

## Emergency contraception: latest changes

Subsequent to the 2002 World Health Organization (WHO) study,<sup>1</sup> the licence for levonorgestrel emergency contraception (EC) in the UK has changed. It now states: 'Two tablets should be taken together, as soon as possible, preferably within 12 hours, and no later than 72 hours after unprotected intercourse'. This simplification should reduce the risk of forgetting or delaying the second dose. Although the initial WHO study<sup>2</sup> that led to the wide licensing of levonorgestrel as the product of choice for EC demonstrated a link between efficacy and length of time since unprotected sexual intercourse (UPSI), this has not been confirmed in any other study, including the latest study from the WHO.<sup>1</sup> There is no harm in suggesting the tablets are taken in the first 12 hours but efficacy is not necessarily reduced as time goes on. In fact the latest study showed that levonorgestrel 1.5 mg is still effective up to 5 days after UPSI. Similar results were obtained in another study that examined combined estrogen-progestogen EC up to 5 days after UPSI.<sup>3</sup> The numbers of women who took EC between 72 and 120 hours was small, so it is imperative that everyone counselling a woman in this situation also mentions the intrauterine device (IUD) as this is known to be more effective at all stages and can be fitted up to 5 days after the earliest predicted ovulation.

In the UK there are two products licensed for EC. They are pharmacologically identical but the first is a pharmacy (P) product and the second a prescription-only medicine (POM). The licence differences are small but significant, in as much as the P product is not recommended for those with certain absorption problems, those taking potentially interacting drugs or patients aged under 16 years, without medical supervision. Also the P product costs £24, the POM £5.50. In France, levonorgestrel EC is available free to women under 18 years in every pharmacy and via school nurses. The US Federal Drug Administration is considering making levonorgestrel EC completely over the counter.

The new summary of product characteristics includes the statement: 'If pregnancy occurs after treatment the possibility of an ectopic pregnancy should be considered. The absolute risk of ectopic pregnancy is likely to be low, as Levonelle®/Levonelle-2® prevents ovulation and fertilisation. Ectopic pregnancy may continue, despite the occurrence of uterine bleeding'. This was included at the request of the Medicines and Healthcare products Regulatory Agency despite the absence of any new data. An editorial in this Journal<sup>4</sup> reported some cases of ectopic pregnancy after EC but evidence shows that the absolute risk of ectopic pregnancy is lower when conceiving after EC than without.<sup>5</sup> If there is any suggestion of ectopic pregnancy, this should be considered whether or not the woman used EC.

EC, mostly levonorgestrel only, is licensed in many countries, but not all. Where there is not a dedicated product it is still possible to use other contraceptives, but it is important to use the correct dosage of hormones. The website [www.not-2-late.com](http://www.not-2-late.com) gives a list of what combinations can be used in most countries. The site is available in many languages and is sited at Princeton University, New Jersey, NY, USA. Increasing availability of EC, be it hormonal or IUD, assists in reducing the risk of unplanned and unwanted pregnancy, which is especially important in countries where abortion is not available or very restricted, as in the Republic of Ireland and Northern Ireland.

EC can work at various levels, including preventing ovulation, fertilisation or implantation. In a judicial review

of EC in 2002, a pregnancy is not recognised to exist legally until implantation is completed.<sup>6</sup> EC has no effect on an implanted pregnancy and therefore does not induce abortion. If a woman believes that life begins when the egg is fertilised she may not wish to use EC. If the clinician has a personal issue about providing EC, they owe a duty of care to the client to refer her immediately to a service where it will be provided.

EC is available in the UK from many venues. Apart from traditional sources of contraception, it may be obtained from walk-in centres (which, in Liverpool, issued EC over 3000 times last year) and many genitourinary medicine and accident and emergency departments. Nurses and pharmacists in many areas are issuing EC via Patient Group Directions (PGDs) at no cost to the client and with no age limits. PGDs provide for onward links where appropriate.

Pregnancy is not the only consequence of UPSI that may be unwanted. Sexually transmitted infections (STIs) are on the rise in the UK. This is probably due to a combination of a genuine rise in prevalence and also an improvement in tests and testing sites available, especially for the most common STI, *Chlamydia trachomatis*. Overall the highest prevalence is in men and women under 25 years but amongst requesters of EC the prevalence remains high up to the age of 30 years.<sup>7</sup> A second-generation, transcription-mediated application test has high sensitivity for chlamydia and gonorrhoea on a first-catch urine sample, which does not always need refrigeration, as well as from self-taken swabs. The possibility of STI should be raised at every EC consultation and testing or effective onward referral offered where appropriate. Ongoing contraception needs to be considered at each occasion. Where EC is used because of missed pills, the packet should be continued; contraceptive cover will be restored as with any missed pills. If the woman wishes to commence pills or an injectable method this can be done at the same visit; although she must be made aware that as hormonal EC can fail, she must have a pregnancy test if she does not have a totally normal period within 3 weeks. Contraceptive cover will be achieved no later than 7 days after starting the ongoing hormonal method. There is no reason why an implant cannot be inserted at the same time, although due to the higher upfront cost many clinicians may prefer to wait until pregnancy is excluded. An IUD covers both immediate and ongoing contraception and, if necessary, the risk of infection can be reduced by using prophylactic antibiotics. A levonorgestrel-releasing intrauterine system does not work as EC and insertion is best delayed until a pregnancy can be definitely excluded.

EC is usually sought after the event although we know that advance issue of EC does not lead to increased use<sup>8</sup> and staff and clients support it.<sup>9</sup> Carrying an umbrella in the British climate is considered sensible, not a wish for rain; maybe having EC available in advance should also be considered sensible and part of 'being prepared'.

In conclusion, the use of hormonal EC is very simple and there are no medical contraindications to its use. However, there are other important issues to consider and improving access to all areas of sexual health still takes time and dedication.

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## Off-licence prescribing in contraception

Did you realise that suggesting a tricycle pill regimen to a woman suffering from dysmenorrhoea, or the use of the Mirena® intrauterine system as part of hormone replacement therapy (HRT), is outside the product licences for these particular medicines? In everyday practice we use licensed products in an unlicensed way but give little thought to the consequences of our actions. What guidance is in place to provide protection for the health professional? How do we ensure safe prescribing?

It is unlikely that we will prescribe an unlicensed medicine in sexual and reproductive health unless we are involved in research. To ensure that medicines are safe and effective, the manufacture, sale or supply of medicinal products is controlled by national and European Economic Community (EEC) (now European Community, EC) legislation.<sup>1,2</sup> Therefore all medicines available in the UK are issued with a Marketing Authorisation (commonly known as a product licence).

If licensed medicines are being used in an 'off-licence' situation the manufacturer cannot generally be held liable for any problems that may arise from such use. Legal liability is therefore likely to rest more heavily with the prescriber and their employer, normally a National Health Service (NHS) Trust.<sup>3</sup> There are many occasions in the field of contraception when licensed medicines are justifiably prescribed for unlicensed indications or to groups of patients not covered by the Marketing Authorisation (Table 1). Very often the off-licence use of a medicine for another therapeutic indication becomes standard practice and it is only when Patient Group Directions (PGDs) are being developed that this comes to light. An example of this is the use of a hormonal contraceptive to treat dysmenorrhoea rather than for birth control.

Many nurses and pharmacists now supply and administer medicines under guidance of a PGD. These are written documents that cover the supply and/or administration of prescription-only medicine by certain classes of health professionals to benefit patient care without compromising safety. PGDs have to be authorised by a Primary Care Trust, NHS Trust or Health Authority and be signed by a doctor or dentist, and a pharmacist who should be involved in their development, in order to be valid.<sup>4</sup> Nurse prescribers are able to prescribe a limited number of medicines. However, nurses can only issue/prescribe licensed medicines for licensed indications.

A number of recommendations for prescribing drugs off-licence have been suggested by the Newcastle Drug and Therapeutics Committee.<sup>5</sup> These recommendations are worth disseminating more widely to ensure safe prescribing.

1. A licensed medicine should not be used outside the terms of its product licence unless its use can be justified; usually one or more of the following scenarios apply:

- The particular unlicensed use is well established, e.g. endorsed by a responsible body of professional opinion such as the Faculty of Family Planning and Reproductive Health Care.
- No product that is licensed for the purpose is available.
- The unlicensed use of a medicine is likely to offer a significant clinical (medical or pharmaceutical) advantage compared with a product licensed for the purpose.

2. Depending on the likely frequency of use and the possible level of risk associated with the unlicensed use of a medicine, the clinician wishing to prescribe the medicine should consider:

- Discussing the matter with a senior colleague, e.g. in difficult clinical circumstances where treatment options are limited and a second opinion is warranted.
- Obtaining clearance for its regular use through the appropriate local drug and therapeutics committee.
- Discussing the unlicensed use and possible risks involved with the patient and/or relative(s), and in some (high-risk) cases obtain their informed consent. This should be recorded in the clinical records together with the points discussed.

**Table 1** Common examples of using licensed products in an unlicensed way

1	Use of the levonorgestrel intrauterine system as the progestogen component of hormone replacement therapy.
2	Use of emergency hormonal contraception beyond 72 hours and up to 120 hours after the earliest time of unprotected sexual intercourse.
3	Use of emergency hormonal contraception more than once in a cycle.
4	Use of 'add-back' oestrogen together with Depo-Provera® to treat hypo-oestrogenic symptoms or management of bleeding problems.
5	Use of Depo-Provera or a combined oral contraceptive (COC) to alleviate menstrual cycle problems such as Mittelschmerz pain and dysmenorrhoea.
6	Advising the use of more than one pill per day when enzyme-inducers are being used with a COC; or two progestogen-only pills daily in the obese young woman.
7	Omission or shortening of the pill-free interval when taking a COC.
8	Use of copper intrauterine devices for longer than their licensed time, particularly after the age of 40 years.