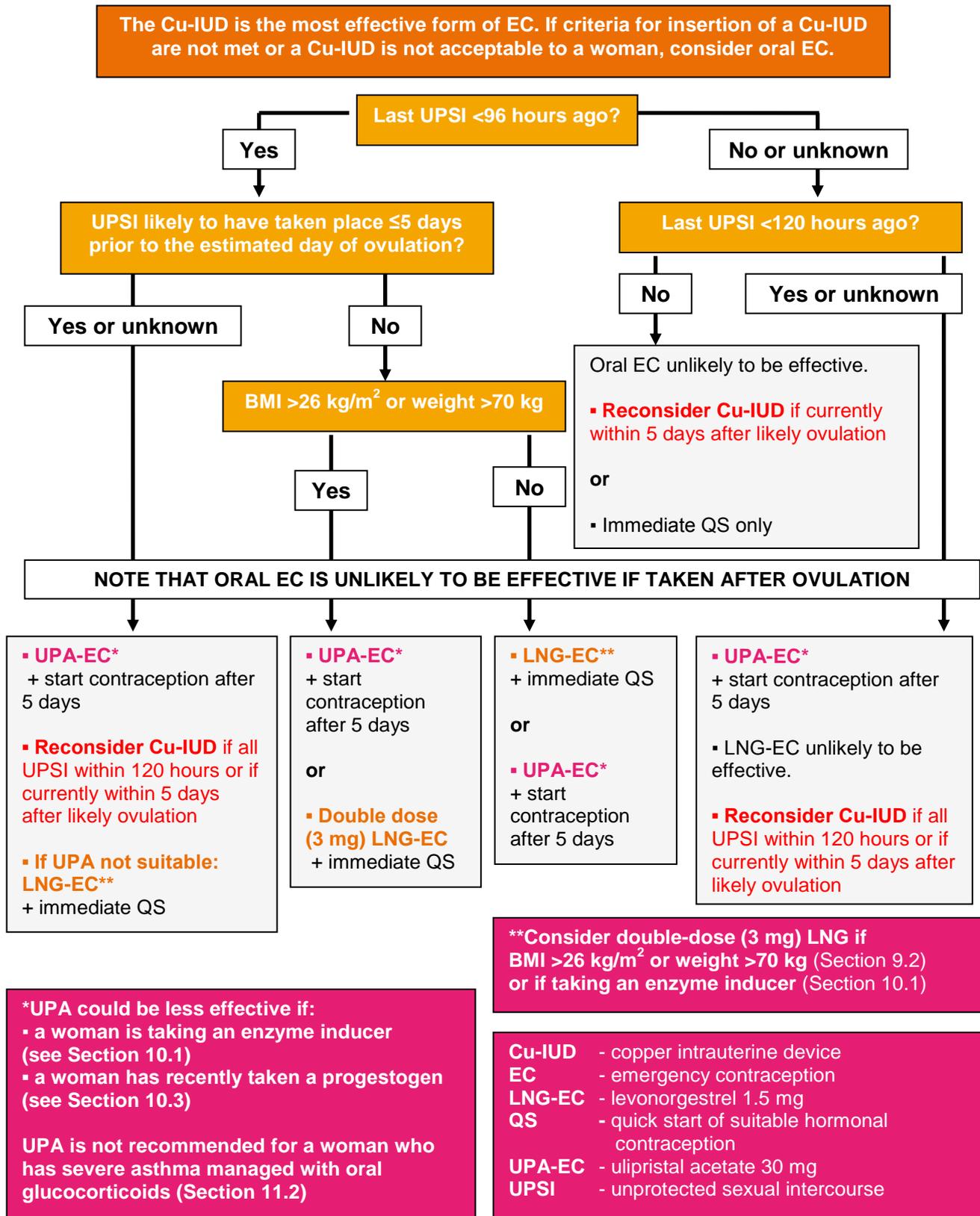
✓	EC providers should advise women that the Cu-IUD provides effective ongoing contraception.
✓	EC providers should advise women that oral EC methods do not provide ongoing contraception.
B	EC providers should advise women that after oral EC there is a pregnancy risk if there is further UPSI and ovulation occurs later in the same cycle.
D	After taking LNG-EC, women should be advised to start suitable hormonal contraception immediately. Women should be made aware that they must use condoms reliably or abstain from sex until contraception becomes effective.
D	Women should be advised to wait 5 days after taking UPA-EC before starting suitable hormonal contraception. Women should be made aware that they must use condoms reliably or abstain from sex during the 5 days waiting and then until their contraceptive method is effective.
✓	If a woman and her EC provider estimate that UPSI is unlikely to have occurred during her fertile period, she may consider the option of using LNG-EC with immediate start of hormonal contraception rather than UPA-EC with delayed start of hormonal contraception.

Decision-making Algorithms for Emergency Contraception

Algorithm 1: Decision-making Algorithm for Emergency Contraception (EC):
Copper Intrauterine Device (Cu-IUD) vs Oral EC



**Algorithm 2: Decision-making Algorithm for Oral Emergency Contraception (EC):
Levonorgestrel EC (LNG-EC) vs Ulipristal Acetate EC (UPA-EC)**



FSRH Guideline (March 2017)

Emergency Contraception

(Revision due by March 2022)

1 Purpose and Scope

This document updates previous Faculty of Sexual & Reproductive Healthcare (FSRH) guidance¹ and aims to summarise the available evidence on emergency contraception (EC). The guidance is intended for use by health professionals providing EC.

1.1 Identification and assessment of the evidence

This guideline was developed in accordance with standard methodology for developing FSRH clinical guidelines. The recommendations made within this document are based on the best available evidence and the consensus opinion of experts and the guideline development group (GDG). The methodology used in developing this guideline and a list of GDG members and other contributors can be found in [Appendix 1](#).

The recommendations included should be used to guide clinical practice but are not intended to serve alone as a standard of medical care or to replace clinical judgement in the management of individual cases.

2 Summary of Guidance and Changes from Previous Guideline

EC is intended for occasional use, to reduce the risk of pregnancy after unprotected sexual intercourse (UPI). It does not replace effective regular contraception.

EC should be considered if a woman does not wish to conceive and has had UPI:

- ▶ On any day of a natural menstrual cycle. Pregnancy is theoretically possible after UPI on most days of the cycle. However, risk of pregnancy is highest after UPI that takes place during the 6 days leading up to and including the day of ovulation.
- ▶ From Day 21 after childbirth unless all criteria for lactational amenorrhoea are met.
- ▶ From Day 5 after miscarriage, abortion, ectopic pregnancy or uterine evacuation for gestational trophoblastic disease (GTD).
- ▶ After regular hormonal contraception has been compromised or used incorrectly. Note that guidance is updated regarding:
 - ▶ Copper intrauterine device (Cu-IUD) insertion after an extended pill-free interval and after a missed progestogen-only pill (POP).
 - ▶ Requirement for EC when intrauterine contraception is removed after recent intercourse.
 - ▶ Pregnancy risk if a progestogen-only implant (IMP) or levonorgestrel-releasing intrauterine system (LNG-IUS) has recently exceeded its recommended duration of use.

The Cu-IUD

- ▶ Is the most effective method of EC and should be considered by **ALL** women who have had UPSI and do not want to conceive.
- ▶ Is the only method of EC that is effective after ovulation has taken place (but is inserted well before the earliest likely date of implantation so that it does not disrupt a pregnancy that has already implanted).
- ▶ Can be inserted for EC within 5 days after the first UPSI in a cycle, or within 5 days of the earliest estimated date of ovulation, whichever is later.
- ▶ Has the advantage of providing immediately effective ongoing contraception.
- ▶ Is not known to be affected by body mass index (BMI)/weight or by other drugs.

Oral EC

- ▶ Should be offered as soon as possible after UPSI if a Cu-IUD is not appropriate or is not acceptable.
- ▶ Is unlikely to be effective if taken >120 hours after the last UPSI, as viable sperm are present in the upper genital tract for only about 5 days after UPSI.
- ▶ Has its effect by delaying ovulation – the evidence suggests that oral EC is not effective after ovulation has taken place.

Choosing between UPA-EC and LNG-EC

Ulipristal acetate EC (UPA-EC) has been demonstrated to be more effective than levonorgestrel EC (LNG-EC) from 0–120 hours after UPSI. It is important to bear in mind that the evidence suggests that both UPA-EC and LNG-EC are ineffective if taken after ovulation. There are also additional factors to consider.

Between 96 and 120 hours after UPSI

The evidence suggests that LNG-EC is ineffective if taken more than 96 hours after UPSI. UPA-EC is therefore the only oral EC that is likely to be effective if UPSI took place 96–120 hours ago.

Between 0 and 96 hours after UPSI

The decision as to whether UPA-EC or LNG-EC is most appropriate depends on the following factors:

- 1 **The risk of pregnancy from the UPSI for which EC is being taken.** If UPSI is likely to have taken place during the 5 days prior to ovulation, risk of pregnancy is very high and UPA-EC should be considered first-line oral EC.
- 2 **The risk of pregnancy resulting from further UPSI if there is a delay in commencing ongoing contraception.** The ability of UPA-EC to delay ovulation is reduced if a progestogen is taken in the following 120 hours. It is therefore recommended that hormonal contraception is not started until 5 days after UPA-EC, whereas hormonal contraception can be started immediately after LNG-EC. If pregnancy risk from UPSI that has already taken place is low, it may be appropriate to prioritise immediate quick start of contraception so that pregnancy risk from further UPSI is reduced. LNG-EC with immediate start of hormonal contraception could be considered in this situation.

- 3 **Recent use of progestogen.** The effectiveness of UPA-EC could theoretically be reduced if a woman has recently taken a progestogen (e.g. If she requires EC because of missed pills). It is unknown whether UPA-EC taken when there may still be circulating progestogen is more or less effective than LNG-EC.
- 4 **BMI/body weight.** The effectiveness of LNG-EC could be reduced if a woman has a BMI >26 kg/m² or weight >70 kg. It is recommended that either UPA-EC or a double dose (3 mg) of LNG-EC is given in this situation. It is unknown which is more effective.
- 5 **Enzyme-inducing drugs.** The effectiveness of both UPA-EC and LNG-EC could be reduced if a woman is using an enzyme inducer. It is not known whether either method is effective in preventing pregnancy in this situation. It is recommended that a double dose (3 mg) of LNG-EC can be used, but effectiveness (and how this compares to UPA-EC) is unknown. Use of double-dose UPA-EC is not currently recommended.

Use of oral EC if there has been UPSI and/or use of oral EC earlier in the cycle

There is evidence that oral EC does not cause abortion or harm to a very early pregnancy. Both UPA-EC and LNG-EC can therefore be used if a woman has also had UPSI earlier in the same cycle. Both UPA-EC and LNG-EC can be used more than once in the same cycle if this is indicated by further UPSI.

Additional responsibilities of EC providers

A consultation regarding EC should include advice regarding the importance of ongoing contraception and information about the available contraceptive methods. EC providers should ensure that after taking EC a woman has access to her contraceptive method of choice. Quick starting of suitable contraception (immediately after LNG-EC or >5 days after UPA-EC) should always be offered and follow-up pregnancy testing arranged. All women requesting EC should be assessed as to their risk of sexually transmitted infection (STI) and offered appropriate testing (or advised as to the testing that is recommended and how to access this).

Please refer to the two [decision-making algorithms for EC](#).

3 Introduction

EC provides women with a means of reducing the risk of conception of an unintended pregnancy following UPSI. EC is the preferred term; other terms include 'postcoital contraception' and 'the morning after pill'. EC is intended for occasional emergency use and should not be considered a substitute for effective regular contraception.

4 When is EC Indicated?

It is recommended that EC is considered for any woman who does not wish to conceive if there is a potential risk of pregnancy after UPSI.

The risk of pregnancy for an individual woman after UPSI is difficult to estimate because it depends on a number of variable factors including the fertility of both partners, the timing and number of episodes of UPSI, cycle length and variability, and whether contraception has not been used or has been used incorrectly.

4.1 Women not using hormonal contraception

D Women who do not wish to conceive should be offered EC after UPSI that has taken place on any day of a natural menstrual cycle.

Pregnancy is extremely unlikely to occur as a result of UPSI in the first 3 days of a natural menstrual cycle.² However, pregnancy is theoretically possible after UPSI on most days of the cycle. Evidence level 2-

A woman's fertile period is considered to be the six consecutive days ending with (and including) the day of ovulation.³ In the days immediately prior to ovulation and on the day of ovulation itself, pregnancy risk following a single episode of UPSI has been estimated to be up to 30%.³ If a woman has one episode of UPSI in a cycle, there is a 25% chance that the UPSI takes place during her fertile period.² Evidence level 2-

It can, however be difficult to predict whether an episode of UPSI has occurred during a woman's fertile period. Estimation of the timing of ovulation using the usual cycle length and date of last menstrual period (LMP) reported by women is imprecise when correlated with serum and ultrasound markers of ovulation.^{2,4-8} Evidence level 2+

The GDG recommends therefore that EC is offered after UPSI on any day of a woman's natural menstrual cycle. Choice of EC method may depend on whether it is considered likely that UPSI may have taken place during the woman's fertile period.

4.2 After pregnancy

✓ Women who do not wish to conceive should be offered EC after:

- UPSI from Day 21 after childbirth (unless the criteria for lactational amenorrhoea are met).
- UPSI from Day 5 after abortion, miscarriage, ectopic pregnancy or uterine evacuation for gestational trophoblastic disease (GTD).

Contraception is required from Day 21 after childbirth (unless a woman is fully breastfeeding, amenorrhoeic **and** within 6 months of delivery; see [Section 12](#)). Contraception is required from Day 5 after abortion, miscarriage, ectopic pregnancy or uterine evacuation for GTD.⁹ If UPSI occurs after this time, EC is required. Evidence level 4

The theoretical risks of insertion of a Cu-IUD generally outweigh the benefits [UK Medical Eligibility Criteria (UKMEC) Category 3] until 28 days after delivery.^{9,10} After GTD, if human chorionic gonadotrophin (hCG) levels are persistently elevated, insertion of a Cu-IUD is contraindicated (UKMEC 4) because of the theoretical risk of perforation and bleeding. IUD insertion is relatively contraindicated (UKMEC 3) while hCG levels are still falling after GTD.^{9,10}

For information regarding use of EC during breastfeeding, see [Section 12](#).

4.3 Women using hormonal contraception incorrectly

 **Women who do not wish to conceive should be offered EC after UPSI if their regular contraception has been compromised or has been used incorrectly.**

EC may be indicated if contraception has been used incorrectly or has been compromised (e.g. by concomitant use of enzyme-inducing drug or vomiting). [Table 1](#) outlines situations in which EC is indicated because of likely failure of hormonal or intrauterine contraception. This is a guide only; there are too many variables relating to incorrect use of contraception to provide advice for every situation.

Table 1: Indications for emergency contraception following potential failure of hormonal and intrauterine methods of contraception (see [Section 13.2 for clarification](#))

Method	Situation leading to possible contraceptive failure	Indication for EC
Hormonal methods of contraception	Failure to use additional contraceptive precautions when starting the method	UPSI or barrier failure during time that additional precautions required as indicated within CEU guidance.
Combined hormonal transdermal patch or combined hormonal vaginal ring	Patch detachment/ring removal for >48 hours Extension of patch-free or ring-free interval by >48 hours	EC is indicated if patch detachment or ring removal occurs in Week 1 and there has been UPSI or barrier failure during the hormone-free interval (HFI) or Week 1. If the HFI is extended, a Cu-IUD can be offered up to 13 days after the start of the HFI assuming previous perfect use (see Section 13.2.1). If CHC has been used in the 7 days prior to EC, the effectiveness of UPA-EC could theoretically be reduced. Consider use of LNG-EC (see Section 10.3).
Combined oral contraceptive pill (monophasic pill containing ethinylestradiol)	Missed pills (if two or more active pills are missed)	EC is indicated if the pills are missed in Week 1 and there has been UPSI or barrier failure during the pill-free interval or Week 1. If the pill-free interval is extended (this includes missing pills in Week 1), a Cu-IUD can be offered up to 13 days after the start of the HFI assuming previous perfect use (see Section 13.2.1). If COC has been taken in the 7 days prior to EC, the effectiveness of UPA-EC could theoretically be reduced. Consider use of LNG-EC (see Section 10.3).

[continued on next page]

Method	Situation leading to possible contraceptive failure	Indication for EC
Combined hormonal contraception, progestogen-only pill and progestogen-only implant	Failure to use additional contraceptive precautions whilst using liver enzyme-inducing drugs or in the 28 days after use	EC is indicated if there is UPSI or barrier failure during, or in the 28 days following, use of liver enzyme-inducing drugs. Offer a Cu-IUD (unaffected by liver enzyme-inducing drugs) or a double dose (3 mg) of LNG-EC. UPA-EC is not recommended in this situation.
Progestogen-only pill	Late or missed pill (>27 hours since last traditional POP or >36 hours since last desogestrel-only pill)	<p>EC is indicated if a pill is late or missed and there has been UPSI or barrier failure before efficacy has been re-established (i.e. 48 hours after restarting).</p> <p>Timing of ovulation after missed pills cannot be accurately predicted. A Cu-IUD is therefore only recommended up to 5 days after the first UPSI following a missed POP (see Section 13.2.1).</p> <p>If POP has been taken in the 7 days prior to EC, the effectiveness of UPA-EC could theoretically be reduced. Consider use of LNG-EC (see Section 10.3).</p>
Progestogen-only injectable	Late injection (>14 weeks since last injection of DMPA)	<p>EC is indicated if there has been UPSI or barrier failure:</p> <ul style="list-style-type: none"> ▶ >14 weeks after the last injection ▶ within the first 7 days after late injection <p>Timing of ovulation after expiry of the progestogen-only injectable is extremely variable (see Section 13.2.1). A Cu-IUD is only recommended up to 5 days after the first UPSI that takes place >14 weeks after the last DMPA injection.</p> <p>The effectiveness of UPA-EC could theoretically be reduced by residual circulating progestogen. Consider use of LNG-EC (see Section 10.3).</p>
Progestogen-only implant	Expired implant	See Section 13.2.2 .
Intrauterine contraception (Cu-IUD and LNG-IUS)	Removal without immediate replacement; partial or complete expulsion; threads missing and IUC location unknown	<p>If UPSI has taken place in the 7 days prior to removal, perforation, partial or complete expulsion. Oral EC is indicated if there has been UPSI in the last 5 days.</p> <p>Depending on the timing of UPSI and time since IUD known to be correctly placed, it may be appropriate to fit another Cu-IUD for EC.</p>

CEU, Clinical Effectiveness Unit; CHC, combined hormonal contraception; COC, combined oral contraception; Cu-IUD, copper intrauterine device; DMPA, progestogen-only injectable: depot medroxyprogesterone acetate; EC, emergency contraception; HFI, hormonal-free interval; IMP, progestogen-only implant; IUC, intrauterine contraception; LNG-EC, levonorgestrel for EC; LNG-IUS, levonorgestrel-releasing intrauterine system; POP, progestogen-only pill; UPA-EC, ulipristal acetate for EC; UPSI, unprotected sexual intercourse.

Table 2: Methods of emergency contraception in the UK

Method	Class	Recommended dose/use	Indications
Copper intrauterine device (Cu-IUD)	Intrauterine contraceptive method	IUD retained until pregnancy excluded (e.g. onset of next menstrual period) or can be kept for ongoing contraception	Within 5 days (120 hours) after the first UPSI in a cycle or within 5 days after the earliest estimated date of ovulation
Levonorgestrel EC (LNG-EC)	Progestogen	1.5 mg single oral dose*	Licensed for use within 72 hours after UPSI or contraceptive failure
Ulipristal acetate EC (UPA-EC)	Progesterone receptor modulator	30 mg single oral dose	Licensed for use within 5 days (120 hours) after UPSI or contraceptive failure

*A double dose (3 mg) of LNG-EC is recommended if a woman is taking an enzyme-inducing drug. A double dose (3 mg) of LNG-EC should be considered if a woman has a body mass index >26 kg/m² or weight >70 kg (see [Section 10.1](#) and [Section 9.2](#)).

EC, emergency contraception; UPSI, unprotected sexual intercourse.

5 What Methods of EC are Available?

In the UK, three methods of EC are currently available: the copper IUD (Cu-IUD), oral ulipristal acetate (UPA) 30 mg (single dose) and oral levonorgestrel (LNG) 1.5 mg (single dose). These are summarised in [Table 2](#).

The combined hormonal Yuzpe method of EC is no longer used in the UK; studies consistently demonstrate Yuzpe to be less effective than LNG-EC.^{11,12}

Use of the LNG-IUS for EC is not currently recommended because there is a lack of evidence of effectiveness of the LNG-IUS for this purpose. A recent prospective cohort study¹³ considered insertion of an LNG-IUS at the time of administration of oral LNG-EC after UPSI. Amongst 110 women who chose LNG-EC plus immediate LNG-IUS insertion rather than a Cu-IUD or oral EC alone, one pregnancy was recorded in a woman who had had multiple episodes of UPSI more than 5 days prior to EC. Of note, twice as many women opted for LNG-EC plus LNG-IUS compared to a Cu-IUD. The study is underpowered to detect important differences between pregnancy rates with the two methods. Larger trials would be required to investigate whether this could be a potential future approach to EC that might increase uptake of long-acting reversible contraception (LARC).

6 Provision of EC

6.1 Where can EC be obtained?

In the UK, LNG-EC and UPA-EC are available from:

- ▶ Community pharmacies (there may be a charge)
- ▶ General practice (GP) surgeries (free of charge)
- ▶ Sexual and reproductive health (SRH) clinics and genitourinary medicine clinics (free of charge).

Oral EC may also be available from:

- ▶ Young people's services (where registered nurses are employed)
- ▶ School nurses
- ▶ Accident and emergency departments
- ▶ National Health Service (NHS) walk-in centres (England only)
- ▶ NHS minor injuries unit
- ▶ Online pharmacies.

Oral EC is available free from pharmacies in Scotland and Wales. The type of oral EC supplied depends upon the clinical presentation. LNG-EC and UPA-EC are available free from many pharmacies in England and some in Northern Ireland. Women aged 16 years or over can purchase LNG-EC from pharmacies for around £25 and all women can purchase UPA-EC from pharmacies for around £35 (prices correct at time of writing, February 2017). Pharmacists are able to supply EC using either the Pharmacy Medicine regulations or a patient group direction (PGD).

Information regarding availability of oral EC outside the UK is available at the International Consortium for Emergency Contraception website (<http://www.cecinfo.org/country-by-country-information/status-availability-database/>).

The Cu-IUD for EC is free of charge and may be available from:

- ▶ SRH clinics
- ▶ Young people's services (where registered nurses are employed)
- ▶ GP practices.

All EC providers should be familiar with their local sexual health services in order to refer or signpost women to the appropriate service or practitioner when needed. For example, services who offer Cu-IUD fittings on certain days each week should know where to refer women presenting for a Cu-IUD on the other days of the week.

6.2 Who can supply EC?

Oral EC is available from a variety of services as described in [Section 6.1](#). Within a service, some providers may be prescribers while others may supply UPA-EC and LNG-EC by PGD.

6.3 What are the responsibilities of EC providers?



EC providers who cannot offer all EC methods should give women information regarding the other methods and signpost them to services that can provide them. If a woman is referred on for a Cu-IUD, oral EC should be given at the time of referral in case the Cu-IUD cannot be inserted or the woman changes her mind.

The GDG recommends that where a provider does not offer a particular method of EC, information regarding all methods of EC should be supplied and a referral pathway should be in place to allow women to access their preferred method. At the time of onward referral for a Cu-IUD, providers should consider provision of oral EC in case Cu-IUD insertion is significantly delayed, not possible or the woman changes her mind.

See [Appendix 2](#) for suggested information which can be provided to women requesting EC.



Providers of oral EC should advise women that oral EC methods do not provide contraceptive cover for subsequent UPSI and that they will need to use contraception or abstain from sex to avoid further risk of pregnancy.



Women requesting EC should be given information regarding all methods of ongoing contraception and how to access these.

Provision of information regarding and access to ongoing contraception is an essential component of any consultation regarding EC. A Scottish study found that amongst women presenting to community pharmacies for EC, women were significantly more likely to be using effective contraception 6–8 weeks later if they were given a month's supply of POPs at the time of receiving EC or were given a rapid access pathway to a local SRH clinic for contraceptive advice.¹⁴ Women welcomed the contraceptive interventions offered. Pharmacists gave positive feedback about their involvement.¹⁵

Evidence level 1-

The GDG recommends that all EC providers should ensure that they also provide information regarding ongoing contraception. If an EC provider cannot themselves offer a woman her contraceptive method of choice, they must be able to give advice as to how she can access local contraceptive services.

Women requesting EC may be at risk of STI. STI risk assessment should be made and testing offered as appropriate, taking window periods into consideration. Antibiotic cover may be considered for Cu-IUD insertion if there is a significant risk of STI that could be associated with ascending pelvic infection.

7 How Does EC Work?

Sperm are viable in the female genital tract for about 5 days after UPSI.^{3,16} If ovulation occurs within those 5 days, fertilisation could take place and a woman is at risk of pregnancy.

A judicial review¹⁷ in 2002 concluded that pregnancy begins at implantation. It is therefore currently accepted that any intervention given for EC must act either to prevent fertilisation or to prevent implantation, rather than by disrupting established implantation. Available data demonstrate that the shortest time from ovulation to implantation is 6 days (although usually longer – over 80% of pregnancies implant 8–10 days after ovulation).¹⁸

Individual women may want to know how a method of EC works. Women may have cultural or religious reasons for avoiding a method of EC that could have its effect after fertilisation.^{19,20} It is important that a woman who raises concerns about EC mechanism of action is given information about what is known and what is uncertain.

7.1 Cu-IUD

The primary mechanism of contraceptive action of the Cu-IUD is inhibition of fertilisation by its toxic effect on sperm and ova. Copper has been shown to adversely affect the motility and viability of sperm and the viability and transport of ova. If fertilisation does occur, the local endometrial

inflammatory reaction resulting from the presence of the Cu-IUD prevents implantation.^{21,22} The Cu-IUD therefore has both pre- and post-fertilisation mechanisms of action.

A Cu-IUD can be inserted up to 5 days after the first UPSI in a cycle. Given that the earliest implantation is believed to occur 6 days after ovulation (and over 80% of implantations occur 8–10 days after ovulation),¹⁸ a Cu-IUD can also be inserted up to 5 days after ovulation, before the process of implantation has begun.

Ovulation occurs about 14 days prior to onset of menstruation.²³ It is established practice that the earliest likely ovulation date is estimated as the date of the start of the LMP plus the number of days in the shortest cycle minus 14. LMP must be accurately known and cycles must be regular in order to make the estimation. A Cu-IUD can be inserted for EC in good faith up to 5 days after this date (e.g. until Day 19 of a regular, 28-day cycle).

7.2 UPA-EC

UPA 30 mg – a selective progesterone receptor modulator – acts by delaying ovulation for at least 5 days, until sperm from the UPSI for which EC was taken are no longer viable. UPA-EC delays ovulation even after the start of the luteinising hormone (LH) surge whereas LNG-EC is no longer effective after the start of the LH surge.²⁴ UPA-EC cannot inhibit ovulation at or after the LH peak.

UPA-EC has not been demonstrated to be effective as EC when administered after ovulation. Li *et al.* found a significant difference between observed and expected pregnancy rates for 364 women who received UPA-EC prior to ovulation, but not for the 329 women studied who received UPA-EC after ovulation.²⁵ Despite this, various theoretical mechanisms of action for a post-ovulation EC effect of UPA have been suggested. Delayed endometrial maturation has been observed after UPA,^{26,27} but the clinical relevance of this in terms of contribution to EC is unclear. *In vitro*, UPA-EC did not inhibit endometrial receptivity or prevent human embryo attachment to the receptive endometrium.²⁸ Munuce *et al.* observed no *in vitro* effect of UPA on sperm function.²⁹ Ko *et al.* demonstrated an *in vitro* dose-dependent suppressive effect of UPA on progesterone-induced acrosome reaction, sperm hyperactivation and calcium influx.³⁰ However the clinical implication of this in the context of EC is uncertain.^{24,31}

Importantly, after UPA-EC, the majority of women will go on to ovulate later in the cycle^{24,31} and are therefore at risk of pregnancy from subsequent UPSI.^{25,32} It is essential that women are made aware of this risk and advised regarding ongoing contraception (see [Section 18](#)).

7.3 LNG-EC

LNG-EC inhibits ovulation, delaying or preventing follicular rupture and causing luteal dysfunction. If taken prior to the start of the LH surge, LNG inhibits ovulation for the next 5 days, until sperm from the UPSI for which it was taken are no longer viable.³³ In the late follicular phase, however, LNG-EC becomes ineffective while UPA-EC is still able to delay ovulation.²⁴

Although post-ovulation effects of LNG-EC have been suggested,³⁴ subsequent studies have not shown a significant EC effect of LNG-EC administered after ovulation.^{4,5} No effect on endometrial receptors was seen in two small studies.^{35,36} *In vitro*, LNG-EC did not impair endometrial receptivity or the attachment of human embryos.³⁷

After taking LNG-EC, women who ovulate later in the cycle are at risk of pregnancy from further UPSI. It is essential that women are made aware of this risk and advised regarding ongoing contraception (see [Section 18](#)).

8 How Effective are the Different Methods of EC?

When making a choice between EC methods, individual women need to know that the risk of pregnancy depends on the timing of intercourse relative to ovulation. EC providers should explain that the observed pregnancy rate after UPSI is significantly lower if a Cu-IUD is inserted than if oral EC is used. If a woman opts for oral EC, it should be taken as soon as possible after UPSI to have the maximum chance of being taken early enough to delay ovulation.

Effectiveness of EC is difficult to study. The overall pregnancy rate after use of a method of EC in a study reports the number of pregnancies that occurred after use of the EC as a percentage of the number of women who used the EC in the study. However, a significant number of the women studied would not have become pregnant in any case. Some studies assessing the effectiveness of EC in preventing pregnancy depend, therefore, on an estimation of the number of pregnancies that would have occurred without the EC intervention.

Randomised, placebo-controlled trials of EC with pregnancy as an endpoint cannot be carried out for ethical reasons. As a result, studies are often designed to compare the pregnancy rate after use of different methods of EC to demonstrate the relative effectiveness of the methods. It is assumed in such studies that women and their partners are equally fertile in the groups receiving the different interventions and that women in all groups are equally at risk of pregnancy (despite the fact that cycle lengths vary, intercourse will have occurred at different times and there may have been multiple episodes of intercourse both prior to and subsequent to administration of EC).

Further information regarding oral EC is obtained from placebo-controlled and comparative studies carried out in women who are not at risk of pregnancy, assessing the risk of ovulation within 5 days (the duration of sperm viability) after administration of EC. Such studies provide no information relating to other possible mechanisms of action.

The way that the effectiveness of a method of EC is explained to an individual woman is extremely important. For example, if 1% of all women receiving a particular method of EC within 72 hours of UPSI at any time in the cycle become pregnant, the overall pregnancy rate is quoted as 1%. However, for a significant proportion of the women included in the study, UPSI would not have occurred during the fertile period and they would not have become pregnant in any case. The pregnancy rate if the EC method is used after UPSI during the fertile period would therefore be significantly higher than 1%. If an individual woman requests the method of EC after UPSI that has taken place just before her likely time of ovulation, it would be inappropriate to tell her that if she uses the method she has only a 1% chance of pregnancy.

8.1 Cu-IUD

C

EC providers should advise women that the Cu-IUD is the most effective method of EC.

The Cu-IUD is the most effective method of EC.¹¹ The GDG recommends that it should be considered for all women requiring EC. If fitted within 5 days after UPSI or ovulation, the pregnancy rate is extremely low. A 2012 systematic review³⁸ reported an overall pregnancy rate of <0.1%; available data were inadequate to allow calculation of the proportion of expected pregnancies prevented.

Evidence level 2+

8.2 Oral EC

B

EC providers should advise women that UPA-EC has been demonstrated to be effective for EC up to 120 hours after UPSI.

B

EC providers should advise women that LNG-EC is licensed for EC up to 72 hours after UPSI. The evidence suggests that LNG-EC is ineffective if taken more than 96 hours after UPSI.

B

EC providers should advise women that UPA-EC has been demonstrated to be more effective than LNG-EC.

B

EC providers should advise women that the available evidence suggests that oral EC administered after ovulation is ineffective.

8.2.1 UPA-EC

UPA-EC has been demonstrated to be effective when taken up to 120 hours after UPSI. No significant reduction in effectiveness is observed with increasing time between UPSI and UPA-EC (up to 120 hours).^{39,40}

Evidence level 1+

The overall pregnancy rate after administration of UPA-EC has been reported to be about 1–2%.^{25,39–42} This means that about 1–2% of all women who take UPA-EC after UPSI will become pregnant. It does not mean that a woman who has taken UPA-EC after UPSI just prior to ovulation has only a 1–2% chance of pregnancy.

Some studies have compared the actual number of pregnancies observed in the study after EC with the estimated the number of pregnancies that would have occurred without EC. This gives an estimate of the percentage of pregnancies that were prevented by the EC intervention. The percentage of pregnancies prevented by UPA-EC has been estimated in different studies to be around 60–80%.^{25,41,42}

Meta-analysis of data from two large randomised controlled trials (RCTs) suggests that UPA-EC is significantly more effective than LNG-EC at preventing pregnancy when taken from 0–120 hours after UPSI³⁹ (see [Table 3](#)).

Evidence level 1+

Table 3: Pregnancy risk after administration of ulipristal acetate versus levonorgestrel for emergency contraception (meta-analysis of data from two large randomised controlled trials)³⁹

Hours since UPSI	OR*	95% CI (p)
0–24	0.35	0.11–0.93 (0.035)
0–72	0.58	0.33–0.99 (0.046)
0–120	0.55	0.32–0.93 (0.025)

*OR = UPA-EC pregnancy rate/LNG-EC pregnancy rate.

CI, confidence interval; LNG-EC, levonorgestrel for EC; OR, odds ratio; UPA-EC, ulipristal acetate for EC.

UPA-EC can delay ovulation even after the start of the LH surge,²⁴ a time when LNG-EC is no longer effective. The GDG recommend that this has implications for choice of oral EC when a woman is likely to be close to ovulation. UPA-EC may be the most suitable choice of oral EC in that situation. Evidence level 1+

The evidence suggests that UPA-EC taken after ovulation is not effective.^{25,31} Evidence level 2+

Importantly, after UPA-EC, the majority of women will go on to ovulate later in the cycle^{24,31} and are therefore at risk of pregnancy from subsequent UPSI.^{25,32,40} It is essential that women are made aware of this risk and advised regarding reliable ongoing contraception (see [Section 18](#)).

8.2.2 LNG-EC

Meta-analysis of data from two large RCTs suggests that UPA-EC is significantly more effective than LNG-EC at preventing pregnancy when taken from 0–120 hours after UPSI³⁹ (see [Section 8.2.1](#)). Evidence level 1+

LNG-EC effectively delays ovulation when taken before the beginning of the LH surge, but (in contrast to UPA-EC) not thereafter.²⁰ This has implications for choice of oral EC when a woman is likely to be close to ovulation. Evidence level 1+

Studies have reported the overall pregnancy rate amongst women taking LNG-EC within 72 hours of UPSI to be about 0.6–2.6%.^{12,39,43–45} In such studies, LNG-EC was taken at any time of the cycle; UPSI may or may not have occurred when women were at risk of pregnancy.

Two large RCTs comparing LNG-EC to other EC regimens estimated the number of pregnancies that would have been expected without the EC intervention and compared this with the number of pregnancies observed after EC in the study.^{43,46} The percentage of pregnancies prevented by LNG-EC taken within 72 hours of a single episode of UPSI was estimated to be about 85%. More recent data from the LNG-EC arms of RCTs comparing LNG-EC with UPA-EC have suggested that the percentage of pregnancies prevented by LNG-EC taken within 72 hours is significantly lower than 85%.^{39,42} Creinin *et al.* estimated 69% [95% confidence interval (95% CI) 46–82].⁴² These studies used revised methods for estimating the expected number of pregnancies and did not exclude women who had had previous episodes of UPSI. In contrast, a large Nigerian study comparing two different regimens of LNG-EC estimated that LNG-EC given within 72 hours of a

single episode of UPSI prevented well over 90% of pregnancies that would have been expected without EC.⁴⁴

A Cochrane review in 2012 concluded that women who took LNG-EC within 72 hours after UPSI were significantly less likely to become pregnant than those who took it more than 72 hours after UPSI [four trials; relative risk (RR) 0.51; 95% CI 0.31–0.84].¹¹ A study analysing data from four World Health Organization (WHO) trials found no significant difference in effectiveness of LNG-EC taken on Days 2, 3 and 4 after UPSI compared to LNG-EC taken within 24 hours of UPSI. However, the risk of pregnancy after LNG-EC taken on Day 5 (96–120 hours) after UPSI was over five times that when LNG-EC was taken on Day 1 [odds ratio (OR) 5.81, 95% CI 2.87–11.76]. The authors caution that the number of women who had taken LNG-EC after 72 hours was relatively small. They note that some studies demonstrated a trend towards increased pregnancy rates with increasing time between UPSI and LNG-EC (up to 72 hours) and advise that LNG-EC is taken as soon as possible after UPSI.⁴⁸ LNG-EC is licensed for use within 72 hours of UPSI. Use of LNG-EC after 72 hours after UPSI is off-licence.^{48,49}

Evidence level 1+

The evidence suggests that LNG-EC is not effective when administered after ovulation.^{4,5}

Evidence level 2+

After LNG-EC, a woman is at risk of pregnancy if she ovulates later in the cycle and has subsequent UPSI. Women should be advised to quick start a suitable, reliable contraceptive method immediately after LNG-EC.

Evidence level 4

9 What is the Effect of Weight/BMI on the Effectiveness of EC?

9.1 Cu-IUD



Women should be informed that the effectiveness of the Cu-IUD is not known to be affected by weight or BMI.

9.2 Oral EC



Women should be informed that it is possible that higher weight or BMI could reduce the effectiveness of oral EC, particularly LNG-EC.

Some studies have suggested that both LNG-EC and UPA-EC could be less effective in women who are overweight, obese or have higher body weight than those with normal or underweight BMI or lower body weight.⁵⁰ The reported negative effect of obesity on effectiveness of LNG-EC is greater than that on effectiveness of UPA-EC.

Evidence level 1+

The European Medicines Agency (EMA) concluded in 2014 that the available evidence was limited and not robust enough to support with certainty a conclusion that oral EC is less effective in women with higher body weight or BMI.⁵¹

9.2.1 UPA-EC

A 2012 meta-analysis⁴⁰ suggests that UPA-EC is less effective for women with a BMI >30 kg/m² than for women with a BMI <30 kg/m² (pregnancy OR for obese versus non-obese women = 2.1 (95% CI 1.0–4.3, *p*=0.04) and for women weighing more than 85 kg, the OR versus women weighing <85 kg = 2.2 (95% CI 1.1–4.6, *p*=0.03). A 2011 meta-analysis by Glasier *et al.*³² reports a non-significantly greater pregnancy risk for obese women (BMI >30 kg/m²) using UPA-EC than for women with BMI <25 kg/m² (OR 2.62, 95% CI 0.89–7.0). The findings have limitations: none of the trials from which the data were taken^{39,41,42} were designed primarily to consider the effect of weight or BMI; weight and height were self-reported by women and may be inaccurate; numbers of pregnancies amongst obese women were small and confidence intervals are wide. Despite these limitations, the GDG concludes that the data suggest that UPA-EC could potentially be less effective for women >85 kg or with a BMI >30 kg/m² than for women <85 kg and with BMI <30 kg/m².

Evidence level 1-

A recently published pharmacokinetic study comparing serum UPA concentrations in 16 obese-BMI women and 16 normal-BMI women after taking UPA 30 mg found no significant difference between the two groups.⁵² This contrasts with the findings for LNG-EC (see [Section 9.2.2](#)). There is no evidence that an increased dose of UPA-EC is more effective than the standard 30 mg dose in these women. Double dosing of UPA-EC is not currently recommended.

9.2.2 LNG-EC

Analysis of data from the LNG-EC comparator arms of RCTs carried out during development of UPA-EC^{39,42} demonstrates a sharp increase in pregnancy rates after LNG-EC for women weighing >70 kg or with BMI >26 kg/m².⁵³ Considering the same data, Glasier *et al.* found that obese women who took LNG-EC were at four times greater risk of pregnancy than women with BMI <25 kg/m² who took LNG-EC (OR 4.41, 95% CI 2.05–9.44, *p*=0.0002).³² These studies considered UK and US women. It should be noted that they were not designed primarily to assess the effect of weight or BMI on effectiveness of oral EC, weights were sometimes self-reported and the number of pregnancies amongst obese women were small.

Evidence level 2+

One analysis of pooled data from three RCTs conducted by the WHO concluded that there is no apparent effect of BMI or body weight on the effectiveness of LNG-EC.⁵⁴ A second analysis of pooled data from these same three RCTs and a fourth WHO RCT suggested a greater risk of pregnancy after LNG-EC amongst women a BMI >30 kg/m² than women with a BMI <25 kg/m². Again, the data were taken from studies that were not primarily designed to consider effect of weight or BMI on effectiveness of oral EC, weights were self-reported and the number of women included in the studies who had a BMI >30 kg/m² is small. A total of only six pregnancies occurred in obese women, all at the same Nigerian study site and all of whom took oral EC after the expected date of ovulation.⁵⁵

A recent study⁵⁶ of the pharmacokinetics of LNG-EC in five obese and five non-obese women demonstrates that obesity adversely impacts maximum serum concentrations of LNG. The authors postulate that this may explain a reduction in effectiveness of LNG-EC in obese women. In this study, doubling the dose of LNG-EC appears to correct the obesity-related pharmacokinetic changes without observed adverse effects. However, it is concluded that “additional research is needed to determine if this also improves EC effectiveness in obese women”. This is supported by very recently published data from a pharmacokinetic study comparing 16 women with obese-BMI and 16 with normal-BMI.⁵² The study concludes that after a single dose of LNG-EC, obese-BMI women are exposed to lower concentrations of LNG when compared to normal-BMI women. This contrasts with the findings for UPA-EC (see [Section 9.2.1](#)).

Evidence level 2-

The GDG considers that the evidence presented above suggests that LNG-EC could be less effective in women weighing >70 kg or with a BMI >26 kg/m². If a Cu-IUD is not indicated or not acceptable, the GDG recommends that such women can be offered UPA-EC. If UPA-EC is not suitable, a double dose (3 mg) of LNG-EC can be used. The effectiveness of 3 mg LNG-EC for these women is unknown. However, the GDG considers that use of 3 mg LNG-EC (which is well tolerated and is supported by pharmacokinetic data)⁵⁶ is justified by its potential ability to prevent unintended pregnancy more effectively than the standard 1.5 mg dose in women weighing >70 kg or with a BMI >26 kg/m². For women weighing >85 kg or with a BMI >30 kg/m², it is not known whether UPA-EC or 3 mg LNG-EC is more effective.

10 What Drug Interactions are Relevant to Use of EC?

The Cu-IUD is unaffected by concomitant use of drugs.

10.1 Inducers of hepatic CYP450 enzymes

D	EC providers should advise women using enzyme-inducing drugs that the effectiveness of UPA-EC and LNG-EC could be reduced.
✓	Women requiring EC who are using enzyme-inducing drugs should be offered a Cu-IUD if appropriate. A 3 mg dose of LNG can be considered but women should be informed that the effectiveness of this regimen is unknown. A double-dose of UPA-EC is not recommended.

The metabolism of both UPA-EC and LNG-EC is increased during and for 28 days after use of drugs that induce liver enzymes.^{48,57,58} The clinical relevance of this interaction in terms of potential reduction in effectiveness is unknown. A Cu-IUD should be recommended for women using enzyme-inducing drugs if the criteria for use are met as the Cu-IUD is unaffected by liver enzyme induction. Alternatively, a single dose of 3 mg LNG (double the licensed dose) can be used off-licence as recommended by the British National Formulary (BNF) and the Medicines and Healthcare products Regulatory Agency (MHRA).^{59,60} The effectiveness of 3 mg LNG for EC in this situation has not been studied. Use of a double dose of UPA-EC is not recommended.

Evidence level 4

See [Resource 1](#) for a list of known enzyme-inducing drugs.

10.1.1 HIV post-exposure prophylaxis

EC may be indicated at the same time as post-exposure prophylaxis for sexual exposure to HIV (PEPSE). The current recommendation from the British Association for Sexual Health and HIV (BASHH) is that Truvada[®] (tenofovir and emtricitabine) and raltegravir are given for PEPSE.⁶¹ This regimen contains no enzyme-inducing drugs that would reduce the effectiveness of oral EC. For other PEPSE regimens it is recommended that potential interactions with oral EC are checked with the online University of Liverpool 'HIV Drug Interactions' Checker (http://www.hiv-druginteractions.org/drug_queries/new).

10.2 Drugs that increase gastric pH

The pharmacokinetics of lower doses of UPA taken for indications other than EC have been shown to be altered by use of esomeprazole.^{58,62} The effectiveness of UPA-EC in women using such medicines has not been studied. The Summary of Product Characteristics (SPC) for ellaOne[®] (UPA 30 mg) advises that the clinical significance of this interaction for single-dose administration of UPA for EC is unknown.⁵⁸

Evidence level 2-

10.3 Progestogens

- ✓ **EC providers should be aware that the effectiveness of UPA-EC could be reduced if a woman takes progestogen in the 5 days after taking UPA-EC.**
- ✓ **EC providers should be aware that the effectiveness of UPA-EC could theoretically be reduced if a woman has taken progestogen prior to taking UPA-EC.**

The ability of UPA-EC (a progesterone receptor modulator) to delay ovulation for at least 5 days has been demonstrated to be significantly reduced by use of a desogestrel POP started immediately after administration of UPA-EC.⁶³

Evidence level 1-

Studies to determine whether this reduces the effectiveness of UPA-EC in preventing pregnancy have not been carried out. It is not known whether other progestogen-containing drugs taken immediately after UPA-EC would have a similar effect. In the absence of evidence, it is recommended by the GDG that all products containing progestogen or progesterone [whether for contraceptive purposes, EC, gynaecological indications or hormone replacement therapy (HRT)] are avoided for 5 days after UPA-EC to avoid compromising the ability of UPA-EC to delay ovulation.

The effect of progestogen taken prior to UPA-EC on UPA-EC effectiveness has not been studied but it is theoretically possible that residual progestogen might reduce the ability of UPA-EC to delay ovulation. Different progestogens administered by different routes are present in the circulation for widely varying lengths of time. The GDG suggests that as a general rule, if a woman has taken any progestogen in the week prior to EC, the effectiveness of UPA-EC could theoretically be reduced by remaining circulating progestogen. Use of LNG-EC rather than UPA-EC may be considered. If UPA-EC is used, progestogen-containing drugs should not be restarted for 5 days afterwards.

11 Are There Any Contraindications/Restrictions to Use of EC?

11.1 Cu-IUD

D

EC providers should be aware that the contraindications to insertion of a Cu-IUD for EC are the same as those for routine IUD insertion.

Use of a Cu-IUD for EC carries the same contraindications as routine Cu-IUD insertion.¹⁰ Importantly, risk of STI (see below), previous ectopic pregnancy, young age (see below) and nulliparity are not contraindications to use. Cu-IUD insertion is relatively contraindicated between 48 hours and 28 days after childbirth.⁹

Evidence level 4

If a woman has known symptomatic *Chlamydia trachomatis* infection or current *Neisseria gonorrhoeae* infection, antibiotic treatment should be completed prior to insertion of a Cu-IUD. Insertion of a Cu-IUD for EC may be considered in the presence of asymptomatic *C. trachomatis* infection after discussion with the woman regarding risk and benefit; treatment with appropriate antibiotics should be given at the time of insertion (or sooner if possible).⁶⁴

All methods of EC including the Cu-IUD should be offered to adolescent girls who are at risk of unwanted pregnancy after UPSI (see [Section 13.1](#)).

11.2 UPA-EC

D

EC providers should be aware that UPA-EC is not suitable for use by women who have severe asthma controlled by oral glucocorticoids.

UKMEC 2016¹⁰ includes no contraindications to the use of UPA-EC. The SPC for ellaOne advises against use in women with severe asthma controlled with oral steroids because of the antiglucocorticoid effect of UPA.

Evidence level 4

The SPC for ellaOne recommends that in the absence of safety data, UPA-EC should be avoided by women with hepatic impairment. However, pregnancy poses a significant risk in women with severe hepatic impairment and expert opinion suggests that use of a single dose of UPA 30 mg is therefore acceptable.

ellaOne contains lactose.⁵⁸

See recommendations regarding use during breastfeeding ([Section 12](#)).

11.3 LNG-EC

UKMEC 2016¹⁰ includes no contraindications to use of LNG-EC. The SPC for Levonelle[®] states that it is not recommended in patients with severe hepatic dysfunction.⁴⁸ However, pregnancy poses a significant risk in women with severe hepatic impairment and expert opinion suggests that use of a single dose of LNG 1.5 mg is therefore acceptable.

Levonelle, Upostelle[®] and Emerres[®] (all 1.5 mg LNG) contain lactose.^{48,65,66}

12 Are There Any Specific Considerations for Women Who are Breastfeeding and Require EC?

In women who are fully breastfeeding and remain amenorrhoeic (lactational amenorrhoea), contraception including EC is not required for 6 months after delivery. However, contraception is required if full breastfeeding ceases, menstruation returns or at 6 months – whichever occurs soonest. Women who do not fully meet the criteria for lactational amenorrhoea require contraception from Day 21 after delivery.⁹

12.1 Cu-IUD

B EC providers should be aware that breastfeeding women have a higher relative risk of uterine perforation during insertion of intrauterine contraception than non-breastfeeding women. However, the absolute risk of perforation is low.

Insertion of a Cu-IUD is relatively contraindicated^{9,10} between 48 hours and 28 days after delivery because of the possible increased risk of uterine perforation and expulsion. Evidence level 4

Clinicians should be aware that there is an increased relative risk of perforation at the time of insertion of intrauterine contraception in the postpartum period and during breastfeeding.^{64,67} However, the absolute risk of perforation remains low. For women who are breastfeeding and within 36 weeks of delivery the risk of uterine perforation was demonstrated by a large European observational study to be about 6 per 1000 insertions.⁶⁷ Evidence level 2+

12.2 UPA-EC

D Breastfeeding women should be advised not to breastfeed and to express and discard milk for a week after they have taken UPA-EC.

UPA is excreted in breast milk. The safety of use of UPA-EC during breastfeeding has not been studied. The SPC for ellaOne advises that breastfeeding is avoided for a week after using UPA-EC; milk should be expressed and discarded during that time.⁵⁸ Evidence level 4

12.3 LNG-EC

C Women who breastfeed should be informed that available limited evidence indicates that LNG-EC has no adverse effects on breastfeeding or on their infants.

The use of LNG-EC is not contraindicated during breastfeeding. The SPC for Levonelle advises that LNG is secreted into breast milk and that potential exposure of the infant to levonorgestrel can be reduced if the woman takes the tablet immediately after feeding and avoids nursing for at least 8 hours.⁴⁸ However studies report no evidence of an adverse effect on the infant or on lactation⁶⁸⁻⁷⁰ and the GDG consider that women can be advised to continue to breastfeed after using LNG-EC. Evidence level 3

A study of 1158 women using the lactational amenorrhoea method (LAM) for postpartum contraception randomised participants to receive either counselling regarding the requirement for contraception when any of the LAM criteria expired or counselling plus an advance supply of LNG-EC. Significantly fewer pregnancies occurred in the LNG-EC group, and significantly more women in that group commenced effective contraception within 6 months after delivery or shortly thereafter.⁷¹ Advance provision of LNG-EC may be considered for women relying on LAM as postpartum contraception.

13 What Method of EC Should be Offered to a Woman Who has had UPSI and Wishes to Avoid Pregnancy?

✓	All women requiring EC should be offered a Cu-IUD if appropriate as it is the most effective method of EC.
✓	EC providers should be aware that a Cu-IUD can be inserted up to 5 days after the first UPSI in a natural menstrual cycle, or up to 5 days after the earliest likely date of ovulation (whichever is later).
✓	If a Cu-IUD is not appropriate or not acceptable, women should be advised that oral EC should be taken as soon as possible if there has been UPSI within the last 5 days.
✓	EC providers should consider UPA-EC as the first-line oral EC for a woman who has had UPSI 96–120 hours ago (even if she has also had UPSI within the last 96 hours).
✓	EC providers should consider UPA-EC as the first-line oral EC for a woman who has had UPSI within the last 5 days if the UPSI is likely to have taken place during the 5 days prior to the estimated day of ovulation.
B	EC providers should advise women that the available evidence suggests that oral EC administered after ovulation is ineffective.

The Cu-IUD is the most effective method of EC (see [Section 8](#)) and the GDG recommends that it should therefore be offered first-line for all women requesting EC who meet the criteria for emergency IUD insertion. In order that the Cu-IUD does not disrupt a pregnancy that has already implanted, insertion is limited to either within the 5 days after the first UPSI in a cycle or up to 5 days after the earliest likely date of ovulation – whichever is later.

If a Cu-IUD is not appropriate or acceptable to a woman, oral EC should be offered as soon as possible after UPSI and effective ongoing contraception commenced (see [Section 18](#)).

Please refer to the two [decision-making algorithms for EC](#) to support choice of EC methods.

13.1 Women not using hormonal contraception

13.1.1 Cu-IUD

If all UPSI since the last natural menstrual period has taken place in the last 5 days, a Cu-IUD can be inserted for EC at any time of the cycle. If a woman is amenorrhoeic, a Cu-IUD can be inserted for EC if all recent UPSI has occurred in the last 5 days, there has been no other UPSI for

>21 days and a highly sensitive urine pregnancy test (able to detect hCG levels around 20 mIU/ml) is negative.

It is established practice that if a woman has had UPSI since her LMP and presents for EC more than 5 days later, a Cu-IUD can be inserted in good faith if she is still within 5 days of her earliest likely date of ovulation (see [Section 7](#)).

The GDG recommends that EC providers who cannot offer Cu-IUD insertion themselves should ensure that they have a clear referral pathway so that women at risk of unwanted pregnancy can access a Cu-IUD if this is their preferred method of EC.

If there is to be a delay before insertion of the Cu-IUD, it is recommended that oral EC is offered at the time of initial attendance in case the woman does not return for the Cu-IUD or the Cu-IUD cannot be fitted.

13.1.2 Oral EC

If a Cu-IUD is not appropriate or not acceptable to a woman, the GDG advises that oral EC should be offered if a woman has had UPSI within the last 5 days. Oral EC should be taken as soon as possible after UPSI to maximise the chances that it is taken before ovulation. It is important to note that oral EC has not been demonstrated to be effective after ovulation has occurred (see [Section 8.2](#)).

UPA-EC is licensed for use up to 120 hours and LNG-EC for use up to 72 hours after UPSI. The evidence suggests that LNG-EC is ineffective if taken more than 96 hours after UPSI⁴⁷ (see [Section 8.2](#)). The GDG therefore recommends that UPA-EC should be considered the first-line oral EC for a woman who has had UPSI 96–120 hours ago (even if she has also had UPSI within the last 96 hours). Use of LNG-EC at 72–96 hours after UPSI is off-licence.^{48,49}

Taken within 120 hours of UPSI, UPA-EC has been demonstrated to be more effective than LNG-EC.³⁹ Therefore the GDG recommends that, in general, UPA-EC should be considered the first-line oral EC if it is thought to be likely that UPSI may have occurred during the 5 days prior to the estimated date of ovulation when risk of pregnancy is highest (see [Section 7.1](#)). A margin for error should be allowed when estimating the timing of ovulation. If it is not possible to establish a likely date of ovulation or a woman does not know where she is in her cycle, use of UPA-EC should be considered.

Effectiveness of oral EC taken more than 120 hours after the most recent episode of UPSI has not been demonstrated. The primary mechanism of action of oral EC is to delay ovulation until sperm are no longer viable. Sperm are viable for about 5 days after UPSI. If ovulation occurs within those 5 days, fertilisation may occur. More than 5 days after the most recent UPSI there is no rationale for giving oral EC to further delay ovulation.

The evidence suggests that oral EC taken after ovulation is ineffective.^{4,5,25} The Cu-IUD is the only method of EC that is known to be effective after ovulation has occurred.

Please refer to the two [decision-making algorithms for EC](#) to support choice of EC methods.

The following factors should also be taken into account when considering choice of oral EC:

- ▶ The effectiveness of UPA-EC (but not of LNG-EC) could be reduced by immediate subsequent use of progestogen-containing contraception or drug (see [Section 10.3](#)). Therefore, ongoing hormonal contraception or hormone therapy should not be started until 5 days after UPA-EC administration (see [Section 18.2](#)).
- ▶ There is a risk of pregnancy from further UPSI occurring during this 5-day waiting period and before ongoing contraception is started and established. If a woman does not subsequently start or return for contraception, an opportunity to initiate an effective ongoing contraceptive method may have been missed. A provider of EC may consider offering LNG-EC with immediate quick start of hormonal contraception (e.g. immediate insertion of an IMP) rather than UPA-EC with delayed start of ongoing contraception if it is likely that a woman might not start contraception after the 5-day delay and she expresses a preference for this. However, if the UPSI for which the woman initially required EC is thought likely to have occurred in the 5 days prior to the estimated date of ovulation, use of UPA-EC should be considered (see above).
- ▶ If a woman has taken progestogen-containing drug within 7 days prior to taking UPA-EC, the effectiveness of UPA-EC may theoretically be reduced, therefore use of LNG-EC rather than UPA-EC can be considered (see [Section 10.3](#)).
- ▶ Metabolism of both UPA-EC and LNG-EC is increased by liver enzyme-inducing drugs. This may reduce their effectiveness as EC. A double dose (3 mg) of LNG-EC can be taken by women using enzyme inducers although its effectiveness is not proven. A double dose of UPA-EC is not recommended (see [Section 10.1](#)) as there are no data to support this regimen.
- ▶ Oral EC, particularly LNG-EC, could be less effective if a woman has a higher body weight or BMI (see [Section 9](#)).

If a woman presents more than 5 days after the most recent UPSI the GDG recommends that it is unlikely that oral EC will be effective. If she declines (or is unsuitable for) a Cu-IUD, she should be offered immediate quick start of suitable hormonal contraception with follow-up pregnancy testing⁷² (see [Section 18.2](#)).

13.2 Women using hormonal contraception

13.2.1 Use of EC for missed pills, late DMPA injection or recently-removed progestogen-only implant or LNG-IUS

A woman may require EC because her compliance with combined hormonal contraception (CHC) (pills, patch or ring), POP or DMPA injections has been poor or an IMP or LNG-IUS has recently been removed. Recommendations for use of the Cu-IUD and oral EC in these situations are outlined in [Table 1](#).

The GDG makes the following recommendations on the basis that the Cu-IUD can be inserted in good faith for EC within 5 days of the earliest likely date of ovulation.

Cu-IUD insertion for EC after incorrect use of CHC

Ovulation may occur if CHC is used incorrectly during Week 1 of pill/patch/ring or if the hormone-free interval (HFI) is extended.

Timing of ovulation after missed pills or detached/removed combined contraceptive patch or ring during Week 1 cannot be predicted for each individual case. Non-compliance with CHC in Week 1 should therefore be considered an extension of the HFI.

A systematic review of studies considering ovulation after an extended HFI in users of combined oral contraception (COC) reports the earliest ovulation at 8 days after the last correctly taken pill in the previous pill packet.⁷³

The largest study included 99 women randomised to one of three treatment groups (i.e. very low-dose monophasic desogestrel, low-dose monophasic gestodene or triphasic gestodene COC), all of which included one cycle of extending the HFI to 10 days. No ovulations and one luteinised unruptured follicle were reported in 98 cycles.

A small study ($n=15$) reported the earliest ovulation after a HFI of 13 days in users of the combined vaginal ring. No data are available for ovulation after an extended HFI amongst users of the combined transdermal patch.⁷³

Based on the fact that the earliest observed ovulation occurred 8 days after stopping CHC (the majority occurred significantly later), the GDG recommends that a Cu-IUD can be inserted for EC up to 13 days after the start of the HFI, provided that the combined hormonal method was used correctly prior to the HFI. This ensures that the Cu-IUD is inserted prior to implantation, even in the unlikely event that ovulation occurs 8 days after stopping CHC.

Cu-IUD insertion for EC after incorrect use of the POP

A recent RCT of 64 women with proven ovulatory cycles demonstrated that the earliest ovulation occurred 9 days after discontinuation of the desogestrel POP following 2 months of correct use.⁷⁴ The GDG considers that the data relating to return of ovulation after the desogestrel POP are too limited to make a definitive recommendation regarding timing of ovulation after missed desogestrel POP.

Provided that the preceding pills have been taken correctly, the cervical mucus effect will have prevented sperm penetration into the upper genital tract until the time of the first missed pill. Therefore, a Cu-IUD can be inserted up to 5 days after the first UPSI following the first missed POP (whether desogestrel or traditional POP).

Cu-IUD insertion for EC after recently-expired DMPA

A systematic review concluded that the return of ovulation following DMPA injection is extremely variable, ranging between 15 and 49 weeks after the last injection.^{75,76} A Cu-IUD is only recommended up to 5 days after the first UPSI that takes place >14 weeks since the last DMPA injection.

Cu-IUD insertion for EC after recently-removed IMP

Ovulation returns rapidly after removal of the IMP Nexplanon[®]. Data relating to earliest ovulation after Nexplanon removal are limited.⁷⁷ The GDG recommends that a Cu-IUD can be inserted up to 5 days after the first UPSI following Nexplanon removal.

Cu-IUD insertion for EC after recently-removed LNG-IUS

Ovulation could have occurred at any time prior to or after removal of the LNG-IUS. Providing that a woman abstained from UPSI during the 5 days prior to removal of the LNG-IUS, a Cu-IUD can be inserted up to 5 days after the first UPSI following LNG-IUS removal.

Oral EC

If a woman requires EC because of non-compliance with hormonal contraception, the possibility must be considered that residual circulating progestogen from the recently-taken contraception could theoretically reduce the effectiveness of UPA-EC (see [Section 10.3](#)). Clinicians may choose to offer LNG-EC in this situation with immediate quick start of a suitable ongoing contraceptive method (see [Section 10.3](#)). The uncertainty surrounding the effectiveness of UPA-EC when there could still be circulating progestogen should be discussed with the woman. If UPA-EC is chosen, hormonal contraception should not be started/restarted for 5 days after the UPA-EC has been taken (see [Section 18](#)).

13.2.2 Recently-expired progestogen-only implant or LNG-IUS

Women can be advised that the risk of pregnancy in the fourth year of use of the progestogen-only implant Nexplanon and the sixth year of use of the 52 mg LNG-IUS Mirena[®] is extremely low.^{64, 78-80} The effectiveness of UPA-EC in the presence of progestogen from a recently expired IMP or LNG-IUS is unknown. Clinicians may consider use of LNG-EC in this situation with immediate quick start of appropriate hormonal contraception. If UPA-EC is given, hormonal contraception should not be started/restarted for 5 days after the UPA-EC has been taken (see [Section 18](#)).

13.3 Adolescents

 **Adolescents who need EC should be offered all methods of EC including the Cu-IUD.**

The GDG advises that all methods of EC including the Cu-IUD should be offered to adolescent girls who are at risk of unwanted pregnancy after UPSI.

There is a growing body of evidence in the professional literature that would support insertion of the Cu-IUD for EC in adolescents. A retrospective case review of emergency Cu-IUD use in 103 women aged 13–19 years found that the vast majority of insertions were straightforward; 96 insertions were rated as ‘easy’ or ‘average’ and only one insertion failed. Twenty-seven (26%) women had their device removed after their next menstrual period (21 due to pain and bleeding and two because of partial expulsion).⁸¹

Evidence level 2+

Other studies investigating acceptability of intrauterine contraception (IUC) amongst adolescents report favourable outcomes but do not specifically consider Cu-IUD use for EC. A recent study of 304 adolescents aged 12–18 years requesting the 13.5 mg IUS (which has an inserter of similar diameter to a non-banded Cu-IUD) reported successful insertion in all but one case. The procedure was well tolerated.⁸² A 2016 review of eight observational studies and one RCT evaluating continuation rates for IUC in women aged 25 years and younger found that 12-month continuation rates of IUC were significantly higher than continuation rates for non-LARC methods ($p=0.001$).⁸³

Evidence level 2+

A 2009 review of six cohort studies and seven case-series reports looking at IUC use in women aged 11–20 years found that continuation rates were high at 12 months (75–88% for Cu-IUD), decreasing over time (39–45% at 36 months). Two studies included in the review compared IUC continuation rates to COC continuation rates and found that women using IUC were at least as likely as COC users to continue using their method.⁸⁴ A 2015 Cochrane review of five moderate- to low-quality RCTs including 1503 women aged ≤ 25 years found no difference in continuation rates between IUC use and other contraceptive methods.⁸⁵

If it is considered likely that a young person might not abstain from UPSI after UPA-EC and thereafter commence effective ongoing contraception, use of LNG-EC with immediate quick start of contraception (e.g. insertion of an IMP) may be discussed as an alternative option. (see [Section 13.1](#)). However, if the UPSI for which the young person initially required EC is thought to be likely to have occurred during the 5 days prior to the day of ovulation, UPA-EC may be considered first-line (see [Section 13.1.2](#)).

13.4 Perimenopausal women

In the perimenopause a woman may still ovulate despite erratic menses. Perimenopausal women should be offered EC after UPSI.

Contraception (including EC) is no longer required by a woman aged >50 years who has been naturally amenorrhoeic for a year.⁸⁶ This does not include women who are amenorrhoeic on hormonal contraception or with HRT. Current FSRH guidance⁸⁶ advises that women aged <50 years can stop contraception after 2 years of natural amenorrhoea for which no other cause is identified. However future ovulation cannot be excluded, particularly in women aged <45 years. The requirement for EC after UPSI should be discussed with these women on an individual basis.

Perimenopausal women who have used hormonal contraception incorrectly should be offered EC after UPSI (see [Section 4.3](#)). Sequential HRT is not contraceptive. Concomitant use of contraception or HRT could reduce the effectiveness of UPA-EC (see [Section 10.3](#)).

13.5 Women requiring EC after sexual assault

✓ Women requiring EC after sexual assault should be offered all methods of EC including the Cu-IUD.

It is recommended that all women at risk of pregnancy after sexual assault are offered a Cu-IUD if within the appropriate timeframe, as it is the most effective method of EC. Antibiotic cover for STI should be considered if a woman opts for Cu-IUD insertion.

The option of forensic examination should be discussed with the woman, with consideration of the timeframe for collection of forensic samples.⁸⁷ If a woman accepts the offer of forensic examination it should be explained that clinical examination and Cu-IUD insertion should be deferred until after forensic examination has taken place in order to maximise potential for capture of assailant DNA. Some women may choose to prioritise pregnancy risk reduction and Cu-IUD insertion above forensic examination if there is to be a delay in arranging the latter. Clinicians should ensure that they provide adequate information to allow a woman to make an informed choice in this regard, dependent on her own priorities; it is important that her decision is respected.

If a woman opts to have a Cu-IUD inserted for EC after forensic examination, her EC provider should arrange for Cu-IUD insertion to be carried out without delay after forensic examination has taken place. Oral EC should be offered in the interim in case the Cu-IUD cannot be inserted or the woman later changes her mind about Cu-IUD insertion.

Women who decline Cu-IUD insertion for EC after sexual assault should be offered oral EC as soon as possible if within the appropriate timeframe.

14 Can Oral EC be Used if There has Also Been UPSI Earlier in the Cycle?

D EC providers can offer a woman UPA-EC or LNG-EC if she has had UPSI earlier in the same cycle as well as within the last 5 days, as evidence suggests that UPA-EC and LNG-EC do not disrupt an existing pregnancy and are not associated with fetal abnormality.

The available data suggest that UPA-EC does not disrupt existing pregnancy or increase the risk of fetal abnormality if taken in very early pregnancy.^{28,88,89} The European Medicines Agency Committee for Medicinal Products for Human Use (CHMP) reviewed the evidence in 2014 and concluded that (1) non-clinical studies demonstrate that UPA-EC is not teratogenic or embryo-lethal and (2) clinical evidence from post-marketing studies (including 568 exposed pregnancies) demonstrates that UPA-EC taken in very early pregnancy does not increase the risk of miscarriage or developmental abnormality. The CHMP noted that during the first 2 weeks after conception, and before the expected date of menses, the developing embryo is not susceptible to teratogenesis.⁸⁹ On the basis of this evidence, pregnancy was removed from the SPC for ellaOne as a contraindication to use.⁵⁸

Evidence level 2+

The GDG recommends therefore that if a woman has had UPSI earlier in the cycle (more than 5 days prior to presenting for EC as well as within the last 5 days) and could be at risk of very early pregnancy, UPA-EC can be used.

Off-licence use of LNG-EC more than 72 hours after UPSI is common practice; there is no evidence that it disrupts existing pregnancy or negatively affects pregnancy outcomes if taken in very early pregnancy.⁴⁸ LNG-EC can therefore be used if there has been UPSI earlier in the cycle as well as within the last 4 days.

Evidence level 4

If a woman requiring oral EC for UPSI in the last 5 days has also had (or may also have had) UPSI more than 21 days ago **AND** has not had a normal menstrual period since the earlier UPSI, a high-sensitivity urine pregnancy test should be done before oral EC is taken.

15 Can Oral EC be Used More Than Once in a Cycle?

- D** If a woman has already taken UPA-EC once or more in a cycle, EC providers can offer her UPA-EC again after further UPSI in the same cycle.
- D** If a woman has already taken LNG-EC once or more in a cycle, EC providers can offer her LNG-EC again after further UPSI in the same cycle.

The significant increased risk of pregnancy with further UPSI later in the cycle in which oral EC has been taken should be explained to women at the time that oral EC is first given. Clear advice regarding the need for effective ongoing contraception must be given. However, women do present requesting EC for further UPSI in the same cycle.

UPA-EC may be used again if a woman has already received UPA-EC earlier in the cycle. Repeated administration of UPA-EC is well tolerated and can continue to delay ovulation for some time.⁹⁰ However, ovulation does eventually occur after UPA-EC in the majority of women.^{31,90} The available evidence demonstrates no risk of disruption of an existing implanted pregnancy or of fetal abnormality if UPA-EC is taken in early pregnancy.^{26,89,90}

Evidence level 2+

Repeated use of LNG-EC in the same cycle and off-licence use of LNG-EC >72 hours after UPSI is common practice; there is no evidence that it disrupts existing pregnancy or negatively affects pregnancy outcomes if taken in very early pregnancy.^{48,91} A recent study considering repeated use of LNG 1.5 mg as pericoital contraception reported that it was well tolerated despite the resulting irregular/frequent bleeding. Side effects were minor (most commonly headache, nausea and abdominal or pelvic pain).⁹²

- ✓** EC providers should be aware that if a woman has already taken UPA-EC, LNG-EC should not be taken in the following 5 days.
- ✓** EC providers should be aware that if a woman has already taken LNG-EC, UPA-EC could theoretically be less effective if taken in the following 7 days.

Use of LNG-EC within 5 days after taking UPA-EC could theoretically reduce the ability of the UPA-EC to delay ovulation after the episode of UPSI for which it was taken (see [Section 10.3](#)). The GDG recommends therefore that LNG-EC should not be taken in the 5 days after UPA-EC. It is recommended that if a woman requests EC for further UPSI within 5 days of taking UPA-EC, a Cu-IUD is offered if appropriate. Alternatively, UPA-EC can be given again.

The GDG recommends that if a woman requests EC having taken LNG-EC within the previous 7 days (the half-life of LNG-EC in the human body is about 26 hours), it is theoretically possible that the effectiveness of UPA-EC could be reduced by residual circulating LNG. In this situation, a Cu-IUD should be offered if appropriate. Alternatively, further administration of LNG-EC may be considered.

16 What are the Side Effects of EC?

Systematic review of safety data for adverse events relating to use of EC by healthy women concludes that such events are rare.⁷⁰ However, evidence for UPA-EC is limited. Headache, nausea and dysmenorrhoea are side effects common to both UPA-EC and LNG-EC and have been reported in around 10% of users.^{39,41,48,58,}

16.1 Vomiting

If vomiting occurs within 3 hours of taking oral EC, a repeat dose should be given.^{48,58}

16.2 Ectopic pregnancy

A Cochrane review in 2012 identified only five cases of ectopic pregnancy amongst over 55 000 oral EC users included in their review.¹¹ A systematic review by Cleland *et al.* concluded that the rate of ectopic pregnancy when LNG-EC or mifepristone (a progesterone receptor modulator) EC failed did not exceed that of the general population.⁹³ A recent large case-control study in China concluded that use of LNG-EC in the current cycle reduced the overall risk of both intrauterine and of ectopic pregnancy. However, the study suggested that amongst pregnancies resulting from failure of LNG-EC, the proportion that were ectopic rather than intrauterine could be higher than amongst pregnancies prior to which no EC had been used.⁹⁴ Absolute numbers of ectopic pregnancies remain very small and LNG-EC reduces absolute risk of ectopic pregnancy by reducing pregnancy risk overall.

A 2014 post-marketing study evaluating adverse events in over 1.4 million women who used UPA-EC found 376 reports of pregnancy, 232 of which had known outcomes. There were four reports of ectopic pregnancies (1.1% of all pregnancies) during the 2.5 years examined.⁸⁸ The rate of ectopic pregnancy in this study did not exceed that of the general population (0.8–2%).⁹³

16.3 Menstrual disturbance

It is recommended that a pregnancy test is carried out if menses are delayed by more than 7 days after EC.

16.3.1 UPA-EC

After UPA-EC, 75% of women in Phase III studies had their next menstrual period at the expected time or within 7 days of the expected time. A small number of women had menses more than

7 days early and about 20% more than 7 days late. The delay was >20 days in 4% of women.^{40,58} Fewer than 10% of women reported intermenstrual bleeding. Similar results are reported by a recent cohort study of 700 women. Delay of menstruation for more than 7 days was significantly more common when UPA-EC was administered prior to ovulation than after ovulation.²⁵

16.3.2 LNG-EC

The majority of women menstruate within 7 days of the expected time after LNG-EC. Menstruation is delayed for over 7 days in fewer than 10% of women.⁴⁸

16.4 Future pregnancy

There is no evidence of adverse pregnancy outcomes or fetal abnormality if pregnancy occurs despite use of LNG-EC^{95,96} or UPA-EC. Evidence relating to UPA-EC is limited.^{28,87,89} If UPA-EC has been taken during a cycle in which a pregnancy is conceived, it should be registered (data are anonymised) at www.hra-pregnancy-registry.com and reported to the MHRA by the Yellow Card scheme.

Use of EC does not affect a woman's long-term fertility.

17 What Investigations are Advised When Providing EC?

A pregnancy test should be considered if a woman has had UPSI earlier in the cycle. Pregnancy testing cannot reliably exclude pregnancy if there has been an episode of UPSI fewer than 21 days previously.

Women requesting EC may be at risk of STI. STI risk assessment should be made and testing offered as appropriate, taking window periods into consideration. Antibiotic cover may be considered for Cu-IUD insertion if there is a significant risk of STI that could be associated with ascending pelvic infection.

18 What Should Women be Advised Regarding Future Contraception?

18.1 Cu-IUD

 **EC providers should advise women that the Cu-IUD provides effective ongoing contraception.**

A Cu-IUD inserted for EC is immediately effective for ongoing contraception. The Cu-IUD offers reliable contraception for its licensed duration. If inserted when a woman is aged >40 years, a Cu-IUD will be effective for contraception until after the menopause.⁶⁴

18.2 Oral EC

 **EC providers should advise women that oral EC methods do not provide ongoing contraception.**

B **EC providers should advise women that after oral EC there is a pregnancy risk if there is further UPSI and ovulation occurs later in the same cycle.**

- D** After taking LNG-EC, women should be advised to start suitable hormonal contraception immediately. Women should be made aware that they must use condoms reliably or abstain from sex until contraception becomes effective.
- D** Women should be advised to wait 5 days after taking UPA-EC before starting suitable hormonal contraception. Women should be made aware that they must use condoms reliably or abstain from sex during the 5 days waiting and then until their contraceptive method is effective.

Studies have demonstrated a higher pregnancy rate after EC amongst women who have further UPSI in the same cycle than amongst women who do not have further UPSI.^{25,32,40,45} Evidence level 1+

It is essential that at the time of provision of oral EC it is explained to the woman that oral EC provides no ongoing protection from pregnancy. The main mechanism of action of oral EC is to delay ovulation, and when ovulation occurs later in the cycle there is a risk of pregnancy if there is further UPSI.

Until recently, it was therefore recommended that suitable hormonal contraception (CHC, POP, IMP or DMPA) should be quick started immediately after oral EC with a pregnancy test 21 days later to exclude pregnancy resulting from EC failure. **This remains the advice after LNG-EC administration.**

However, it has been demonstrated that starting a desogestrel POP immediately after UPA-EC reduces the ability of the UPA-EC to delay ovulation.⁶³ Studies to investigate whether this affects pregnancy rates or whether quick starting CHC, IMP and DMPA after UPA-EC has the same effect have not been done. Evidence level 1+

Extrapolating from this evidence, the GDG recommend that **after UPA-EC, commencement of CHC, POP, IMP and DMPA be delayed for 5 days** (at least 120 hours) after UPA-EC has been given (see [Table 4](#)).⁷² This ensures that the UPA-EC is as effective as possible in preventing pregnancy resulting from the episode(s) of UPSI for which it was taken. Importantly, there is a risk of pregnancy if there is further UPSI before ongoing contraception is started and becomes effective.

Table 4: When to start hormonal contraception after ulipristal acetate emergency contraception (UPA-EC)

Start hormonal contraception >120 hours after UPA-EC	
If UPA taken on...	120 hours later falls on...
Sunday	Friday
Monday	Saturday
Tuesday	Sunday
Wednesday	Monday
Thursday	Tuesday
Friday	Wednesday
Saturday	Thursday

Table 5: Time to contraceptive effectiveness when starting 120 hours after ulipristal acetate emergency contraception (UPA-EC)

Contraceptive method	Requirement for additional contraception after starting method
Combined oral contraceptive pill*	7 days
Combined vaginal ring/transdermal patch	7 days
Progestogen-only pill (traditional/desogestrel)	2 days
Progestogen-only implant or injectable	7 days

*Except Qlaira which requires 9 days of additional contraceptive precautions.

Data from Brache *et al.*⁶³ and Cameron *et al.*⁹⁷ demonstrate that the ability of the desogestrel POP to induce ovarian quiescence and produce a cervical mucus effect and the ability of COC to induce ovarian quiescence is not reduced if they are started immediately after UPA-EC. Evidence level 1+

The GDG advises that CHC (except Qlaira[®]), IMP and DMPA commenced 5 days after administration of UPA-EC will be effective 7 days after starting and POP 2 days after starting (see [Table 5](#)). Additional contraceptive precautions are required until the contraception becomes effective.

It is currently recommended that the LNG-IUS should not be inserted unless pregnancy can be reasonably excluded.

 **If a woman and her EC provider estimate that UPSI is unlikely to have occurred during her fertile period, she may consider the option of using LNG-EC with immediate start of hormonal contraception rather than UPA-EC with delayed start of hormonal contraception.**

If the UPSI for which a woman originally required EC is considered likely to have occurred in the 5 days prior to ovulation (see [Section 7.1](#)), the most effective method of EC should always be considered. If UPSI is unlikely to have occurred during the fertile period, and after discussion with her EC provider a woman thinks that she is likely to have further UPSI after oral EC, or may not commence (or return for) effective contraception after a delay, she could consider LNG-EC in preference to UPA-EC so that suitable ongoing hormonal contraception can be immediately quick started.⁷²

19 What Aftercare is Recommended?

Pregnancy testing is advised if, after EC, the next menstrual period is delayed by more than 7 days, is lighter than usual or is associated with abdominal pain that is not typical of the woman's usual dysmenorrhoea.

Women who start hormonal contraception soon after use of EC should be advised to have a pregnancy test even if they have bleeding; bleeding associated with the contraceptive method may not represent menstruation. Pregnancy can be excluded by a urine pregnancy test taken 21 days after the last episode of UPSI.

If pregnancy occurs after Cu-IUD insertion, management is as described in the FSRH *Intrauterine Contraception* guideline.⁶⁴ If a pregnancy is conceived in a cycle in which oral EC has been taken, the woman should be reassured that evidence suggests that there is no harmful effect on pregnancy outcomes and no increase in the risk of congenital abnormality (see [Section 14](#)). If UPA-EC has been taken during a cycle in which a pregnancy is conceived, it should be registered (data are anonymised) at www.hra-pregnancy-registry.com and reported to the MHRA via the Yellow Card scheme.

EC providers must ensure that if ongoing contraception is not commenced at the time that EC is used, a woman is given information regarding contraceptive choices and has a clear pathway to access her contraception of choice.

20 Can EC be Supplied in Advance of Need?

A Cochrane review in 2010⁹⁸ and a systematic review in 2013⁹⁹ concluded that advance provision of oral EC did not reduce pregnancy rates when compared to conventional provision, although EC was taken more frequently and sooner after UPSI if supplied in advance. However, many women in the included trials did not use EC after UPSI despite having a supply. Advance provision did not lead to increased frequency of UPSI, change in contraceptive method use or increased risk of STI. A randomised trial of advance provision of LNG-EC (plus condoms and an information leaflet) to Swedish teenagers suggested that advance provision shortened the time between UPSI and EC over the following year, without adverse effects on sexual risk-taking or contraceptive use. There was, however, significant loss to follow-up in the study.¹⁰⁰

Access to EC has improved with ‘behind the counter’ availability of LNG-EC and UPA-EC. Routine advance provision would not be cost effective. Providers should always recommend use of the extremely effective LARC methods so that the need for future EC is minimised.

However, there may be individual circumstances in which it is considered that advance supply of either LNG-EC or UPA-EC is appropriate. This should be accompanied by information regarding use, effectiveness, alternative EC and follow-up after use, as well as advice regarding effective ongoing contraception and the STI risk associated with UPSI.

21 Does the Availability of EC Increase Sexual Risk-taking?

The bulk of the available evidence suggests that increased accessibility of oral EC does not increase the frequency of UPSI, the likelihood of sexual risk-taking or the risk of STI and does not make women less likely to use effective contraception.^{98,100-105}

However, a trial that randomised almost 1500 US women to either free, unrestricted access to oral EC or to standard access concluded that some women appeared to substitute free oral EC for their usual contraceptive method.¹⁰⁶

22 What is the Comparative Cost-effectiveness of Different Methods of EC?

A UK cost-effectiveness model calculated the savings associated with avoidance of unintended pregnancy with use of UPA-EC versus use of LNG-EC. The authors concluded that UPA-EC is a cost-saving alternative to LNG-EC despite being itself more expensive. The study received funding from the manufacturer of ellaOne.¹⁰⁷ Similar models in the USA¹⁰⁸ and France (the latter supported by money from the manufacturer of ellaOne)¹⁰⁹ also found use of UPA-EC to be more cost-effective than LNG-EC. However, such models rely on the assumption that women will indeed use oral EC when they are at risk of pregnancy and do not take into account the risk from previous or subsequent UPSI.

As a public health measure, increased access to EC has not yet demonstrated a proven effect in terms of reduction of rates of unplanned pregnancy.¹¹⁰⁻¹¹² Since EC became widely available free of charge, women presenting for abortion in Scotland appear to be no more likely to have used EC to try to prevent the unplanned pregnancy.¹¹³ It may be the case that the women most at risk of unplanned pregnancy do not use EC¹¹⁴ or present late when requesting EC.

Oral EC provides no ongoing contraception and the risk of pregnancy after oral EC is significantly greater amongst women who have further UPSI in the same cycle than amongst those who do not.^{11,25,32,40,45} The Cu-IUD is not only an extremely effective EC method, but offers highly effective ongoing LARC. A study of 542 women reported significantly lower pregnancy rates at a year after EC amongst women who opted for a Cu-IUD than amongst those opting for LNG-EC. Some 64% of Cu-IUDs inserted in the study were retained at 1 year.¹¹⁵ The Cu-IUD may therefore represent a very cost-effective option for EC.

An EC consultation is an important opportunity to provide information regarding future contraception and to consider quick starting contraception so that future UPSI is avoided.

Recommendations for Future Research

High-quality studies are needed to inform clinical recommendations. Specific areas for future research are suggested below.

- ▶ Effectiveness of UPA-EC followed by commencement of hormonal contraception (HC) after 5 days compared with LNG-EC followed by quick start of HC for prevention of pregnancy after UPSI.
- ▶ Comparison of the effectiveness of double-dose LNG-EC versus standard-dose UPA-EC for prevention of pregnancy after UPSI in women with higher body weight or BMI.
- ▶ Safety and effectiveness of standard-dose UPA-EC compared with double-dose UPA-EC in delaying ovulation in women with higher body weight or BMI.
- ▶ Effectiveness of meloxicam with LNG-EC or UPA-EC for prevention of pregnancy after UPSI.
- ▶ Safety, acceptability and effectiveness for prevention of pregnancy of quick starting LNG-IUS at the time of LNG-EC administration.

Useful Links

- ▶ [The International Consortium for Emergency Contraception](#)

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Appendices

Appendix 1 – FSRH Clinical Guideline Development Process

Who has developed the guideline?

This guideline is produced by the Clinical Effectiveness Unit (CEU) with support from the Clinical Effectiveness Committee (CEC) of the Faculty of Sexual & Reproductive Healthcare (FSRH). The FSRH is a registered charitable organisation which funds the development of its own clinical guidelines. NHS Lothian is contracted to host the CEU in the Chalmers Centre and to provide the CEU's services using ring-fenced funding from the FSRH. No other external funding is received. Chalmers Centre supports the CEU in terms of accommodation, facilities, education, training and clinical advice for the members' enquiry service. As an organisation, NHS Lothian has no editorial influence over CEU guidelines, although staff members may be invited to join the CEU's multidisciplinary guideline development groups (GDGs) in an individual professional capacity.

Development of the guideline was led by the secretariat (CEU staff) and involved the intended users of the guidelines (contraception providers) and patient/service user representatives as part of a multidisciplinary group. The scope of the guideline was informed by a scoping survey conducted amongst members of the FSRH and amongst service users from three sexual and reproductive health services across the UK [Sandyford (Glasgow), Scotland; Brook (Liverpool & Wirral), England; Aneurin Bevan University Health Board (Gwent), Wales]. The first draft of the guideline was produced based on the final scope of the guideline agreed by the GDG. The first draft of the guideline (version 0.1) was reviewed by the GDG and discussed at a face-to-face meeting held at the CEU (Edinburgh, Scotland) on 24 May 2016. A revised draft guideline (version 0.2) was produced in response to comments received at the meeting. The draft guideline was revised again after further comments from the GDG, after which the draft guideline (version 0.3) was sent to international and UK-based external independent reviewers suggested by the GDG at the face-to-face meeting. A further revision to the draft guideline was made to produce draft guideline (version 0.4) which was put on the FSRH website for public consultation between 9 November and 7 December 2016. The revised draft guideline (version 0.5) was sent to the GDG for final comments and to reach consensus on the recommendations (details of this process given later). Service users were consulted at both the scoping stage and during the late drafting stages to ensure that their input was considered throughout the process.

Below is the list of contributors involved in the development of this clinical guideline.

Guideline development group (GDG)

Secretariat

- | | |
|-----------------------------|--|
| ▶ Dr Ailsa Gebbie | Director, Clinical Effectiveness Unit |
| ▶ Dr Sarah Hardman | Deputy Director, Clinical Effectiveness Unit |
| ▶ Mrs Valerie Warner | Researcher, Clinical Effectiveness Unit |

Multidisciplinary group

- | | |
|---------------------------|---|
| ▶ Dr Aisling Baird | Consultant in Sexual and Reproductive Healthcare
(Abacus Community Sexual Health Service, Liverpool) |
|---------------------------|---|

- ▶ **Ms Alison Craig** Nurse Consultant in Sexual and Reproductive Healthcare (Chalmers Centre, NHS Lothian)
- ▶ **Dr Lynne Gilbert** Associate Specialist in Sexual and Reproductive Healthcare (iCASH Cambridgeshire); Vice Chair Clinical Standards Committee FSRH
- ▶ **Dr Jennifer Heathcote** Associate Specialist (East Cheshire Centre for Sexual Health, Macclesfield)
- ▶ **Dr Diana Mansour** Consultant in Community Gynaecology and Reproductive Healthcare, Head of Clinical Service, (Sexual Health, Newcastle); FSRH Vice-President Clinical Quality
- ▶ **Dr Anatole S Menon-Johansson** Clinical Lead for Sexual & Reproductive Health (Guy's & St Thomas' NHS Foundation Trust, London)
- ▶ **Dr Lucy Michie** Specialty Trainee in Community Sexual and Reproductive Health (Sandyford Sexual Health Service, Glasgow)
- ▶ **Dr Sarah Millar** Community Sexual and Reproductive Health Trainee (Chalmers Centre, NHS Lothian)
- ▶ **Dr Priyanka Patel** Specialty Trainee in Community Sexual and Reproductive Health (Homerton Hospital)
- ▶ **Mr Andrew Radley** Consultant in Public Health Pharmacy (Kings Cross Hospital, Dundee, NHS Tayside)
- ▶ **Professor James Trussell** Senior Research Demographer (Princeton University); Honorary Fellow (University of Edinburgh)

Independent reviewers

- ▶ **Dr Sharon Cameron** Director (Clinical Effectiveness Unit); Consultant Gynaecologist (Chalmers Centre, NHS Lothian)
- ▶ **Dr Alison Edelmann** Professor OB/GYN, Director Section of Family Planning and the Fellowship in Family Planning (Oregon Health & Science University)
- ▶ **Professor Kristina Gemzell-Danielsson** Professor and Chair (Division of Obstetrics and Gynecology, Department of Women's and Children's Health, Karolinska Institutet); Senior Consultant (Karolinska University Hospital)
- ▶ **Dr Raymond Li** Associate Professor in Obstetrics and Gynaecology, (The University of Hong Kong) and Honorary Medical Consultant (The Family Planning Association of Hong Kong)
- ▶ **Dr Clare Spencer** GPwSI in Gynaecology and GP Partner (Meanwood Practice, Leeds)
- ▶ **Professor Alison Strath** Professor of Community Pharmacy Practice (School of Pharmacy and Life Sciences, Robert Gordon University, Aberdeen)

Declaration of interest

Dr Baird received an honorarium from HRA Pharma for a presentation at their symposium at Current Choices 2013 entitled “EC: Is choice achievable?”. Dr Mansour has received financial support to attend pharmaceutical advisory board meetings, undertake research studies and speak at educational meetings and conferences along with travel grants from Aspen, Astellas, Bayer, Consilient Healthcare, HRA Pharma, Merck, Mithra, Pfizer and Vifor Pharma. Professor Gemzell-Danielsson serves on advisory boards and has been an invited speaker at scientific meetings for Bayer AG, MSD/Merck, HRA Pharma, Exelgyn, Actavis, NaturalCycles and Gedeon Richter on an *ad hoc* basis. Her institution has conducted studies sponsored by HRA Pharma, Mithra, Bayer and MSD/Merck. None of the individuals involved had competing interests that prevented their active participation in the development of this guideline.

Partner contributors

We would like to thank the British Association for Sexual Health and HIV (BASHH) Sexual Violence Group for their helpful contribution regarding women who have experienced sexual assault.

Public consultation contributors

We would like to thank the contributors who provided their valuable feedback during the public consultation.

Guideline development methodology

This FSRH guideline was developed in accordance with the standard methodology for developing FSRH clinical guidelines (outlined in the FSRH’s *Framework for Clinical Guideline Development* which can be accessed [here](#)). The methodology used in the development of this guideline has been accredited by the National Institute for Health and Care Excellence (NICE).

Systematic review of evidence

A systematic review of the literature was conducted to identify evidence to answer the clinical questions formulated and agreed by the GDG. Searches were performed using relevant medical subject headings and free-text terms using the following databases: PubMed, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, the Cumulative Index to Nursing and Allied Health Literature (CINAHL) and POPLINE®. Further, the National Guideline Clearinghouse (NGC) and Scottish Intercollegiate Guideline Network (SIGN) were also used to identify relevant guidelines produced by other organisations; these guidelines were checked to identify missing evidence. No language restrictions were applied to the searches.

Search date: The databases were initially searched up to 21 October 2016. The evidence identified up to this point was used to develop the first draft of the guideline. Any evidence published after this date was not considered for inclusion.

Search strategy: The literature search was performed separately for the different sub-categories covered in this clinical guideline. The search terms used are listed below:

EC efficacy: pregnancy	(emergency contracept*) AND pregnancy (<i>n</i> =568) (emergency contracept*) AND efficacy (<i>n</i> =240) (levonorgestrel AND emergency) AND pregnancy (<i>n</i> =286) (levonorgestrel AND emergency) AND efficacy (<i>n</i> =112) (copper AND emergency) AND pregnancy (<i>n</i> =105) (copper AND emergency) AND efficacy (<i>n</i> =53) (ulipristal AND emergency) AND pregnancy (<i>n</i> =67) (ulipristal AND emergency) AND efficacy (<i>n</i> =47) delay AND ovulation AND emergency [human]
Adverse events	Ulipristal AND gastric (enzyme AND inducer) AND ulipristal (enzyme AND inducing) AND ulipristal (emergency AND contracept*) AND ectopic [humans]
Special populations	(intrauterine AND (device OR system)) AND (adolescent OR teen OR youth) AND (nulli*) (emergency AND contraception) AND (lactati* OR breastfeeding OR infant) breastfeed* AND (“ulipristal acetate” OR levonorgestrel) (emergency contracept*) AND (body mass index) (emergency contracept*) AND (weight)
Quick starting	ulipristal AND (progestogen OR progesterone OR progestin) AND contracept* [filtered for humans] levonorgestrel AND exposure AND (child* OR babies OR baby OR fetus OR fetal) ulipristal AND exposure AND (child* OR babies OR baby OR fetus OR fetal)

Articles identified from the search were screened by title and abstract and full-text copies were obtained if the articles addressed the clinical questions relevant to the guideline. A full critical appraisal of each article was conducted. Studies that did not report relevant outcomes or were not relevant to the clinical questions were excluded.

Summary tables of evidence are available upon request.

Synthesis of evidence and making clinical recommendation

The recommendations are graded (A, B, C, D and Good Practice Point) according to the level of evidence upon which they are based. The highest level of evidence that may be available depends on the type of clinical question asked. The CEU adopts the comprehensive methodology developed by the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) (<http://www.gradeworkinggroup.org/>) to assess the strength of the evidence collated and for generating recommendations from evidence.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

Classification of evidence levels		Grades of recommendations	
1++	High-quality systematic reviews or meta-analysis of randomised controlled trials (RCTs) or RCTs with a very low risk of bias.	A	At least one systematic review, meta-analysis or RCT rated as 1++, and directly applicable to the target population; <i>or</i> A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results.
1+	Well-conducted systematic reviews or meta-analysis of RCTs or RCTs with a low risk of bias.		
1-	Systematic reviews or meta-analysis of RCTs or RCTs with a high risk of bias.		
2++	High-quality systematic reviews of case-control or cohort studies or high-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal.	B	A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results; <i>or</i> Extrapolated evidence from studies rated as 1++ or 1+.
2+	Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal.		
2-	Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal.	C	A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; <i>or</i> Extrapolated evidence from studies rated as 2++.
3	Non-analytical studies (e.g. case report, case series).		
4	Expert opinions.	D	Evidence level 3 or 4; <i>or</i> Extrapolated evidence from studies rated as 2+.
			Good Practice Points based on the clinical experience of the guideline development group.*

*On the occasion when the guideline development group find there is an important practical point that they wish to emphasise but for which there is not, nor is there likely to be, any research evidence. This will typically be where some aspect of treatment is regarded as such sound clinical practice that nobody is likely to question it. It must be emphasised that these are NOT an alternative to evidence-based recommendations, and should only be used where there is no alternative means of highlighting the issue.

Considerations when making recommendations

FSRH clinical guidelines are produced primarily to recommend safe and appropriate clinical practice in relation to the provision of different contraceptive methods. Therefore, when formulating the recommendations, the GDG takes into consideration the health benefits, side effects and other risk associated with implementing the recommendations, based on the available evidence and expert opinion. Further, the GDG takes into consideration the different financial and organisational barriers that clinicians and services may face in the implementation of recommendations to ensure that the recommendations are realistic and achievable.

Reaching consensus on the recommendations

When further revisions based on public consultation feedback have been made, members of the GDG were asked to complete a form to indicate whether they agree or disagree with the recommendations proposed. The consensus process is as follows:

- ▶ Consensus will be reached when 80% of the GDG members agree with the recommendation.
- ▶ Recommendations where consensus is not reached will be redrafted in the light of any feedback.
- ▶ The recommendation consensus form will be sent again for all recommendations. Consensus will be reached when 80% of the GDG members agree with the recommendation.
- ▶ If consensus is not reached on certain recommendations, these will be redrafted once more.
- ▶ If after one more round of consultation, consensus is still not reached, the recommendation will be taken to the CEC for final decision.
- ▶ Any group member who is not content with the decision can choose to have their disagreement noted within the guideline.

Updating this guideline

Clinical guidelines are routinely due for update 5 years after publication. The decision as to whether update of a guideline is required will be based on the availability of new evidence published since its publication. Updates may also be triggered by the emergence of evidence expected to have an important impact on the recommendations. The final decision on whether to carry out a full or partial clinical guideline update is taken by the CEU in consultation with the CEC of the FSRH.

Appendix 2 – Information for Women Requesting Emergency Contraception

Emergency Contraception

You have been supplied with the emergency contraceptive pill.

The emergency contraceptive pill when taken correctly reduces the chances that you will get pregnant after unprotected sex. But

- ▶ It is **not** 100% effective at preventing pregnancy after unprotected sex.
- ▶ It does not prevent pregnancy if you have unprotected sex again after you have taken it.
- ▶ You need to make sure you start using effective contraception immediately.

If you have unprotected sex again after taking the emergency contraceptive pill you are again at risk of getting pregnant. It is very important that you start using effective contraception as soon as possible. The person giving you this leaflet should be able to advise you on where you can go to get effective contraception and advice.

What is the emergency contraceptive IUD?

The copper intrauterine device (IUD) used for emergency contraception is the most effective method. It is more effective in preventing pregnancy after you have had unprotected sex than the emergency contraceptive pill.

The copper IUD as emergency contraception needs to be inserted into the womb as soon as possible after unprotected sex. **It can be used even if you have been given the emergency contraceptive pill.** Once it has been inserted, it also works as an ongoing contraceptive method to prevent pregnancy. The copper IUD is one of the most effective contraceptive methods and it can stay in place for several years. You can have it taken out any time if you want to become pregnant.

If you would like to have a copper IUD for emergency contraception – **ACT NOW**. The person giving you this leaflet will be able to advise you where to go to get more advice and have an emergency IUD fitted. You need to be aware that sometimes it may be too late to fit a copper IUD for emergency contraceptive purposes.

What do I do if I think I am pregnant after using the emergency contraceptive pill?

The emergency contraceptive pill is not 100% effective at preventing pregnancy after unprotected sex. To check you are not pregnant, it is important that you do a pregnancy test if your next period is more than 7 days late or if your period is much lighter than usual. You should seek medical advice if you have any lower abdominal pain that is different from your usual period pain or if you are worried about anything.

Resource

Resource 1: FSRH Drug Interactions with Hormonal Contraception¹¹⁶

- ▶ Available on the FSRH website: <http://www.fsrh.org/standards-and-guidance/documents/ceu-clinical-guidance-drug-interactions-with-hormonal/>
- ▶ Examples of enzyme-inducing drugs

Examples:

Antiepileptics	carbamazepine, eslicarbazepine, oxcarbazepine, phenobarbital, phenytoin, primidone, rufinamide topiramate
Antibiotics	rifabutin, rifampicin
Antiretrovirals	<i>Always use the HIV Drug Interaction Checker (www.hiv-druginteractions.org) to identify potential interactions</i>
Antidepressants	St John's wort
Others	modafinil, bosentan, aprepitant

Questions for Continuing Professional Development

The following multiple choice questions (MCQ) have only one correct answer and have been developed for continuing professional development (CPD). The answers to the questions and information on claiming CPD points can be found in the 'members-only section' of the FSRH website (www.fsrh.org), which is accessible to all Diplomates, Members, Associate Members and Fellows of the FSRH.

- 1 **During a woman's fertile period, the pregnancy risk following a single episode of unprotected sexual intercourse (UPSI) has been estimated to be up to:**
 - a. 10%
 - b. 20%
 - c. 30%
 - d. 40%

- 2 **How does emergency contraception (EC) work? Which of the following statements is false?**
 - a. The primary mechanism of contraceptive action of the copper intrauterine device (Cu-IUD) is inhibition of fertilisation by its toxic effect on sperm and ova.
 - b. If fertilisation does occur, the local endometrial inflammatory reaction resulting from the presence of the Cu-IUD prevents implantation.
 - c. Given that the earliest implantation is believed to occur 6 days after ovulation, a Cu-IUD can be inserted up to 6 days after the first UPSI in a cycle.
 - d. The mechanism of contraceptive action of oral EC is to delay or inhibit ovulation for at least 5 days.

- 3 **The Cu-IUD is the most effective method of EC. A 2012 systemic review reported an overall pregnancy rate of:**
 - a. <0.01%
 - b. <0.1%
 - c. <1%
 - d. <10%

- 4 **Which of the following statements is false? EC providers should consider ulipristal acetate EC (UPA-EC) as first-line oral EC for a woman who:**
 - a. Has had UPSI 96–120 hours ago (even if she has also had UPSI within the last 96 hours).
 - b. Has had UPSI within the last 5 days and it is likely to have taken place during the 5 days prior to ovulation.
 - c. Has a weight >70 kg and BMI >26 kg/m².
 - d. Has had UPSI 2 days ago, on Day 3 of a regular, 28-day cycle and is keen to have Nexplanon insertion today.

- 5 **A woman requesting EC is taking hepatic enzyme-inducing drugs. Which of the following statements is false:**
- A single dose of 60 mg UPA-EC (double the licensed dose) can be used off-licence.
 - The effectiveness of UPA-EC and levonorgestrel EC (LNG-EC) could be reduced.
 - A Cu-IUD should be recommended if the criteria for use are met.
 - A single dose of 3 mg LNG (double the licensed dose) can be used off-licence.
- 6 **Regarding oral EC, which of the following is false?**
- Regular contraception should be started as soon as possible after EC because of the risk of pregnancy due to delayed ovulation in the same cycle.
 - Oral EC can be offered if there has been UPSI or oral EC has already been given earlier in the same cycle.
 - Use of LNG-EC rather than UPA-EC may be considered if the woman has taken any progestogen in the week prior to EC.
 - If LNG-EC is used, progestogen-containing drugs should not be restarted for 5 days afterwards.
- 7 **Contraindications to the insertion of a Cu-IUD for EC are the same as those for routine IUD insertion. Which of the following is a relative contraindication?**
- Between 48 hours and 28 days after childbirth
 - Risk of sexually transmitted infection
 - Previous ectopic pregnancy
 - Young age and nulliparity
- 8 **Which of the following is true? UPA-EC may be less effective if a woman:**
- Has severe asthma managed with oral glucocorticoids.
 - Is taking truvada and raltegravir given for post-exposure HIV prophylaxis after sexual exposure (PEPSE).
 - Commences a hormonal contraceptive on the same day.
 - Takes UPA-EC between 0 and 72 hours after UPSI.
- 9 **A woman presents for a Cu-IUD for EC after using her combined hormonal contraception incorrectly only during Week 1. A Cu-IUD can be inserted for EC up to how many days after the start of the hormone-free interval?**
- 5 days
 - 10 days
 - 13 days
 - 15 days
- 10 **Regarding oral EC, which of the following is false?**
- 10% of women experience side effects of headache, nausea and dysmenorrhoea.
 - Repeat EC should be given if a woman vomits within 3 hours of taking oral EC.
 - After UPA-EC, 75% of women will have their next menstrual period within 7 days of the expected time.
 - After LNG-EC, 30% of women will have a delay in their menstruation by more than 7 days.

Auditable Outcomes

The following auditable outcomes have been suggested by the FSRH Clinical Standards Committee.

Auditable outcome	Target
Percentage of women presenting for emergency contraception (EC) who, subject to eligibility, are advised that a copper intrauterine device (Cu-IUD) is the most effective method.*	97%
Percentage of women whose preferred method is a Cu-IUD who are advised of alternative pathways if the provider is unable to meet their request.	97%
Percentage of women prescribed oral EC who are advised about the importance of starting a reliable method of contraception and are given information about contraceptive methods.	97%
Percentage of women resuming or quick starting a hormonal method of contraception after taking ulipristal acetate EC (UPA-EC) or levonorgestrel EC (LNG-EC) who are advised to do a pregnancy test no sooner than 3 weeks after the most recent episode of unprotected sexual intercourse.	97%
Percentage of women presenting for EC who have a sexual health risk assessment and are offered screening at the appropriate interval if indicated.	97%

Comments and Feedback on Published Guideline

All comments on published guideline can be sent directly to the Clinical Effectiveness Unit (CEU) of the Faculty of Sexual & Reproductive Healthcare (FSRH) via the FSRH website (www.fsrh.org).

The CEU may not respond individually to all feedback. However, the CEU will review all comments and provide an anonymised summary of comments and responses, which are reviewed by the Clinical Effectiveness Committee and any necessary amendments made subsequently.

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