



RICHTER GEDEON

**Escapelle 1500 microgram tablet
(levonorgestrel)
Brochure for healthcare professionals**

For further information and additional details on Escapelle, please see the Summary of Product Characteristics (SmPC).

Malta Medicines Authority Approval 18th Jan 2021

The following list of questions is designed to support you in providing information during consultation with women who require levonorgestrel-containing emergency contraception.

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I Definition

I.1. What is emergency contraception?

Emergency contraception (EC), also known as postcoital contraception refers to contraceptive methods that can be used after unprotected or inadequately protected act of sexual intercourse. It provides women with an additional opportunity to prevent unintended pregnancy following unprotected sexual intercourse (UPSI) or failure of a contraceptive method.

I.2. Why should emergency contraception be used only in case of emergency?

It is not as effective as a conventional regular method of contraception. It is an occasional method which does not provide ongoing contraception. It should in no instance replace a regular contraceptive method.

I.3. What methods of emergency contraception are available?^{1 2 3}

Emergency contraception methods include emergency contraceptive pills (ECPs) as well as insertion of a copper intrauterine device (Cu-IUD).

There are four types of emergency contraceptive pills:

- levonorgestrel-only pills (LNG EC),
- pills containing ulipristal acetate (UPA),
- combined oral contraceptive (COC) pills taken in specific amounts, also known as Yuzpe method,
- mifepristone, which is only approved for EC use in a few countries (e.g. Armenia, China, Russia, Vietnam).

The Cu-IUD is the most effective method of EC. Studies have demonstrated Yuzpe method to be less effective than LNG EC, additionally COCs are not labelled for EC use.

I.4. What is Levonorgestrel emergency contraceptive (LNG EC) pill and what is it used for?

It is an emergency contraceptive pill which safely prevents unintended pregnancy within 72 hours (three days) after UPSI or failure of a contraceptive method.

I.5. What brands of LNG EC pills are available around the world?

LNG EC pills are marketed under many brand names and authorised with the following strengths and formulation:

- two tablets of 0.75 mg: Rigesoft, Postinor(-2 / -Duo), Plan B, Escapel-2
- single tablet of 1.5 mg: Escapelle, Levonelle(-1 / 1500), Levonelle One Step, Ramonna, Upostelle, Postinor(-1 or One), Emergency Contraceptive Consilient, Take Action, Aftera, Evitta, Plan B One Step.

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II Indication, Posology

II.1. Who can use the emergency contraception pill?

Any woman or girl of reproductive age should be offered EC if there is a potential risk of an unintended pregnancy after UPSI.^{1 2} There is no relevant use of LNG for children of pre-pubertal age in the indication emergency contraception.⁴

II.2. Is there an age limit for taking LNG EC?

The only limit regarding age is pre-pubertal age as LNG EC is not indicated for use before the first menstrual bleeding (menarche). Thus LNG EC can be given to women under 16 years provided that she is judicious according to the health care professionals' assessment (usually pharmacists).^{3 4}

II.3. What should women be advised requiring LNG EC after delivery or abortion?⁵

Contraception should be considered from the first 21 days after giving birth (unless a woman is fully breastfeeding, amenorrhoeic and within 6 months of delivery). If UPSI occurs after this time, EC should be considered. LNG EC is safe to use from 21 days after childbirth.

Contraception is required from Day 5 after abortion, miscarriage, ectopic pregnancy or uterine evacuation for gestational trophoblastic disease. If UPSI occurs after this time, EC is required. Any method of EC can be safely used after an uncomplicated abortion.

II.4. Can it be used during breastfeeding?

According to the SmPC of Escapelle is secreted into breast milk (about 0.1 %). Potential exposure of an infant to LNG can be reduced if the breastfeeding woman takes the tablet immediately after feeding and avoids nursing at least 8 hours following LNG administration.

The FSRH Guideline Emergency Contraception states that use of LNG EC is not contraindicated during breastfeeding. In addition, some studies report no evidence of an adverse effect on the infant or on lactation.¹ For example, a study conducted in 2013 supports the safety of using LNG as an emergency contraceptive during lactation without the need for withholding breastfeeding for 8 hours. There were no reported side effects in infants exposed to LNG during breastfeeding and only transient, mild and infrequent side effects in mothers. Breastfeeding was reinitiated within less than 8 hours in 75% of the LNG group women. Adverse infant effects were rare.^{6 7}

II.5. In what situations should EC be used?²

Emergency contraception can be used in a number of situations following sexual intercourse. These include:

- When no contraceptive has been used.
- Sexual assault when the woman was not protected by an effective contraceptive method.

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- When there is concern of possible contraceptive failure, from improper or incorrect use, such as:
 - condom breakage, slippage, or incorrect use;
 - 3 or more consecutively missed combined oral contraceptive pills;
 - more than 3 hours late from the usual time of intake of the progestogen-only pill (minipill), or more than 27 hours after the previous pill;
 - more than 12 hours late from the usual time of intake of the desogestrel-containing pill (0.75 mg) or more than 36 hours after the previous pill;
 - more than 2 weeks late for the norethisterone enanthate (NET-EN) progestogen-only injection;
 - more than 4 weeks late for the depot-medroxyprogesterone acetate (DMPA) progestogen-only injection;
 - more than 7 days late for the combined injectable contraceptive (CIC);
 - dislodgment, breakage, tearing, or early removal of a diaphragm or cervical cap;
 - failed withdrawal (e.g. ejaculation in the vagina or on external genitalia);
 - failure of a spermicide tablet or film to melt before intercourse;
 - miscalculation of the abstinence period, or failure to abstain or use a barrier method on the fertile days of the cycle when using fertility awareness-based methods; or
 - expulsion of an intrauterine contraceptive device (IUD) or hormonal contraceptive implant.

II.6. When should it be taken under medical supervision only?

- If the woman has previously experienced an allergic reaction after taking a product containing LNG (it is not recommended to take this product).
- In case of liver or bowel disease (the efficacy of the product can be changed).
- If the product is taken together with certain medicines (e.g. barbiturates (including primidone), phenytoin, carbamazepine, herbal medicines containing *Hypericum perforatum* (St. John's Wort), rifampicin, ritonavir, and rifabutin may prevent LNG EC from working properly).
- LNG has no effect on an existing pregnancy; therefore, the use of LNG EC is not recommended if the woman is already pregnant.
- Use of the product is not recommended for women who are at risk of ectopic pregnancy (previous history of salpingitis or ectopic pregnancy). If this applies to a woman and/or she develops severe abdominal pain after taking LNG EC, it is important to see the doctor urgently.

II.7. How to take the single-dose and two-dose regimen of LNG EC?

LNG EC is authorised for 1.5 mg dose administered as either a single 1.5 mg dose or two 0.75 mg doses taken 12 hours apart or at the same time. The CMDh recommends taking the 0.75 mg tablets at once after UPSI instead of following the outdated frequency of administration (taken 12 hours apart).⁸

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A systematic review proved that emergency contraceptive regimen of single-dose LNG is not inferior in efficacy to the two-dose regimen. Single LNG 1.5 mg dose can substitute two 0.75 mg doses 12 hours apart. With either regimen, the earlier the treatment is given, the more effective it seems to be.⁹

II.8. Is physical examination or any lab tests needed to get emergency contraception?

No. However, if there is uncertainty about the timing of the unprotected intercourse or if the woman has had unprotected intercourse more than 72 hours earlier in the same menstrual cycle, conception may have occurred. In such case pregnancy testing prior to EC administration should be considered. On the other hand, a pregnancy test cannot reliably exclude pregnancy if there has been an episode of UPSI less than 3 weeks previously. If menstrual periods are delayed by more than 5 days or abnormal bleeding occurs at the expected date of menstrual periods or pregnancy is suspected for any other reason, pregnancy should be excluded before taking LNG EC.¹

II.9. Should woman wait 72 hours to take LNG EC?

The sooner LNG EC is taken, the more effective it is. Thus, it should be taken as soon as possible, preferably within 12 hours, and no later than 72 hours after unprotected intercourse.

Some studies demonstrated a trend towards increased pregnancy rates with increasing time between UPSI and LNG EC (up to 72 hours).¹⁰

II.10. What should be done in case of vomiting/diarrhoea?

If vomiting occurs within three hours of taking the tablet, another tablet should be taken immediately.

Three hours are usually enough for the total absorption of the tablet. Therefore, if vomiting occurs more than three hours after taking LNG EC, no need for another tablet.

In case of severe diarrhoea, an additional tablet is also recommended.

II.11. How often can LNG EC be used? / What happens if a woman takes LNG EC more than once in a cycle?

Repeated administration within a menstrual cycle is not advisable due to increased risk of side effects, such as menstrual irregularities, although LNG EC frequent use poses no known health risks. Available evidence indicates that LNG EC is safe and effective in preventing unwanted pregnancy over multiple uses and it could still reflect a reasonable risk-benefit for women who need to take it.^{11 12 13 14}

On the other hand, emergency contraceptives have higher possibility of failure compared to regular contraceptives; therefore, they are suitable only for occasional use after UPSI. Additionally, the efficacy decreases significantly after further acts of UPSI. Women should be advised that LNG will not provide contraceptive cover for subsequent acts of UPSI and that they will need to use contraception or refrain from sex to avoid further risk of pregnancy. LNG EC can be used more than once in the same cycle if this is indicated by further UPSI. Women

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who present for repeated courses of emergency contraception should be advised to consider long-term methods of contraception.²

II.12. If woman has several unprotected intercourses within 72 hours of taking LNG EC will she be still protected against unwanted pregnancy?

If another unprotected intercourse takes place after the use of LNG EC, the tablet will not provide contraceptive cover and there is the risk of pregnancy again. Ongoing contraception will need to be used or refraining from sex to avoid further risk of pregnancy. After using emergency contraception, it is recommended to use a local barrier method (e.g. condom, diaphragm, spermicide, cervical cap) until the next menstrual period starts. Furthermore, use of LNG does not contraindicate the continuation of regular hormonal contraception. If the woman is already using regular oral contraceptive, she can continue to take this at the regular times. She also should be advised to use additional contraceptive precautions for 7 days (2 days for POP, 9 days for Qlaira).¹

No data were identified regarding a minimum time interval between successive LNG treatments. However, efficacy was examined when further acts of unprotected intercourse occurred after using LNG EC. 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.^{15 16 17 18}

The general advice is to use barrier contraception (such as condom or diaphragm) after using LNG EC or consult a doctor for a long-term contraceptive method.

III Concomitant medical condition, concomitant drug use

III.1. What should women with polycystic ovarian syndrome (PCOS) requiring LNG EC be advised?

According to the SmPC of Escapelle, LNG EC can be used within 72 hours of UPSI, at any time during the menstrual cycle unless menstrual bleeding is overdue. As women with polycystic ovarian syndrome usually do not have regular periods, pregnancy should be excluded before taking the tablet. As there is no information about using LNG EC in cases of polycystic ovarian syndrome, medical consultation is required and alternative non-hormonal emergency contraception (i.e. Cu-IUD) might be considered.

III.2. May women using other contraception take LNG EC? What to recommend woman who use regular oral contraceptives and forgot to take the pill in two to three days in a row?

The use of LNG EC does not contraindicate the continuation of regular hormonal contraception. If the woman is already using regular oral contraceptive, she can continue to take this at the regular times.

Following administration of LNG EC, women continuing to use a hormonal method of contraception should be advised to use additional contraceptive precautions (barrier method) until the next menstrual period starts.¹

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III.3. How should LNG EC be taken in case of HIV-infected patients?

For women who have used enzyme-inducing drugs in the past 4 weeks and need emergency contraception, the use of non-hormonal emergency contraception (i.e. a Cu-IUD) should be considered. Taking a double dose of LNG (i.e. 3mg within 72 hours after the unprotected intercourse) is an option for women who are unable or unwilling to use a Cu-IUD, although this specific combination (a double dose of LNG during concomitant use of an enzyme inducer) has not been studied.¹⁹

III.4. Can other medicines change the effect of LNG EC (i.e. doxycycline, rifampicin, carbamazepine, levothyroxine)?

The metabolism of LNG is enhanced by concomitant use of liver enzyme inducers, mainly CYP3A4 enzyme inducers. Concomitant administration of efavirenz has been found to reduce plasma levels of LNG (AUC) by around 50 %. Drugs suspected of having similar capacity to reduce plasma levels of LNG include barbiturates (including primidone), phenytoin, carbamazepine, herbal medicines containing *Hypericum perforatum* (St. John's Wort), rifampicin, ritonavir, rifabutin, and griseofulvin.

The metabolism of LNG EC is increased during and for 28 days after use of drugs that induce liver enzymes. Women who have used enzyme-inducing drugs during the last 4 weeks and need emergency contraception are recommended to use a non-hormonal EC, i.e. Cu-IUD. If they are unable or unwilling to use Cu-IUD, they could take a double dose of LNG (i.e. 2 tablets of 1.5 mg taken together as soon as possible within 72 hours).¹⁹

III.5. Does St John's Wort (*Hypericum perforatum*) interact with LNG EC?

Yes, herbal medicines containing St. John's Wort interact with LNG EC. St. John's Wort has a liver enzyme (cytochrome P450) inducing effect which results in reduced efficacy of emergency hormonal contraceptives.

Therefore, women, who require emergency contraception whilst using St. John's Wort or have used during the last 28 days, should be advised to use a non-hormonal EC, i.e. Cu-IUD. Taking a double dose of LNG (i.e. 3 mg within 72 hours after the UPSI) is an option for women who are unable or unwilling to use a Cu-IUD.

III.6. Does LNG EC have an effect on the metabolism of cyclosporin?

Medicines containing LNG may increase the risk of cyclosporin toxicity due to possible inhibition of cyclosporin metabolism. However, women on cyclosporin therapy are under medical supervision. Sex steroid hormones may increase plasma levels of cyclosporin leading to toxic effects. The mechanism of the increased cyclosporin concentrations is unclear but might be related to an inhibition of hepatic drug metabolism. The mechanism of the hepatotoxicity is unknown. Thus, it cannot be excluded that medicines containing LNG may increase the risk of cyclosporin toxicity due to possible inhibition of cyclosporin metabolism.^{20 21}

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IV Efficacy

IV.1. How does LNG EC prevent pregnancy?

At the recommended regimen, LNG works mainly by preventing or delaying ovulation. Research also indicates that there may be other mechanisms of action in play besides interruption of ovulation. Additional mechanisms of action include preventing fertilization of an egg by affecting the cervical mucus or the ability of sperm to bind to the egg.

LNG is not effective once the process of implantation has begun. It is not an “abortion pill” as it does not interrupt a pregnancy.² Error! Bookmark not defined.³³

IV.2. How effective is it?

Emergency contraception can be very effective especially if the emergency contraceptive pill is taken soon after unprotected sex. Efficacy appears to decline with time after intercourse.

However, emergency contraception does not prevent a pregnancy in every instance. The fact that LNG EC tablets have no proven effect on implantation explains why they are not 100 % effective in preventing pregnancy and are less effective the later they are taken. If there is uncertainty about the timing of the unprotected intercourse or if the woman has had unprotected intercourse more than 72 hours earlier in the same menstrual cycle, conception may have occurred. LNG administration following the second act of intercourse may therefore be ineffective in preventing pregnancy. If menstrual periods are delayed by more than 5 days or abnormal bleeding occurs at the expected date of menstrual periods or pregnancy is suspected for any other reason, pregnancy should be excluded.

It was estimated from the results of an earlier clinical study that 0.75 mg of levonorgestrel (taken as two 0.75 mg doses with a 12-hour interval) prevents 85% of expected pregnancies. Efficacy appears to decline with time of start of treatment after intercourse (95% within 24 hours, 85% 24-48 hours, 58% if started between 48 and 72 hours).¹⁴

Results from another randomised, double-blind clinical study showed 1.34% (16/1198) pregnancy rate with two 0.75mg tablets of LNG taken at the same time (and within 72 hours of unprotected sex) compared with 1.69% (20/11832) when two 0.75mg tablets were taken 12 hours apart.¹⁵

Meta-analysis on three WHO studies showed that the pregnancy rate of LNG is 1.01% (59/5863) which means it could prevent pregnancy in 99% of situations.²²

IV.3. When can a woman take a pregnancy test and be sure that it is accurate?

When the next period has occurred and it seemed like a normal period, the unintended pregnancy is likely to be prevented. If there is any doubt about whether menstruation has occurred, a pregnancy test should be performed ≥ 3 weeks after UPSI has occurred. A pregnancy test cannot reliably exclude pregnancy if there has been an episode of unprotected sex less than 3 weeks previously.¹

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IV.4. Does body weight influence the efficacy of LNG EC?

There is limited and inconclusive data on the effect of increasing body weight/BMI on the contraceptive efficacy of LNG EC. In three WHO studies²² no trend for a reduced efficacy with increasing body weight/BMI was observed, whereas in two other studies (Creinin et al., 2006²³ and Glasier et al., 2010²⁴) a reduced contraceptive efficacy was observed with increasing body weight or BMI. Both meta-analyses excluded intake later than 72 hours after unprotected intercourse (i.e. off-label use of LNG EC) and women who had further acts of unprotected intercourse.

In 2014 the Committee for Medicinal Products for Human Use (CHMP) after reviewing all data on the efficacy of emergency contraceptives containing levonorgestrel (LNG) or ulipristal acetate (UPA), with regards to the relation of body weight/body mass index (BMI) of women has stated that the limited data available do not support the conclusion that the contraceptive effect is reduced in women with high bodyweight. As a conclusion, no adjustment of the dose has been recommended at that stage.²⁵

A recently published analysis of four WHO studies (above mentioned three plus one) showed that there was an increase in pregnancy rates among obese women ($BMI \geq 30 \text{ kg/m}^2$), but it was influenced by pregnancies all coming from one study site in Nigeria. Furthermore, data were collected up to 120 hours of UPSI which could have an impact on the pregnancy rates. Delay in drug intake is significantly associated with reduced efficacy of LNG EC and the product is licensed to use within 72 h following UPSI. According to the conclusion of this analysis provision of LNG should not be restricted in any weight or BMI category based on these data.²⁶ Recent pharmacokinetic results suggest that BMI could have an impact on serum concentration of LNG, however direct conclusion about the relationship between efficacy and body weight or BMI cannot be drawn. Current PK data are considered not to be an evidence for impaired efficacy, as these studies did not measure endpoints more directly related to effectiveness (e.g. ovulation or pregnancy).^{27 28} Recent safety data retrieved from Gedeon Richter Plc.'s validated safety database does not suggest an increased risk for LNG EC failure resulting unwanted pregnancy in overweight/obese women.

In all women, emergency contraception should be taken as soon as possible after unprotected intercourse, regardless of the woman's body weight or BMI.

IV.5. How does EC differ from abortion?

EC is not the same as early medical abortion. LNG EC can only prevent pregnancy before the implantation of fertilised egg. It is not effective once the process of implantation has begun. Medical abortion is an option for women in the early stage of an established pregnancy but requires a different drug from LNG.

LNG is not an 'abortion pill' as it cannot terminate pregnancy. Evidence suggests that LNG EC does not interrupt an established pregnancy or harm a developing embryo.^{29 30 27}

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V Safety

V.1. Are there any contraindication?

Yes, the only contraindication is hypersensitivity to the active substance or to any of the excipients.

There are no medical contraindications to the use of LNG EC.²⁷

V.2. When is the next period expected after taking the morning after pill?

After LNG intake, menstrual periods are usually normal and occur at the expected date. Some women might experience cycle disturbances. For instance, intermenstrual bleeding or spotting and/or their next period may occur earlier or later than expected by a few days. Clinical experiences and studies as well show that menstrual cycle length may be shortened or lengthened and the period of the bleeding also could be shorter, longer, and/or stronger by using emergency contraceptives. At the same time changes experienced in the menstrual cycle are transient and resolve, probably in the next cycle. However, if the next period is more than five days late or abnormal bleeding occurs, seeking medical advice is recommended to exclude pregnancy.

After taking LNG EC other local barrier contraceptive methods (e.g. condom) should be applied until the next menstrual period starts. Following EC administration women using hormonal contraception should be advised to rule out pregnancy in case of missed withdrawal bleeding in the next hormone-free period.³¹

V.3. What is the VTE risk of LNG EC?

Based on the scientific literature, there is no evidence to suggest that use of progestogen-only emergency contraception is associated with an increased risk of venous thromboembolism. Such risk is mainly associated with the oestrogen component and the regular dosage of regularly (daily) used COCs. On the other hand, studies showed that progestogen component in combined hormonal contraceptives (CHCs) also has some impact on thromboembolic risk, but LNG is a second-generation progestogen, which is the safest choice for hormonal contraception regarding this issue.³²

According to Medical Eligibility Criteria for Contraceptive Use published by WHO, women with history of severe cardiovascular disease, including ischaemic heart disease, cerebrovascular attack, or other thromboembolic conditions, can generally use LNG for emergency contraception. This is also supported by UK Medical Eligibility Criteria which says that venous thromboembolism (including pulmonary embolism) is a condition where the advantages of using LNG EC method generally outweigh the theoretical or proven risks. The duration of use of emergency contraception is less than that of regular use of COCs or progesterone-only pills (POPs) and thus would be expected to have a lower risk for adverse health outcomes.⁷

Emergency oral contraceptives should be administered only once in a cycle instead of continuous long-term usage, which is responsible for the effect on haemostatic changes. The amount of the active hormone in one course of LNG emergency contraceptive pills is less than half of that found in a cycle of most common contraceptive pills. WHO Statement published in

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2011 also supported the above-mentioned findings that no such risk is associated with LNG-containing emergency contraceptive pills.^{33 34}

Additionally, it is important to highlight that the associated risk of a venous thrombosis with pregnancy is higher than the risk in women who use emergency hormonal contraceptive method.

V.4. Are there any serious side effects of using LNG EC?

There are no serious short or long-term side effects when taking LNG EC.

There were three reports of serious adverse events during one of the WHO trials (von Hertzen et al. 2002) in the LNG groups: one ectopic pregnancy that required surgical treatment (two-dose LNG group); one case of pyelonephritis and one of a ruptured corpus luteum cyst that required surgery between treatment and follow-up (single-dose LNG group). Except ectopic pregnancy, there is no evidence of any relation between these events and trial treatment. During other WHO sponsored trials (Arowojolu et al. 2002; Dada et al. 2010) there was no report about serious adverse events. The observed side effects were minimal and all were well-known from the product profile.^{17 18 18}

V.5. What are the common side effects?

Headache, nausea and altered bleeding patterns are side effects very common to LNG EC use and have been reported in around 10 % of users. After taking LNG EC, bleeding patterns may be temporarily disturbed, but most women will have their next menstrual period within 7 days of the expected time. Irregular menstruation and delay of menses more than 7 days are among the common side effects. However, in case of any serious or unusual event (e.g. more than 5 days delay of the next period) immediate gynaecologic examination and pregnancy test should be performed,

Other reported side effects of LNG EC include lower abdominal pain, fatigue, breast tenderness, dizziness, diarrhoea and vomiting. If a woman vomits within three hours of taking LNG EC, she should take a further dose as soon as possible.

V.6. Will use of LNG EC affect future fertility?

LNG EC use increases the possibility of cycle disturbances which can sometimes lead to earlier or later ovulation date. These changes can result in modified fertility date. After treatment with LNG EC a rapid return to fertility is expected as EC does not affect the long-term fertility.^{1 33}

V.7. Can LNG EC harm a foetus or cause birth defects if taken by a woman who is already pregnant?

Although there is no evidence that LNG could cause harm to either a pregnant woman or her foetus if pregnancy occurs despite use of LNG EC, the tablet should not be taken in case of a confirmed pregnancy. LNG EC can prevent unintended pregnancy but does not interrupt one. However, it is important to seek medical examination in order to exclude ectopic pregnancy.

Clinical studies have shown that no foetal malformations or abnormalities of the foetal development were found in women exposed to LNG EC during pregnancy. Failure of LNG as

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an emergency contraceptive was not associated with an increased risk of major congenital malformations, pregnancy complications or any other adverse pregnancy outcomes.^{29 33 7 35 36}

V.8. Does LNG EC pill increase the risk of having an ectopic pregnancy?

The absolute risk of ectopic pregnancy is likely to be low, as LNG prevents ovulation and fertilisation. Ectopic pregnancy may continue, despite the occurrence of uterine bleeding. Therefore, LNG is not recommended for patients who are at risk of ectopic pregnancy (history of salpingitis or ectopic pregnancy).

The WHO Fact Sheet in 2010 stated that LNG EC does not increase the risk of ectopic pregnancy. A comprehensive search of the published literature evaluating 23 studies of LNG EC use in 216 pregnancies found that fewer than 1% (0.9%) were ectopic, which is less than or comparable to general ectopic pregnancy rates. A Cochrane review identified only five cases of ectopic pregnancy amongst over 55 000 oral EC users included in their review. Absolute numbers of ectopic pregnancies remain very small and LNG EC reduces absolute risk of ectopic pregnancy by reducing pregnancy risk overall.^{1 10 7 33}

V.9. Do women need to see a healthcare professional after LNG EC administration?

- Women should be advised to seek medical advice if they vomit within 3 hours of taking LNG EC.
- Women should be advised to make a medical appointment to initiate or adopt a method of regular contraception.
- If the next menstrual period is delayed with more than five days or abnormal bleeding occurs, seeking medical advice is recommended to exclude pregnancy.
- If no withdrawal bleed occurs in the next pill-free period following the use of LNG EC after regular hormonal contraception, pregnancy should be ruled out.
- If pregnancy occurs after LNG EC intake, the possibility of an ectopic pregnancy should be considered.

V.10. Does LNG EC protect against STIs?

Use of emergency contraception does not replace the necessary precautions against STIs.* Male and female condoms, when used correctly and consistently, offer an effective protection against STIs, including HIV.^{1 7}

VI Pharmacokinetics

VI.1. Can food or alcohol affect LNG EC?

The absorption of the drug is not affected significantly if it is taken before or after the meal, therefore LNG EC can be taken anytime irrespective to the time of meals.

Data is lacking as food-drug interactions were not investigated in the clinical trials. Related information is neither included in the SmPCs of LNG containing COCs. Relevant data cannot be found in the scientific literature either.

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VI.2. How long does it take for the LNG EC to be eliminated from the body?

After reaching maximum serum levels, the concentration of LNG decreases with a mean elimination half-life of about 26 hours.

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Healthcare Professionals are asked to report any suspected adverse reactions.

Suspected adverse reactions and medication errors should be reported.

Report forms can be downloaded from:

www.medicinesauthority.gov.mt/adrportal

and sent to:

E: postlicensing.medicinesauthority@gov.mt or

E: pv@alfredgera.com

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