

Faculty of Sexual & Reproductive Healthcare Clinical Guidance



Emergency Contraception

Clinical Effectiveness Unit

August 2011

ABBREVIATIONS USED

BMI	body mass index
CEU	Clinical Effectiveness Unit
CHC	combined hormonal contraception
Cu-IUD	copper-bearing intrauterine device
DMPA	depot medroxyprogesterone acetate
EC	emergency contraception
FSRH	Faculty of Sexual and Reproductive Healthcare
LNG	levonorgestrel
LNG-IUS	levonorgestrel-releasing intrauterine system
NET-EN	norethisterone enantate
PEPSE	post-exposure HIV prophylaxis after sexual exposure
POP	progestogen-only pill
SPC	Summary of Product Characteristics
STI	sexually transmitted infection
UKMEC	<i>UK Medical Eligibility Criteria for Contraceptive Use</i>
UPA	ulipristal acetate
UPSI	unprotected sexual intercourse
WHOMEK	<i>World Health Organization Medical Eligibility Criteria for Contraceptive Use</i>

GRADING OF RECOMMENDATIONS

- A** Evidence based on randomised controlled trials
- B** Evidence based on other robust experimental or observational studies
- C** Evidence is limited but the advice relies on expert opinion and has the endorsement of respected authorities
- ✓** Good Practice Point where no evidence exists but where best practice is based on the clinical experience of the multidisciplinary group

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SUMMARY OF KEY RECOMMENDATIONS

What methods should be offered to women requesting emergency contraception?

- ✓ Health professionals should discuss individual need for emergency contraception (EC) and inform women about the different methods with regard to efficacy, adverse effects, interactions, medical eligibility and need for additional contraceptive precautions.
- C** The copper-bearing intrauterine device (Cu-IUD) can be inserted up to 120 hours after the first episode of unprotected sexual intercourse (UPSI) or within 5 days of the earliest expected date of ovulation.
- A** The efficacy of ulipristal acetate (UPA) has been demonstrated up to 120 hours and can be offered to all eligible women requesting EC during this time period. It is the only oral EC licensed for use between 72 and 120 hours.
- A** The efficacy of levonorgestrel (LNG) has been demonstrated up to 96 hours; between 96 and 120 hours efficacy is unknown. Use of LNG beyond 72 hours is outside the product licence.
- ✓ If a service or health professional is unable to provide a method of EC, local referral mechanisms should facilitate timely access to a service that can provide the woman's preferred method.
- ✓ Ideally an emergency intrauterine device (IUD) should be inserted at first presentation, but where this is not possible oral EC can be given in the interim, and the woman advised to return at the earliest appropriate time.

Future/ongoing contraception

- B** Women should be advised that oral EC methods do not provide contraceptive cover for subsequent UPSI and that they will need to use contraception or refrain from sex to avoid further risk of pregnancy.
- ✓ If a woman is likely to continue to be at risk of pregnancy or has expressed a preference to start contraception immediately after EC, a health professional may 'quick start' combined hormonal contraception (excluding co-cyprindiol), the progestogen-only pill (POP) or implant, providing the woman has been appropriately informed and advised to have a pregnancy test in ≥ 3 weeks.
- ✓ Women requesting the progestogen-only injectable after EC should ideally be offered an alternative method until pregnancy can be excluded. The injectable should be started immediately only if other methods are not appropriate or acceptable and the woman has been appropriately informed and advised to have a pregnancy test in ≥ 3 weeks.
- C** Following administration of LNG, women continuing to use a hormonal method of contraception should be advised to use additional contraceptive precautions for 7 days (2 days for POP, 9 days for Qlaira®).
- ✓ Following administration of UPA, women continuing to use a hormonal method of contraception should be advised to use additional contraceptive precautions for 14 days (9 days for POP, 16 days for Qlaira®).

Drug interactions

- A** Women taking liver enzyme-inducing drugs (or who have stopped taking this medication within the last 28 days) should be advised that a Cu-IUD is the only method of EC not affected by these drugs.
- C** Women taking liver enzyme-inducing drugs, including post-exposure HIV prophylaxis after sexual exposure (or who have stopped within the last 28 days), and who decline or are not eligible for a Cu-IUD, should be advised to take a dose of 3 mg LNG (two Levonelle® tablets) as soon as possible within 120 hours of UPSI (outside the product licence). The efficacy of LNG after 96 hours is uncertain.
- C** Women taking liver enzyme-inducing drugs should be advised not to use UPA during or within 28 days of stopping taking this medication.
- C** Women should be advised not to use UPA if they are currently taking drugs that increase gastric pH (e.g. antacids, histamine H₂ antagonists and proton pump inhibitors).

Side effects

- ✓ Women should be advised to seek medical advice if they vomit within 2 hours of taking LNG or 3 hours of UPA administration. A repeat dose of the same method or a Cu-IUD may be offered if appropriate.
- ✓ Women should be advised about menstrual disturbances after oral EC use. If there is any doubt about whether menstruation has occurred, a pregnancy test should be performed ≥3 weeks after UPSI has occurred.

Multiple use in the same cycle

- C** LNG can be used more than once in a cycle or for a recent indication even if there has been an earlier episode of UPSI outside the treatment window (>120 hours).
- ✓ The CEU does not currently support use of UPA more than once per cycle or if there has been another episode of UPSI outside the treatment window (>120 hours).

Clinical examinations and investigations

- C** Women attending for EC should be offered the opportunity to undergo testing for sexually transmitted infections (STIs) including HIV.
- ✓ For women at risk of STIs, if test results are unavailable before IUD insertion, health professionals should consider prophylactic antibiotics at least to cover *Chlamydia trachomatis*.

Advance provision

- ✓ Health professionals should inform women about availability of EC and when it can be used. Advance supply may be considered but there is no evidence to support routine provision.



Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit

A unit funded by the FSRH and supported by NHS Greater Glasgow & Clyde to provide guidance on evidence-based practice

FSRH Guidance (August 2011) Emergency Contraception

(Update due by August 2016)

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. Recommendations are based on available evidence and consensus opinion of experts. A key to the Grading of Recommendations, based on levels of evidence, is provided on the inside front cover of this document. The recommendations should be used to guide clinical practice but they 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 Changes

The most significant change from previous Faculty guidance on EC¹ is that a new oral method has become available. The progesterone receptor modulator, ulipristal acetate (UPA) (ellaOne®) was introduced into the UK in 2009 and is licensed for use up to 5 days (120 hours) after unprotected sexual intercourse (UPSI).²

3 Introduction

EC provides women with a means of preventing unintended pregnancy following any UPSI. EC is the preferred term; other terms include 'postcoital contraception' and 'the morning after pill'. Currently there are three methods that can be used in the UK as EC (Table 1).

Table 1 Methods of emergency contraception in the UK

Method	Class	Products	Recommended dose/use	Indications
Copper-bearing intrauterine device (Cu-IUD)	Intrauterine contraceptive method	Various types licensed for contraception	IUD retained until pregnancy excluded (e.g. onset of period) or for licensed duration of IUD (5–10 years)	Within the first 5 days (120 hours) following first UPSI in a cycle or within 5 days from the earliest estimated date of ovulation
Levonorgestrel (LNG)	Progestogen hormone	Levonelle One Step® (P) Levonelle1500® (POM)	1.5 mg single oral dose	Licensed for use within 72 hours of UPSI or contraceptive failure
Ulipristal acetate (UPA)	Progesterone receptor modulator	ellaOne® (POM)	30 mg single oral dose	Licensed for use within 120 hours of UPSI or contraceptive failure

EC, emergency contraception; P, pharmacy medicine; POM, prescription-only medicine; UPSI, unprotected sexual intercourse.

EC is commonly supplied for 'off licensed' indications (i.e. outside the terms of the product licence). We have indicated where Faculty recommendations fall outside the product licence. Health professionals should be aware of practices that constitute 'off licence' use of medicines but it may not be necessary to inform the patient if off licence use is supported by clinical guidance. (See Appendix 1 for further guidance.)³

4 When is EC Indicated?

Determining a woman's precise risk of pregnancy is complex as it depends on a number of factors including when ovulation is likely to occur, the fertility of both partners and whether contraception has not been used or has been used incorrectly.

In clinical practice it can be difficult to determine the precise timing of ovulation. The length of the luteal phase (ovulation to menstruation) is relatively constant at 14 days. The follicular phase is more variable, hence the different cycle lengths observed between and within individual women. Discrepancies have been shown between self-reported cycle day and hormonal data,^{4,5} therefore risk of pregnancy calculated from cycle day may not always reflect actual risk.

Conception is most likely to occur following UPSI on the day of ovulation or in the preceding 24 hours.⁶ Due to the natural variation in timing of ovulation, the timing of the 'fertile period' is highly variable, particularly among women with more irregular cycles,⁶ and there are few days in the menstrual cycle when women are not theoretically at risk of pregnancy.⁶ However, the probability of pregnancy from a single act of intercourse in the first 3 days of the cycle appears to be negligible.⁷

Table 2 Indications for emergency contraception following potential failure of hormonal and intrauterine methods of contraception

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 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 the Cu-IUD (unaffected by liver enzyme-inducing drugs) or a double dose (3 mg) of LNG. UPA is not recommended with liver enzyme-inducing drugs
Combined oral contraceptive pill (other than Qlaira®)	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 Week 1 or the pill-free interval If the pill-free interval is extended an emergency IUD can be considered up to 15 days after taking the 21st pill in the last packet providing the preceding pills have been taken correctly
Progestogen-only pill	Late or missed pill (>27 hours since last traditional POP or >36 hours since last desogestrel-only pill)	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). Timing of ovulation after missed pills cannot be accurately predicted. An emergency IUD is therefore only recommended up to 5 days after UPSI
Progestogen-only injectable	Late injection (>14 weeks since last injection of DMPA or >10 weeks since NET-EN)	UPSI during time that additional precautions required as indicated within CEU guidance
Intrauterine methods (Cu-IUD and LNG-IUS)	Removal without immediate replacement; partial or complete expulsion; threads missing and IUD/IUS location unknown	If UPSI has occurred in the 5 days prior to removal, perforation, partial or complete expulsion. Depending on the timing of UPSI and time since IUD known to be correctly placed, it may be appropriate to fit another IUD for EC

CEU, Clinical Effectiveness Unit; Cu-IUD, copper-bearing intrauterine device; DMPA, depot medroxyprogesterone acetate; EC, emergency contraception; LNG-IUS, levonorgestrel intrauterine system; NET-EN, norethisterone enantate; POP, progestogen-only pill; UPA, ulipristal acetate; UPSI, unprotected sexual intercourse.

Given the difficulties in accurately determining risk of pregnancy and the consequences of an unintended pregnancy, all requests for EC should be considered and care individualised. Health professionals should consider the following factors when assessing a woman's need for EC:

- The timing of all episodes of UPSI in the current cycle
- The most likely date of ovulation based on the date of the last menstrual period and the usual cycle length
- Details of potential contraceptive failure (e.g. how many pills were missed and when)
- Use of medications that may affect contraceptive efficacy.

Table 2 summarises some potential indications for EC use with hormonal and intrauterine contraception.

5 How Does EC Work?

In 2002, a judicial review ruled that pregnancy begins at implantation, not fertilisation.⁸ The possible mechanisms of action should be explained to the patient as some methods may not be acceptable, depending on individual beliefs about the onset of pregnancy and abortion.

5.1 Copper-bearing intrauterine device (Cu-IUD)

Copper is toxic to the ovum and sperm and thus the copper-bearing intrauterine device (Cu-IUD) is effective immediately after insertion and works primarily by inhibiting fertilisation.^{9–11} A systematic review on mechanisms of action of IUDs showed that both pre- and post-fertilisation effects contribute to efficacy.¹¹ If fertilisation has already occurred, it is accepted that there is an anti-implantation effect.^{12,13} In a study of 221 women trying to conceive the mean time from ovulation to implantation was 9 (range 6–18) days.¹⁴ Therefore, to ensure that an IUD is inserted before the process of implantation begins an emergency Cu-IUD should be fitted within the first 5 days (120 hours) following first UPSI in a cycle or within 5 days from the earliest estimated date of ovulation.¹⁵ A Cu-IUD can be fitted in good faith, providing appropriate steps have been taken to try and establish a woman's earliest estimated date of ovulation. Appendix 2 illustrates when a Cu-IUD can be inserted for EC in relation to a woman's menstrual cycle.

The Clinical Effectiveness Unit (CEU) does not support the use of the levonorgestrel-releasing intrauterine system (LNG-IUS) for EC as there is no evidence of effectiveness.

5.2 Levonorgestrel (LNG)

The precise mode of action of levonorgestrel (LNG) is incompletely understood but it is thought to work primarily by inhibition of ovulation.^{16,17} Administration of LNG appears to prevent follicular rupture or cause luteal dysfunction.^{16–21} LNG taken prior to the luteinising hormone surge has been shown to result in ovulatory dysfunction in the subsequent 5 days.¹⁷ LNG can thus inhibit ovulation for 5–7 days, by which time any sperm in the reproductive tract will have become non-viable. The closer to ovulation treatment is given, the less likely the probability of interfering with this process. Indeed LNG has been shown to be no better than placebo at suppressing ovulation when given immediately prior to ovulation¹⁷ and is not thought to be effective once the process of fertilisation has occurred.^{22–25}

Studies looking at the effect of LNG on endometrial markers of receptivity have found little to no effect using different modes of administration.^{16,26,27} Evidence from an *in vitro* study indicates that LNG does not affect embryo-endometrial attachment.²⁸

The available evidence suggests that pregnancies occurring after LNG failure are not associated with any major congenital malformations, pregnancy complications or other adverse pregnancy outcomes.²⁹

5.3 Ulipristal acetate (UPA)

UPA's primary mechanism of action is thought to be inhibition or delay of ovulation.² If administered immediately before ovulation UPA has been shown to suppress growth of lead follicles.^{30,31} There is evidence³¹ to suggest that UPA can prevent ovulation after the LH surge has started, delaying follicular rupture until up to 5 days later. Administration of UPA at the time of the LH peak or after has been shown to be ineffective in delaying follicular rupture.³¹

Although there have been studies that have shown an endometrial effect,^{32,33} the contribution of these endometrial changes to the efficacy of UPA (e.g. by inhibiting implantation) is as yet unknown.

There is currently a lack of evidence on the effect of UPA if inadvertently administered after implantation has occurred, but there have been no associated adverse outcomes in the small numbers of inadvertent pregnancies that have been reported to date.² As a new drug, it is still under the Black Triangle Scheme. A variety of measures are in place to monitor adverse effects, including a European register to monitor outcomes of exposure during pregnancy.²

6 How Effective are the Different EC Methods?

In order to estimate the number of pregnancies prevented by EC, the pregnancy rates observed in clinical trials are compared to published reports of conception rates in a reference population of women having UPSI on different days of the menstrual cycle. Because of the assumptions inherent in this method (e.g. the study population are equally fertile and that they have accurately reported their menstrual cycle dates) bias and errors cannot be excluded.

The difficulties in determining absolute effectiveness should not significantly influence observed differences in randomised comparative trials but they may affect how accurately pregnancy rates and cost effectiveness can be predicted in routine clinical practice and in different populations.

Although EC has been shown to reduce the risk of pregnancy at an individual level,^{34–38} provision of EC has not yet been shown to impact on overall unintended pregnancy or abortion rates in women with increased access,³⁹ including advance provision,^{40–42} or at a population level.⁴³ This may in part be because even with advance provision women do not use EC on every occasion of UPSI, and EC is used too infrequently by those women most at risk of pregnancy.^{42–44} Tackling the problem of unintended pregnancies requires a multidimensional approach of which EC provision is only one aspect.

6.1 Cu-IUD

Data from non-randomised trials suggest that the failure rate for use of the Cu-IUD as EC is considerably lower than 1%.^{38,45–49} There are no published data to suggest which type of Cu-IUD is most effective for EC. A prospective observational cohort study⁵⁰ has shown that the CU-T380A[®] is very effective with no pregnancies reported in the first month after insertion amongst 1963 women (nulliparous and parous) who received it for the purpose of EC. For ongoing contraception, the most effective Cu-IUDs contain at least 380 mm² of copper and have banded copper on the arms.⁵¹

6.2 LNG

The efficacy of LNG has been demonstrated up to 72 hours after UPSI. There has been uncertainty about its effectiveness thereafter and whether or not efficacy decreases with time since intercourse.^{1,36,37,52,53} A study⁵⁴ has tried to address these concerns by combining data from four World Health Organization (WHO) randomised controlled trials (RCTs). The risk of pregnancy on Days 2, 3 and 4 after UPSI [odds ratio (OR) 0.68, 95% confidence interval (CI) 0.36–1.28; 1.74, 95% CI 0.94–3.19; and 0.87, 95% CI 0.26–2.89, respectively] was not significantly different from that on Day 1, suggesting that LNG is effective up to 96 hours⁵⁴ and that delay in treatment up to this time did not appear to affect efficacy. Compared to Day 1, however, LNG administered on Day 5 increased the risk of pregnancy nearly six-fold (OR 5.81, 95% CI 2.87–11.76) and the percentage of women becoming pregnant was not statistically different from the rates (6–8%)⁵⁵ that might be expected without treatment. It is therefore not certain whether LNG administration on Day 5 offers protection against unintended pregnancy.⁵⁴

6.3 UPA

The efficacy of UPA has been demonstrated up to 120 hours after UPSI^{2,56,57} and there is no apparent decline in efficacy within that time period.⁵⁶ Two randomised, non-inferiority trials^{53,57} have found UPA to be no less effective than LNG in preventing pregnancy when administered within 72 hours of UPSI.^{53,57} In both trials there was a non-significant trend towards lower pregnancy rates with UPA.^{53,57} One of these two studies also demonstrated

Table 3 Results of randomised trials and meta-analysis of ulipristal acetate versus levonorgestrel^a

Authors	Design	Time since UPSI (hours)	Ulipristal acetate			Levonorgestrel			OR (95% CI)	p
			Exposed (n)	Pregnancies (n)	Rate (%)	Exposed (n)	Pregnancies (n)	Rate (%)		
Creinin <i>et al.</i> ⁵³	Phase II randomised non-inferiority trial	0–72	773	7	0.9	773	13	1.7	0.50 (0.18–1.24)	0.135 NS
Glasier <i>et al.</i> ⁵⁷	Phase III randomised non-inferiority trial	0–120	941	15	1.6	958	25	2.6	0.57 (0.29–1.09)	0.091 NS
Glasier <i>et al.</i> ⁵⁷	Meta-analysis	0–24	584	5	0.9	600	15	2.5	0.35 (0.11–0.93)	0.035
		0–72	1617	22	1.4	1625	35	2.2	0.58 (0.33–0.99)	0.046
		0–120	1714	22	1.3	1731	38	2.2	0.55 (0.32–0.93)	0.025

^aIn the meta-analysis the efficacy-evaluable population excluded women aged older than 35 years as recommended by the US Food and Drug Administration, therefore subject numbers may differ from the original papers. CI, confidence interval; NS, no significant difference; OR, odds ratio; UPSI, unprotected sexual intercourse.

non-inferiority up to 120 hours.⁵⁷ In order to increase statistical power, the data from these two non-inferiority trials were combined in a meta-analysis.⁵⁷ The authors concluded that the pregnancy rate was significantly lower in the UPA group than the LNG group.⁵⁷ The difference in pregnancy rates was significant in all time periods analysed up to 120 hours (Table 3). The authors did not report data for the 72–120-hour period.

The meta-analysis combined two non-inferiority trials that were not designed to show superiority of one product over another and contained a small number of subjects presenting between 73 and 120 hours. Table 3 summarises the findings of the meta-analysis.

Although neither of the individual studies was specifically designed to look at factors affecting efficacy of EC, the meta-analysis demonstrated that pregnancies were significantly related to where in the cycle intercourse took place and whether further incidents of UPSI occurred. There was no difference in the efficacy of UPA and LNG with respect to the cycle day on which intercourse took place or whether further acts of UPSI occurred.⁵⁸

6.4 Efficacy and body weight

No studies have specifically looked at the effect of body weight on the efficacy of oral EC. However, in the meta-analyses of UPA and LNG studies⁵⁷ subgroup analysis revealed an association between pregnancy risk and body mass index (BMI).⁵⁸ Obese women (BMI >30) using LNG were at greater risk of pregnancy compared with those using LNG with a normal or low BMI.⁵⁸ Whilst an increased risk was also noticed amongst UPA users, the difference was not statistically significant.⁵⁸ The numbers of women falling pregnant using either method was small ($n = 60$) and even smaller among obese women ($n = 20$, 6/227 UPA, 14/242 LNG).⁵⁸ It is not clear whether confounding factors such as multiple episodes of UPSI, indication for EC or subsequent episodes of UPSI played a role in the findings. More evidence is needed before specific recommendations can be made for obese women. The CEU supports the use of all EC methods in obese women and does not recommend increasing the dose of oral EC.

7 What are the Side Effects of EC?

7.1 Cu-IUD

Pain is a common side effect associated with insertion.⁵⁹ Pain relief may facilitate insertion and should be discussed with all women in advance of the procedure.⁵⁹ Analgesics commonly used are non-steroidal anti-inflammatory drugs, topical lidocaine (Instillagel®) and cervical

local anaesthetic block. Further information on side effects of the Cu-IUD can be found in existing Faculty guidance.⁵⁹

7.2 LNG/UPA

Headache, nausea and altered bleeding patterns are side effects common to oral EC.^{2,23,24} Nausea is reported by less than 20% of women using LNG EC and vomiting occurs in only 1%.³⁴ According to the *UK Selected Practice Recommendations for Contraceptive Use*, if a woman vomits within 2 hours of taking LNG she should take a further dose as soon as possible⁶⁰ [the Summary of Product Characteristics (SPC) advises 3 hours].^{23,24} A repeat dose of UPA should be given if vomiting occurs within 3 hours of administration.²

Most women experience bleeding within 7 days of the expected time.^{2,23,24} Menstruation has been observed as occurring on average 1.2 days earlier than might be expected when using LNG, and on average 2 days later than expected when using UPA.⁵⁷ Around 20% of women in clinical trials reported a delay of more than 7 days with use of UPA.² There is no significant change to the duration of bleeding.⁵⁷

A systematic review⁶¹ has concluded that emergency contraceptives containing LNG or mifepristone (another progesterone receptor modulator not licensed for use in the UK as EC) do not increase the chance that a pregnancy will be ectopic. Moreover, in common with all contraceptive methods, EC reduces the absolute risk of ectopic pregnancy by preventing pregnancy in general.⁶¹ A previous ectopic pregnancy is not a contraindication to use.⁶²

Other reported side effects of UPA and LNG include headaches, abdominal pain, dysmenorrhoea and dizziness.^{34,35,53,56,57}

✓ Women should be advised to seek medical advice if they vomit within 2 hours of taking LNG or 3 hours of UPA administration. A repeat dose of the same method or a Cu-IUD may be offered if appropriate.

✓ Women should be advised about menstrual disturbances after oral EC use. If there is any doubt about whether menstruation has occurred, a pregnancy test should be performed ≥ 3 weeks after UPSI has occurred.

8 Are There Any Contraindications/Restrictions to EC Use?

8.1 Cu-IUD

Use of an Cu-IUD for EC carries the same contraindications as routine Cu-IUD insertion.^{59–62} Risk of sexually transmitted infections (STIs), previous ectopic pregnancy, age and nulliparity are not contraindications to use.⁶²

8.2 LNG

The *UK Medical Eligibility Criteria for Contraceptive Use* (UKMEC) advises that there are no medical contraindications to LNG, including breastfeeding.⁶²

8.3 UPA

There are currently no recommendations on the use of UPA within UKMEC. Although there has been limited inclusion of under-18s in clinical trials of UPA, age is not listed as a contraindication within the SPC.² UPA is licensed for use in under-18s and the CEU supports the use of all EC methods in young people.

The SPC states that contraindications to use include a hypersensitivity to UPA or any of the other components, and also pregnancy.² Use is not recommended in women with severe asthma insufficiently controlled by oral glucocorticoids. In addition the SPC advises caution in women with hepatic dysfunction, hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.²

The SPC states that after intake of UPA, breastfeeding is not recommended for up to 36 hours.²

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

9.1 LNG

Giving repeated doses of LNG may be effective and further UPSI may be an indication for repeat LNG use.¹⁷ A Cochrane review has suggested that LNG administered on a regular basis for pre- and postcoital contraception seemed reasonably efficacious and was safe.⁶³ As

there is no evidence to indicate LNG is not safe in pregnancy, the CEU recommends that LNG can be used more than once in the same cycle or can be used for a recent episode of UPSI even if there has been an earlier episode of UPSI outside the treatment window (>120 hours) (outside product licence) (Table 2).

No data were identified regarding a minimum time interval between successive LNG treatments. However, the CEU advises that if further UPSI occurs within 12 hours of a dose of LNG, further EC treatment is not required.

9.2 UPA

The SPC for ellaOne states that UPA should not be used more than once in a cycle or concomitantly with LNG,² and the CEU currently supports this advice. There are limited data on its safety in pregnancy, therefore where multiple episodes of UPSI have occurred and there is a risk that a woman may already be pregnant, the CEU does not currently support the use of UPA (Table 2). If a Cu-IUD is declined or is not appropriate, the CEU supports giving LNG for another episode of UPSI after administration of UPA (outside product licence). It is not known if UPA reduces the efficacy of LNG or how long after UPA administration any such interaction has an effect.

C LNG can be used more than once in a cycle or for a recent indication even if there has been an earlier episode of UPSI outside the treatment window (>120 hours).

✓ The CEU does not currently support use of UPA more than once per cycle or if there has been another episode of UPSI outside the treatment window (>120 hours).

10 What Drug Interactions are Relevant to EC Use and What Should be Advised?

10.1 Cu-IUD

The efficacy of Cu-IUDs is unaffected by concomitant drug use^{59,64} (Table 2).

10.2 LNG

Drugs that induce enzymes have the potential to decrease the contraceptive efficacy of LNG⁶⁵ whilst using them and for 28 days afterwards. Women on liver enzyme-inducing drugs or who have stopped using them (≤ 28 days ago) who require EC should be offered a Cu-IUD as the efficacy is not affected by drugs. However, in women who are ineligible or who do not wish an intrauterine method a single 3 mg dose of LNG (two Levonelle[®] tablets) may be administered (outside product licence),⁶⁵ although there is no empirical evidence to support this. In certain circumstances HIV post-exposure prophylaxis after sexual exposure (PEPSE) and EC may be required simultaneously. Although it can take several days for liver enzyme-inducing drugs to take effect, the exact mechanisms of LNG's action are unknown and there have been no interaction studies looking at the impact of dual administration of LNG and PEPSE. Therefore, the CEU recommends 3 mg LNG (two tablets) if a Cu-IUD is not available or not acceptable (Table 2).

10.3 UPA

The SPC states that it is not advisable to use UPA with liver enzyme-inducing drugs² and the CEU therefore recommends that it is not used in women using liver enzyme-inducing drugs and for 28 days after these drugs are stopped.⁶⁴ The SPC² also states that UPA should not be used concomitantly with drugs that increase gastric pH.² The CEU does not currently support doubling the dose of UPA when using drugs that may reduce UPA's efficacy.⁶⁴ (Table 2).

UPA itself may reduce the contraceptive efficacy of ongoing hormonal contraception.² As a progesterone receptor modulator it blocks the action of progestogen and therefore in theory could reduce the efficacy of contraceptives containing progestogen.² The half-life of UPA is 32.4 hours.² No interaction studies have been carried out to date, therefore the CEU has taken a pragmatic approach in developing its recommendations, which may need to be amended if new evidence becomes available. The CEU currently recommends additional precautions for 7 days in addition to the 7 days [2 days for the progestogen-only pill (POP), 9 days for Qlaira[®]] for starting hormonal contraception (i.e. 14 days total) [9 days if starting or continuing the POP, 16 days for Qlaira].⁶⁶ Theoretically there is a risk that progestogen could also block the action of UPA but to date there is no evidence to support or refute this. Starting contraception immediately after UPA is off licence.

- A** Women taking liver enzyme-inducing drugs (or who have stopped within the last 28 days) should be advised that a Cu-IUD is the only method of EC not affected by these drugs.
- C** Women taking liver enzyme-inducing drugs including PEPSE (or who have stopped within the last 28 days), and who decline or are not eligible for a Cu-IUD, should be advised to take a dose of 3 mg LNG (two Levonelle tablets) as soon as possible within 120 hours of UPSI (outside the product licence). The efficacy of LNG after 96 hours is uncertain.
- C** Women taking liver enzyme-inducing drugs should be advised not to use UPA during or within 28 days of stopping treatment.
- C** Women should be advised not to use UPA if they are currently taking drugs that increase gastric pH (e.g. antacids, histamine H₂ antagonists and proton pump inhibitors).

11 What Methods Should be Offered to Women Requesting EC?

A number of factors should be considered when informing women about EC options. These include:

- Medical eligibility
- Efficacy of method
- Last menstrual period and cycle length
- Number and timing of episodes of UPSI
- Previous EC use within cycle
- Need for additional precautions/ongoing contraception
- Drug interactions
- Individual choice.

All eligible women should be offered the Cu-IUD as it is considered the most effective method of EC due to the low documented failure rate.^{38,45-49}

Both oral methods of EC are licensed and effective between 0 and 72 hours. UPA is the only oral method licensed for use between 72 and 120 hours. Use of LNG beyond 72 hours after UPSI would be unlicensed use but the CEU supports use up to 96 hours.

- ✓** Health professionals should discuss individual need for EC and inform women about the different methods with regard to efficacy, adverse effects, interactions, medical eligibility and need for additional contraceptive precautions.
- C** The copper-bearing intrauterine device can be inserted up to 120 hours after the first episode of UPSI or up to 5 days after the earliest expected date of ovulation.
- A** The efficacy of UPA has been demonstrated up to 120 hours and can be offered to all eligible women requesting EC during this time period. It is the only oral EC licensed for use between 72 and 120 hours.
- A** The efficacy of LNG has been demonstrated up to 96 hours; between 96 and 120 hours its efficacy is unknown. Use of LNG beyond 72 hours is outside the product licence.
- ✓** If a service or health professional is unable to provide a method of EC, local referral mechanisms should facilitate timely access to a service that can provide the woman's preferred method.
- ✓** Ideally an emergency IUD should be inserted at first presentation, but where this is not possible oral EC can be given in the interim, and the woman advised to attend for insertion at the earliest appropriate time.

12 What Investigations are Advised When Providing EC?

Consideration may be given to pregnancy testing prior to EC administration if a woman has been at risk earlier in the cycle. A pregnancy test cannot reliably exclude pregnancy if there has been an episode of UPSI less than 3 weeks previously.

Women presenting for EC may be at risk of STIs. Studies looking at the prevalence of *Chlamydia trachomatis* infection amongst women presenting for EC have reported figures up to 9.1% in women aged under 25 years.^{67,68} Women presenting for EC should be offered the opportunity to undergo testing for STIs including HIV. Women tested for STIs when they present for EC should be made aware that recently acquired STI may not be detected and that they

may need to be retested after the appropriate window period. Health professionals should avoid making assumptions about risk and should offer STI testing to all women irrespective of age, relationship or ethnicity.

Antibiotics should be considered for women presenting for an emergency IUD.^{59,69}

C Women attending for EC should be offered the opportunity to undergo testing for STIs including HIV.

✓ For women at risk of STIs, if test results are unavailable before IUD insertion, health professionals should consider prophylactic antibiotics at least to cover *Chlamydia trachomatis*.

13 What Should Women be Advised Regarding Future Contraception?

Women should be advised that neither LNG nor UPA will provide contraceptive cover for subsequent acts of UPSI.

Ongoing contraception should be discussed with all women even if they do not plan to have sex in the foreseeable future. Information should include typical use failure rates⁷⁰ for all methods of contraception, and the benefits of some long-acting reversible contraception methods over shorter-acting methods.

Women choosing a Cu-IUD for EC may opt to continue using the Cu-IUD for ongoing contraception. If the woman does not require contraception or prefers another method, the Cu-IUD can be removed after pregnancy has been excluded and providing there has been no UPSI in the 7 days prior to removal and guidance for switching methods is followed.

13.1 Women starting contraception

Women may prefer to wait until pregnancy can be excluded before starting a hormonal method of contraception. However, the CEU supports starting some methods of contraception immediately after EC. The woman should be informed of the theoretical risks and the importance of pregnancy testing. Detailed information is provided in Faculty guidance on *Quick Starting Contraception*.⁶⁶ A health professional may initiate combined hormonal contraception (CHC) (excluding co-cyprindiol), the POP or implant.⁶⁶ The progestogen-only injectable should only be quick started after EC if other methods are not appropriate or not acceptable.⁶⁶ The LNG-IUS should never be inserted following administration of EC and an alternative 'bridging' method should be offered until pregnancy can be excluded. The Cu-IUD should only be inserted following oral EC administration if the conditions of its use as an EC are still met.⁶⁶

13.2 Women already using contraception

The SPCs for both LNG^{23,24} and UPA² indicate that use does not contraindicate the continued use of regular contraception.

In the event of EC administration because of missed pills, women should be advised to resume their oral hormonal contraception. Following use of LNG, additional precautions (condoms or refraining from sex) should be advised for 7 days when continuing CHC, 2 days for POP and 9 days for Qlaira. Following UPA administration, additional precautions should be advised for 14 days for CHC, 9 days for POP and 16 days for Qlaira (outside terms of product licence).

Table 4 highlights the need for additional precautions if continuing or starting any hormonal contraception after EC.

Table 4 Requirements for additional contraception after emergency contraception in women using hormonal contraception

EC option	Additional contraceptive precautions (condom or avoidance of sex)
Cu-IUD	Not applicable. [If Cu-IUD to be removed at time of starting an alternative method the woman should use additional precautions for the 7 days prior to removal. Health professionals should follow guidance in relation to starting hormonal contraception.]
LNG	7 days (2 for POP, 9 for Qlaira®)
UPA	14 days (9 for POP, 16 for Qlaira)

Cu-IUD, copper-bearing intrauterine device; EC, emergency contraception; LNG, levonorgestrel; POP, progestogen-only pill; UPA, ulipristal acetate.

- B** Women should be advised that oral EC methods do not provide contraceptive cover for subsequent UPSI and that they will need to use contraception or refrain from sex to avoid further risk of pregnancy.
- ✓ If a woman is likely to continue to be at risk of pregnancy or has expressed a preference to start contraception immediately after EC, a health professional may 'quick start' combined hormonal contraception (excluding co-cyprindiol), the progestogen-only pill or implant, providing the woman has been appropriately informed and advised to have a pregnancy test in ≥ 3 weeks.
- ✓ Women requesting the progestogen-only injectable after EC should ideally be offered an alternative method until pregnancy can be excluded. The injectable should be started immediately, only if other methods are not appropriate or acceptable and the woman has been appropriately informed and advised to have a pregnancy test in ≥ 3 weeks.
- C** Following administration of LNG, women continuing to use a hormonal method of contraception should be advised to use additional contraceptive precautions for 7 days (2 days for POP, 9 days for Qlaira).
- ✓ Following administration of UPA, women continuing to use a hormonal method of contraception should be advised to use additional contraceptive precautions for 14 days (9 days for POP, 16 days for Qlaira).

14 What Aftercare is Advised?

Women may be offered follow-up if they want a pregnancy test, STI screening, Cu-IUD removal or have any concerns or difficulties with their contraception. If a Cu-IUD is to be used as an ongoing contraceptive method, women are advised to return for a follow-up visit after the first menses (or 3–6 weeks) after insertion.⁵⁹

Failure of an emergency Cu-IUD should be managed as described in the FSRH guidance on intrauterine contraception.⁵⁹

Pregnancies arising from failed oral EC need to be managed differently from other pregnancies. If a woman chooses to continue her pregnancy after exposure to UPA this should be reported to the manufacturer of ellaOne for inclusion in their European register to monitor outcomes of exposure during pregnancy.

15 Who Can Supply EC?

Oral EC is available from a variety of services including general practitioners, accident and emergency departments, pharmacies and sexual health services. Where a service does not provide a particular method of EC, local referral pathways should be in place to ensure timely access if the method is requested. Health professionals should consider providing oral EC in the interim to women being referred for a Cu-IUD. EC can be supplied by doctors and non-medical prescribers (e.g. nurses, school nurses and pharmacists). LNG and UPA can also be supplied by patient group direction (PGD).

16 Can EC be Supplied in Advance of Need?

Advance provision of EC has not been shown to reduce pregnancy rates when compared to conventional provision.³⁹ However the WHO recognises that in certain circumstances an advance supply of EC is appropriate and acceptable.¹⁵ Women who have EC in advance have been shown to be more likely to report use of the medication, and to use it sooner after sex.³⁹ Health professionals may consider advance provision on an individual basis for women who may be at risk (e.g. women relying on barrier methods or travelling abroad). Qualitative research⁷¹ suggests that women can be reluctant to ask for advance supply of EC due to concerns about being judged, and thus professionals should be more proactive in providing women with information about the use of EC. EC provision should be backed up with advice and information about ongoing contraceptive provision and advice on condom use for STI protection.

- ✓ Health professionals should inform women about availability of EC and when it can be used. Advance supply may be considered but there is no evidence to support routine provision.

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APPENDIX 1: JOINT STATEMENT FROM THE FSRH CLINICAL STANDARDS COMMITTEE, CLINICAL EFFECTIVENESS COMMITTEE AND ASSOCIATE MEMBERS' WORKING GROUP ON THE PRESCRIPTION, ADMINISTRATION OR SUPPLY OF CONTRACEPTIVE MEDICINES FOR USE OUTSIDE THE TERMS OF THEIR LICENCES³

There are many generally accepted off licence ('off-label') usages of contraception.

The General Medical Council guidance document *Good Practice in Prescribing Medicines* (2008) states that:

"When prescribing a medicine for use outside the terms of its licence, you must be satisfied that there is sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy, and make a clear, accurate, legible record of all medicines prescribed and, where you are not following common practice, your reasons for prescribing the medicine. Some medicines are routinely used outside the scope of their licence. ... Where current practice supports the use of a medicine in this way it may not be necessary to draw attention to the licence when seeking consent..."

The above mentioned Committees have agreed that Clinical Effectiveness Unit (CEU) guidance on use of contraceptives is guidance on "common practice" and "**current practice**" in the use of these medicines and devices. Therefore it is recommended that it may not be necessary for clinicians to document every occasion when a contraceptive preparation is prescribed outside the product licence if such use falls within current guidance issued by the Faculty's CEU. Similarly, current guidance from the Royal College of Obstetricians and Gynaecologists (RCOG) and the National Institute for Health and Clinical Excellence (NICE) should be regarded as common practice.

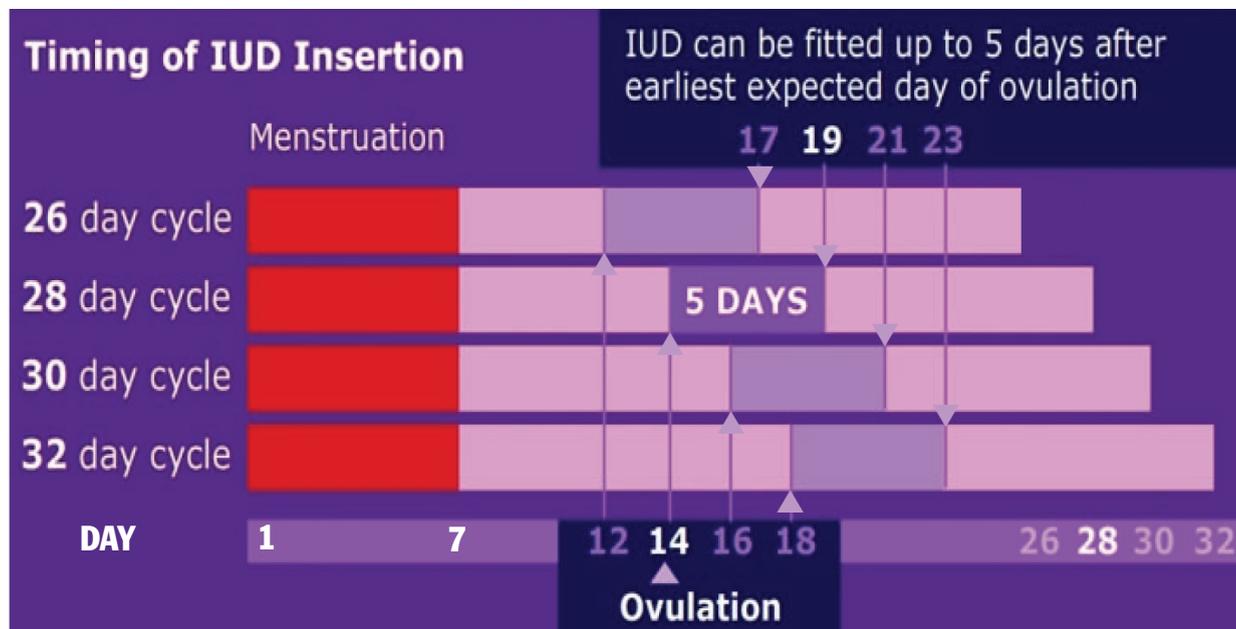
Current guidance to nurse/midwife prescribers is different. The Nursing and Midwifery Council (NMC) advises that nurse or midwife independent prescribers may prescribe off-label if they are satisfied that this better serves the patient's/client's needs, if they are satisfied that there is sufficient evidence-base and that they have explained to the patient/client the reasons why medicines are not licensed for their proposed use, and document accordingly.

The NMC also states it is acceptable for medicines used outside the terms of the licence to be included in Patient Group Directions (PGDs) when such use is justified by current best clinical practice and the direction clearly describes the status of the product.

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APPENDIX 2: CALCULATING THE LATEST MENSTRUAL CYCLE DAY ON WHICH AN INTRAUTERINE DEVICE (IUD) CAN BE INSERTED FOR EMERGENCY CONTRACEPTION



[NB. In women with variable cycle lengths, calculations should be based on the shortest cycle length. An IUD can be inserted on any menstrual cycle day if all episodes of unprotected sexual intercourse occurred within the previous 120 hours.]

APPENDIX 3: DEVELOPMENT OF CEU GUIDANCE

GUIDELINE DEVELOPMENT GROUP

Dr Louise Melvin – Director, Clinical Effectiveness Unit

Ms Julie Craik – Researcher, Clinical Effectiveness Unit

Dr Pauline McGough – Joint Clinical Director, Sandyford, Glasgow

Dr Najia Aziz – FSRH Education Committee representative; Speciality Trainee, Community Sexual & Reproductive Health, Ella Gordon Unit, St Mary's Hospital, Portsmouth

Dr Sharon Cameron – Consultant Gynaecologist, Family Planning and Well Woman Clinic, Chalmers Sexual Health Centre, Edinburgh

Dr Charlotte Cogswell – Associate Specialist, Department of Sexual and Reproductive Health, Llanyrafon House, Cwmbran, Gwent

Ms Caroline Donnelly – Practice Development Nurse, Sandyford, Glasgow

Dr Miranda Farmer – General Practitioner, Sex, Drugs and HIV Group of the Royal College of General Practitioners, Manchester Road Medical Centre, Knutsford, Cheshire

Dr Kate Guthrie – Consultant in Sexual and Reproductive Health, Conifer House, Hull

Mrs Lynn Hearton – FSRH Clinical Effectiveness Committee and user representative; Helpline and Information Services Manager, Family Planning Association, London

Dr Praveen Jayadeva – FSRH Clinical Standards Committee representative; Career Grade Trainee in Sexual and Reproductive Health, Lewisham Healthcare NHS Trust, London

Dr Noreen Khan – Consultant in Community Gynaecology Sexual and Reproductive Health, Palatine CASH Services, Manchester

Dr Paul O'Brien – Associate Specialist, Westside Contraceptive Services, St Charles Hospital, London

Miss Joanna Peacham – Community Pharmacist, Brocklehurst Chemists Ltd, Hull

Dr Rudiger Pittrof – Consultant in Community Sexual and Reproductive Health, Streatham Hill Health Centre, London

Dr Rashmi Ronghe – Subspecialty Trainee in Sexual and Reproductive Health, Sandyford, Glasgow

Professor James Trussell – Professor of Economics and Public Affairs, Princeton University and Visiting Professor, The Hull York Medical School, Hull

Dr Anne Webb – Consultant in Sexual and Reproductive Healthcare, Central Abacus, Liverpool

Administrative support to the CEU team was provided by **Ms Janice Paterson**.

Declared interests: Dr Sharon Cameron and Dr Anne Webb were principal investigators for an EC study funded by HRA Pharma.

INDEPENDENT PEER REVIEWERS

Professor PC Ho Pak Chung – Head of Reproductive Medicine, of Obstetrics and Gynaecology, Queen Mary Hospital, Hong Kong

Dr Clare Lipetz – Consultant Gynaecologist, Department of Sexual and Reproductive Health, Aneurin Bevan Health Board, Wales

CEU guidance is developed in collaboration with the Clinical Effectiveness Committee of the FSRH. The CEU guidance development process employs standard methodology and makes use of systematic literature review and a multidisciplinary group of professionals. The multidisciplinary group is identified by the CEU for their expertise in the topic area and typically includes health professionals working in family planning, sexual and reproductive health care, general practice, other allied specialities, and user representation. In addition, the aim is to include representatives from the FSRH Clinical Effectiveness, Education and Clinical Standards Committees and FSRH Council in the multidisciplinary group.

Evidence is identified using a systematic literature review and electronic searches are performed for: MEDLINE (CD Ovid version) (1996–2011); EMBASE (1996–2011); PubMed (1996–2011); The Cochrane Library (to 2011) and the US National Guideline Clearing House. The searches are performed using relevant medical subject headings (MeSH), terms and text words. The Cochrane Library is searched for relevant systematic reviews, meta-analyses and controlled trials relevant to emergency contraception. Previously existing guidelines from the FSRH (formerly the Faculty of Family Planning and Reproductive Health Care), the Royal College of Obstetricians and Gynaecologists (RCOG), the World Health Organization (WHO) and the British Association for Sexual Health and HIV (BASHH), and reference lists of identified publications, are also searched. Similar search strategies have been used in the development of other national guidelines. Selected key publications are appraised using standard methodological checklists similar to those used by the National Institute for Health and Clinical Excellence (NICE). All papers are graded according to the Grades of Recommendations Assessment, Development and Evaluation (GRADE) system. Recommendations are graded as in the table on the inside front cover of this document using a scheme similar to that adopted by the RCOG and other guideline development organisations. The clinical recommendations within this guidance are based on evidence whenever possible. Summary evidence tables are available on request from the CEU. An outline of the guideline development process is given in the table on the inside back cover of this guidance document.

Discussion Points for Emergency Contraception Guidance

The following discussion points have been developed by the FSRH Education Committee.

Discussion Points

- 1 Discuss the key aspects of counselling for quick starting hormonal contraception after supplying levonorgestrel (LNG) or ulipristal acetate (UPA).
- 2 What do you consider are the key aspects of counselling for a woman presenting for emergency contraception (EC) and taking a liver enzyme-inducing drug? How might you ensure that the counselling is undertaken in a consistent manner in your service?

Questions for Emergency Contraception Guidance

The following questions and answers have been developed by the FSRH Education Committee.

Indicate your answer by ticking the appropriate box for each question

	True	False
1 Administration of levonorgestrel (LNG) between 72 and 120 hours is outside the product licence.	<input type="checkbox"/>	<input type="checkbox"/>
2 Women should be advised to seek medical advice if they vomit within 3 hours of taking ulipristil acetate (UPA).	<input type="checkbox"/>	<input type="checkbox"/>
3 UPA is recommended for use more than once in a cycle if there has been unprotected sexual intercourse earlier (>120 hours) in the same cycle.	<input type="checkbox"/>	<input type="checkbox"/>
4 Women taking drugs that increase gastric pH should be advised not to use UPA.	<input type="checkbox"/>	<input type="checkbox"/>
5 The progestogen-only injectable can be started immediately after EC, if other methods are not appropriate or acceptable.	<input type="checkbox"/>	<input type="checkbox"/>
6 Following administration of UPA, women continuing to use a progestogen-only pill should be advised to use additional contraceptive precautions for 9 days.	<input type="checkbox"/>	<input type="checkbox"/>
7 UPA can be used in women using liver enzyme-inducing drugs.	<input type="checkbox"/>	<input type="checkbox"/>
8 In the event of further UPSI, additional EC is not required if UPSI occurs within 12 hours of LNG administration.	<input type="checkbox"/>	<input type="checkbox"/>
9 Following use of LNG, additional precautions (condoms or refraining from sex) should be advised for 7 days when continuing with Qlaira®.	<input type="checkbox"/>	<input type="checkbox"/>
10 Women choosing a copper-bearing intrauterine device (Cu-IUD) for EC who do not wish to continue can have the Cu-IUD removed if there has been UPSI in the 7 days prior to removal.	<input type="checkbox"/>	<input type="checkbox"/>

Answers

1 True	2 True	3 False	4 True	5 True	6 True
9 True	7 False	8 True	9 False	10 False	10 False

Auditable Outcomes from Emergency Contraception Guidance

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

Auditable Outcomes

- 1 What percentage of women presenting for emergency contraception (EC) had documentation that they were offered an intrauterine device (IUD) or the reason for not offering an IUD? (Target 100%)
- 2 Where an emergency IUD could not be inserted at the time of first presentation, what percentage of women were given interim emergency hormonal contraception? (Target 100%)
- 3 What proportion of women attending for EC had a discussion regarding future contraception? (Target 100%)
- 4 What proportion of women attending for EC were offered the opportunity for STI testing? (Target 100%)

STEPS INVOLVED IN THE DEVELOPMENT OF THIS GUIDANCE DOCUMENT

STEP	TIME TAKEN
<p>Formulation of key clinical questions by the Clinical Effectiveness Unit (CEU).</p> <p>Systematic literature review involving searching electronic, bibliographic databases by CEU researcher.</p> <p>Obtaining and reviewing copies of the full papers of all relevant publications identified through the searches.</p> <p>Formal, critical appraisal of key papers and development of short evidence tables.</p>	<p>This process must be completed in a maximum of 8 weeks.</p>
<p>Draft one guidance document is written providing recommendations and good practice points based on the literature review.</p>	<p>The CEU has overall responsibility for writing the guidance document. The multidisciplinary group and other peer reviewers should highlight inconsistencies, errors, omissions or lack of clarity.</p>
<p>Peer review by multidisciplinary group comprising stakeholders and including service user representation; representation from the FSRH Education Committee; and where possible representation from the FSRH Clinical Effectiveness Committee (CEC) and FSRH Council.</p>	<p>At this stage the CEU convenes a one-day meeting of the multidisciplinary group.</p>
<p>Preparation of draft two guidance document based on written comments from the multidisciplinary group.</p>	
<p>Peer review of draft two guidance document by the multidisciplinary group, the FSRH CEC and two independent peer reviewers.</p>	
<p>Preparation of draft three guidance document based on written comments from the peer reviewers.</p>	
<p>Peer review of draft three guidance document by multidisciplinary group and FSRH CEC.</p>	
<p>Preparation of draft four guidance document based on written comments from the peer reviewers.</p>	
<p>Peer review of draft four guidance document by multidisciplinary group using a consensus process.</p>	
<p>Preparation of draft five guidance document based on consensus scoring and comments of peer reviewers.</p>	
<p>Draft document posted on Faculty website for 1 month for public consultation.</p>	
<p>CEU's response to consultation approved by FSRH CEC. Final draft prepared.</p>	<p>Proofreading of the guidance document is then performed by three members of the CEU team independently and comments collated and sent back by the Unit Director.</p>
<p>The final guidance document is published by the FSRH.</p>	<p>PDF versions of the guidance document and the CEU's response to consultation comments are available on the FSRH website.</p>

COMMENTS AND FEEDBACK ON PUBLISHED GUIDANCE

All comments on published guidance can be sent directly to the Clinical Effectiveness Unit (CEU) at **ceu.members@ggc.scot.nhs.uk**. You will receive an automated acknowledgment on receipt of your comments. If you do not receive this automated response please contact the CEU by telephone [+44 (0) 141 232 8459/8460] or e-mail (**ceu.members@ggc.scot.nhs.uk**). The CEU is unable to 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.