

Bayer HealthCare
Bayer Schering Pharma



Your ref:
Our ref: SC/EB

Date: 5th February 2008

Dear Mr Taylor

Thank you for your e-mail.

Our Summary of Medical Product Characteristics (SmPC) for Levonelle[®] 1500 (levonogestrel) states that "Levonelle 1500 is not recommended in children" and that "very limited data are available in women under 16 years of age".

It also states that "Levonelle 1500 is not as effective as a conventional regular method of contraception and is suitable only as an emergency measure. It should in no instance replace a regular contraceptive method. Women who present for repeated courses of emergency contraception should be advised to consider long-term methods of contraception".

Nurses and other health care professionals (such as pharmacists) have been allowed to supply Levonelle 1500 to under 16 year old girls by way of patient group directions (PGDs) for some time. However introduction was not universal and the initiation date varied across Primary Care Trusts.

Patient group directions have been developed to allow nurses and other health care professionals to supply and administer medicines.

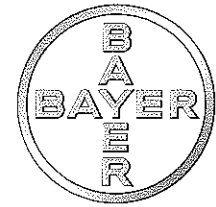
A PGD is developed locally by doctors, pharmacists and other health care professionals and must meet certain legal criteria. Each PGD must be signed by a doctor (or dentist) and a pharmacist, and approved by an appropriate body, usually a primary care NHS trust (on a local level). A PGD will lay down the clinical situations in which the medicine may be supplied; the clinical criteria under which a person is eligible for treatment; circumstances under which further advice should be sought from a doctor; any specific warnings such as side effects; necessary follow-up arrangements; arrangements for referral for medical advice; and details of the record of supply and administration. Medicines used outside the product licence can be included in PGDs provided such use is justified by current best practice.

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If a young person (aged <16 years) requests emergency contraception, under the Fraser ruling (Department of Health guidelines specifically relating to contraceptive provision for those aged under 16 years) a healthcare professional may give advice and treatment without parental consent, provided that he/she has confirmed that the young person is competent and that the Fraser criteria (the advice has been understood, the young person has been advised to inform her parents, the action is in their best interest) are met ¹

With regard to your question, would there be an increased risk for ectopic pregnancies? We currently have the following advice in our SmPC: If pregnancy occurs after treatment with Levonelle 1500, the possibility of an ectopic pregnancy should be considered. The absolute risk of ectopic pregnancy is likely to be low, as Levonelle 1500 prevents ovulation (the release of an egg) and fertilisation.

Very limited data derived from the scientific literature do not point towards an increased risk of ectopic pregnancies in association with levonogestrel emergency contraception in adolescents.

Risk of ectopic pregnancies in association with Levonelle/Postinor:

Several case reports on ectopic pregnancies related to the failure of using levonogestrel as emergency contraception have been published^{2 3}, but all these cases occurred in female patients over 16 years of age

In the large WHO multicenter study⁴ on emergency contraception one case of an ectopic pregnancy in an adult female patient using levonogestrel emergency contraception was reported. This patient was randomized in the single dose levonogestrel group (1.5 mg levonogestrel, n = 1379). In the two-dose levonogestrel group (0.75 mg levonogestrel, 12 hours apart, n = 1356) and in the mifepristone group (n = 1356) no ectopic pregnancies occurred.

¹ Journal of Family Planning and Reproductive Healthcare 2006; 32(2):121-128

² Sheffer-Mimouni G, Pazner D, Maslovitch S, Lessing JB, Gamzu R. Ectopic pregnancies following emergency levonogestrel contraception. Contraception. 2003 Apr;67(4):267-9

³ Jian Z, Iinan C. Ectopic gestation following emergency contraception with levonogestrel. The European Journal of Contraception and Reproductive Health Care 2003;8:225-228

⁴ von Herzen H, Piaggio G, Ding J et al for the WHO Research Group on postovulatory Methods of Fertility Regulation. Low dose mifepristone and two regimens of levonogestrel for emergency contraception: a WHO multicentre randomised trial. Lancet 2002;360:1803-10.

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These data derived from the WHO-study confirm the common estimation that the risk of ectopic pregnancies related to levonogestrel emergency contraception is to be considered low.

Experience with Levonelle/Postinor in adolescents

In a single-centre, open-label observational trial Harper et al⁵ evaluated 52 adolescent females aged 13-16 regarding the tolerability of 0.75 mg levonorgestrel emergency contraception (Plan B[®] Gedeon Richter). The adolescents tolerated the medication well, experiencing transient side effects, no case of ectopic pregnancy was reported.

In a clinical study by Kolarov et al⁶ involving 49 girls with regular menstrual cycle at the age between 15 and 19, 0.75 mg levonogestrel were administered within 72nd hour, repeated after 12 hours due to unprotected or faulty protected sexual intercourse. One intrauterine pregnancy was registered of a girl with first intake at the 67th hour with a pregnancy rate of 2.0%. No ectopic pregnancy could be diagnosed.

In answer to your question who would be accountable for any problems that occur:

Patient safety is of paramount importance to us. We have a comprehensive system in place to collate and investigate reports of any adverse events suffered by patients taking any of our products which are regularly reviewed.

I hope this information has helped you. If you have any other queries please don't hesitate to contact us.

Kind regards

Yours sincerely

Dr Sarah Cross
**Head of Medical
Women's Health**

⁵ Harper CC, Rocca CH, Darney PD et al. Tolerability of levonorgestrel emergency contraception in adolescents. Am J of Obstetrics and Gynecology 2004, 191:1158-63

⁶ Kolarov G, Dimitrov A, Cherev I, Kamernov Z, Sirakov M, Nikolov A. Emergency contraception with levonorgestrel for teenagers--efficacy, tolerability, and level of information awareness. Akusherstvo i ginekologijia 2004 VOL: 43 (1), P: 26-31