Complete Summary

GUIDELINE TITLE

The use of contraception outside the terms of the product licence.

BIBLIOGRAPHIC SOURCE(S)

Penney G, Brechin S, Allerton L. The use of contraception outside the terms of the product licence. J Fam Plann Reprod Health Care 2005 Jul;31(3):225-41; quiz 242. [150 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory information has been released.

On April 7, 2005, the U.S. Food and Drug Administration (FDA) asked manufacturers of non-prescription (over the counter [OTC]) non-steroidal anti-inflammatory drugs (NSAIDs) to revise their labeling to include more specific information about potential gastrointestinal (GI) and cardiovascular (CV) risks, and information to assist consumers in the safe use of the drugs. See the FDA Web site for more information.

Subsequently, on June 15, 2005, the FDA requested that sponsors of all NSAIDs make labeling changes to their products. FDA recommended proposed labeling for both the prescription and OTC NSAIDs and a medication guide for the entire class of prescription products. See the FDA Web site for more information.

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SCOPE

DISEASE/CONDITION(S)

- Unintended pregnancy
- Menorrhagia
- Dysmenorrhea
- Menstrual bleeding abnormalities
- Acne vulgaris
- Hypo-oestrogenism

GUIDELINE CATEGORY

Counseling
Evaluation
Prevention

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Nurses
Patients
Pharmacists
Physicians

GUIDELINE OBJECTIVE(S)

- To provide information for clinicians and women considering the use of contraception outside the terms of the product license
- To provide recommendations on prescribing outside the terms of product licenses and support for clinicians and women using contraceptive methods outside their licensed indications

TARGET POPULATION

Women using contraceptive methods outside their licensed indications

INTERVENTIONS AND PRACTICES CONSIDERED

1. Taking appropriate clinical history and assessing a woman's priorities and preferences
2. Developing Patient Group Directions (PGDs)
3. Counseling women about using contraceptive methods outside product licence, including
    - When to start hormonal contraception (combined hormonal methods, progestin-only pill [POP], implants, injectables, levonorgestrel-releasing intrauterine system [LNG-IUS]) and when to start non-hormonal contraception (copper-bearing intrauterine contraceptive device [IUD], condoms)
    - What to do if hormonal contraception is late or missed
    - When the dose of oral contraceptives is increased
    - When the hormone-free interval is delayed, shortened, or omitted
    - Extended use of intrauterine methods
    - When progesterone-only emergency contraception (POEC) is used outside the terms of the product licence
    - The use of contraceptive agents for non-contraceptive unlicensed indications (e.g., management of menorrhagia, dysmenorrhoea, endometriosis, menstrual bleeding abnormalities, acne vulgaris, hypo-oestrogenism)
    - Benefits, risk, and precautions of contraceptive use outside the terms of product license

MAJOR OUTCOMES CONSIDERED

Effectiveness of contraception used outside the terms of the product licence

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Electronic searches were performed for: MEDLINE (CD Ovid version) (1996-2005); EMBASE (1996-2005); PubMed (1996-2005); the Cochrane Library (to February 2005) and the US National Guideline Clearing House. The searches were performed using relevant medical subject headings (MeSH), terms, and text words. The Cochrane Library was searched for systematic reviews, meta-analyses, and controlled trials relevant to use of contraceptive methods for contraception and other conditions outside the terms of the product license. Previously existing guidelines from the Faculty of Family Planning and Reproductive Health Care (FFPRHC), the Royal College of Obstetricians, and Gynaecologists (RCOG), the World Health Organization (WHO) and reference lists of identified publications were also searched. Similar search strategies have been used in the development of other national guidelines.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Selected key publications were appraised according to standard methodological checklists before conclusions were considered as evidence. Evidence was graded using a scheme similar to that adopted by the Royal College of Obstetricians and Gynaecologists (RCOG) and other guideline development organizations.

Evidence tables are available on the Faculty for Family Planning and Reproductive Health Care (FFPRHC) Web site (http://www.ffprhc.org.uk/). These summarise relevant published evidence on use of contraception outside product licence, which was identified and appraised in the development of this Guidance. The clinical recommendations within this Guidance are based on evidence whenever possible.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendation

A Evidence based on randomized controlled trials (RCTs)

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 expert group

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The grades of recommendation (A-C, Good Practice Point) definitions are provided at the end of the "Major Recommendations" field.

How Should Clinicians Prescribe Contraceptives for Uses Other than Those Stated in the Product Licence?

1. Contraceptive, sexual, and reproductive health care services should ensure that their organisational policy on use of medicines outside the terms of the product licence is incorporated into clinical practice **(Grade C)**.
2. When prescribing contraceptives outside the terms of the product licence doctors should: take an appropriate clinical history; assess a woman's priorities and preferences; discuss the evidence supporting use outside licence; document all this information clearly in the case records; and advise the woman of the benefits of informing her general practitioner (GP) **(Grade C)**.
3. Nurse prescribers cannot prescribe medicines outside the terms of the product licence **(Grade C)**.
4. Women should be informed when contraceptives are used outside the terms of the product licence and should be given appropriate and complementary written information in addition to the manufacturers' Patient Information Leaflets (PILs) **(Grade C)**.
5. Patient Group Directions (PGDs) can be developed to allow nurses and other health care professionals to supply and administer contraceptives. This may include use outside the terms of the product licence provided such use is justified by current best practice. The PGD must clearly describe the status of the product and when it is being used outside licence, and should include the reasons why such use is necessary **(Grade C)**.
6. Pharmacists can dispense medicines outside the terms of the product licence if: the medicine is prescribed by a medical practitioner; in the best interests of the patient; and reasonable steps have been taken to ensure that the

prescribing clinician knew that the medicine was to be used outside the terms of the product licence **(Grade C)**.

When Are Contraceptives Prescribed Outside the Terms of the Product Licence?

Starting Hormonal Contraception Outside Product Licence

7. Women can be advised that, ideally, hormonal methods should be started on Day 1 of the menstrual cycle but can be started up to and including Day 5 [unlicensed for combined hormonal methods and progestogen-only pills (POPs)] without the need for additional contraception (as the risk of pregnancy is small and does not warrant the routine use of additional contraception) **(Grade C)**.
8. Women can be advised that hormonal contraception (combined hormonal methods, POPs, implants and injectables) can be started at any other time in the cycle if it is reasonably certain they are not pregnant, but additional contraception is required for 7 days (or 2 days for POPs) **(Grade C)**.
9. Women can be advised that the levonorgestrel-releasing intrauterine system (LNG-IUS) can be inserted at any time in a cycle if it is reasonably certain that they are not pregnant. Additional contraceptive protection is required for 7 days if inserted after Day 7 **(Grade C)**.

Starting Non-Hormonal Contraception

10. Women can be advised that an intrauterine contraceptive device (IUD) can be inserted at any time in the menstrual cycle if it is reasonably certain she is not pregnant **(Grade C)**.

Starting Contraceptives in Special Circumstances

Following Miscarriage or Abortion (Less than 24 Weeks' Gestation)

11. Women can be advised that all contraceptive methods can be started immediately following miscarriage or induced abortion occurring at less than 24 weeks' gestation **(Grade C)**.

Postpartum (not Breastfeeding)

12. Contraception is not required before Day 21 postpartum. Ideally, hormonal contraception should be started on Day 21 to provide immediate contraceptive protection. However, progestogen-only methods can be started before Day 21 if requested **(Grade C)**.
13. All intrauterine methods can be inserted from 4 weeks postpartum; they can also be inserted within 48 hours of delivery **(Grade C)**.

Breastfeeding

14. Breastfeeding women can be advised that: combined hormonal contraception can be used from 6 weeks to 6 months postpartum if no other method is acceptable; POPs can be started before Day 21 postpartum but if started after

Day 21 additional contraceptive protection is required for 2 days; progestogen-only implants can be inserted before Day 21 postpartum but bleeding may be a problem; progestogen-only injectables can be given less than 6 weeks postpartum but should ideally be delayed until Day 21 postpartum **(Good Practice Point)**.

Starting Contraception Following Use of Progestogen Only Emergency Contraception (POEC)

15. After progestogen only emergency contraception (POEC) use, clinicians and women should discuss and consider individually the option of initiating a regular method of contraception prior to the onset of the next menstruation **(Good Practice Point)**.

When Hormonal Contraception Is Late or Missed

Combined Oral Contraceptive Pill

16. Women can be advised that if one or two 30 to 35 microgram ethinylestradiol (EE)-containing combined oral contraceptives (COCs) are missed (or one 20 microgram EE-containing COC): the last missed pill should be taken as soon as remembered; pills should be continued daily at the usual time; additional contraceptive protection is not required; and emergency contraception (EC) is not indicated **(Grade C)**.
17. Women can be advised that if three 30 to 35 microgram EE-containing COCs are missed (or two 20 microgram EE-containing COCs) the last missed pill should be taken as soon as remembered and daily pill taking continued. Additional contraceptive protection, such as condoms, is advised for 7 days. EC is only indicated if pills are missed in Week 1 and unprotected sexual intercourse (UPSI) occurred in the pill-free week or in Week 1. If pills are missed in Week 3, the pill-free interval should be omitted **(Grade C)**.

Progestin-Only Pill

18. Women taking POPs containing levonorgestrel, norethisterone or ethynodiol diacetate can be advised that if more than 27 hours have elapsed since taking the last POP (i.e., more than 3 hours late): the late pill should be taken as soon as remembered; the next pill should be taken at the usual time; additional contraceptive protection such as condoms is advised for 2 days; and if UPSI has occurred in the 2 days since late POP, EC is indicated **(Grade C)**.
19. Women taking desogestrel-only pills can be advised that if more than 36 hours have elapsed since taking the last pill (i.e. more than 12 hours late): the late pill should be taken as soon as remembered; the next pill should be taken at the usual time; additional contraceptive protection such as condoms is advised for 2 days; and if UPSI has occurred in the 2 days since late pills, EC is indicated **(Grade C)**.

Late Progestogen-Only Injectables

20. Should a woman present late for her next contraceptive injection (i.e., more than 12 weeks to less than 14 weeks for depot medroxyprogesterone acetate [DMPA], and more than 8 weeks to less than 10 weeks for norethisterone enanthate [NETEN]) the risk of pregnancy is extremely small. Additional contraceptive protection need not be recommended **(Grade C)**.

When the Dose of Oral Contraceptives Is Increased

21. Women taking liver enzyme-inducing drugs who wish to use COC should choose a regimen containing at least 50 microgram EE daily. Additional contraceptive protection, such as condoms, should be used until 4 weeks after the liver enzyme-inducing drug has been stopped (Grade C).
22. Women using POPs containing levonorgestrel, norethisterone, or ethynodiol diacetate who weigh more than 70 kg are advised to take two pills together every day **(Good Practice Point)**.

When the Hormone-Free Interval Is Delayed, Shortened, or Omitted

23. Women may be given advice regarding "tricycling" combined hormonal contraception to avoid withdrawal bleeds, extending the active hormone-taking days to delay menses, or shortening the pill-free interval if using liver enzyme-inducing drugs **(Good Practice Point)**.

Extended Use of Intrauterine Methods

24. After counselling about declining fertility, contraceptive efficacy and risks associated with IUD insertion, women who have an IUD with more than 300 mm^2 of copper inserted at age greater than or equal to 40 years can be advised to retain the device until the menopause **(Grade C)**.
25. Women can be advised that if the LNG-IUS is inserted at greater than or equal to 45 years of age (and not being used in combination with oestrogen replacement therapy) it may continue to be used to provide contraception for 7 years **(Grade C)**.

<u>When is POEC Used Outside the Terms of the Product Licence?</u>

Use of POEC Beyond 72 Hours

26. POEC may be considered for use between 73 and 120 hours after UPSI, but women should be informed of the limited evidence of efficacy and offered the alternative option of an IUD **(Good Practice Point)**.

Use of POEC More Than Once in a Cycle

27. Women can be advised that POEC can be used more than once in a cycle if clinically indicated **(Good Practice Point)**.

Increased Dose of POEC for Women Using Liver Enzyme-Inducers

28. Women using liver enzyme-inducing drugs should be advised to increase the dose of POEC and take 2.25 milligrams as a single dose as soon as possible and within 72 hours of UPSI **(Grade C)**.

Advance Provision of POEC

29. Advance provision of POEC and instructions on use can be offered to those women attending family planning and sexual health services to increase early use when required **(Grade A)**.

What Evidence is Available to Support the Use of Contraceptive Agents for Non-Contraceptive Unlicensed Indications?

Combined Oral Contraceptives

Management of Menorrhagia

30. Women may be advised that menstrual blood loss may be reduced with COC use **(Grade C)**.

Management of Dysmenorrhoea and Endometriosis

31. Women may be advised that menstrual pain may be reduced with COC use **(Grade C)**.

Management of Menstrual Bleeding Abnormalities Associated with Progestogen-Only Implants or Injectables

32. Women using progestogen-only implants or injectables who have menstrual abnormalities may consider the short-term use of a COC or non-steroidal anti-inflammatory drugs (NSAID) after gynaecological problems and infection have been excluded **(Grade C)**.

Management of Acne Vulgaris

33. Women can be informed that COCs improve acne vulgaris **(Grade A)**.

Management of Hypo-Oestrogenism

34. Combined hormonal contraception may be useful in preserving bone mineral density (BMD) for women with a premature menopause but has no beneficial effect on bone mineral density in women with anorexia nervosa **(Grade B)**.

Progestogen-Only Pills and Implants

Management of Menstrual Bleeding

35. POPs and implants are ineffective in the management of menstrual bleeding problems and should not be used for this purpose **(Good Practice Point)**.

Progestogen-Only Injectables

Management of Menorrhagia

36. Progestogen-only injectables can induce amenorrhoea and may be considered by women with menorrhagia **(Grade B)**.

Levonorgestrel-Releasing Intrauterine System

Duration of Use in Management of Menorrhagia

37. Women can be advised that if the LNG-IUS is used to treat menorrhagia (and when not relying on it for contraception or in combination with oestrogen replacement therapy) then it may be continued beyond the usual 5 years of licensed use, if bleeding patterns remain acceptable **(Good Practice Point)**.

Definitions:

Grades of Recommendation

A Evidence based on randomized controlled trials (RCTs)

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 expert group

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document on advice for women missing combined oral contraceptives (30-35 micrograms and 20 micrograms ethinylestradiol formulations).

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Improved knowledge and appropriate support for clinicians and women using contraceptive methods outside their licensed indications

POTENTIAL HARMS

- Side effects of hormonal contraception and risk of unintended pregnancy in case of contraception failure.
- The risks associated with copper-bearing intrauterine contraceptive device (IUD) insertion include infection, perforation, and expulsion and potential loss of contraceptive efficacy if used beyond the recommended life of the device.

CONTRAINDICATIONS

CONTRAINDICATIONS

Summary of Product Characteristics (SPCs) suggest combined hormonal methods should be avoided when breastfeeding.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Penney G, Brechin S, Allerton L. The use of contraception outside the terms of the product licence. J Fam Plann Reprod Health Care 2005 Jul;31(3):225-41; quiz 242. [150 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Jul

GUIDELINE DEVELOPER(S)

Faculty of Sexual and Reproductive Healthcare - Professional Association

SOURCE(S) OF FUNDING

Faculty of Family Planning and Reproductive Health Care

GUIDELINE COMMITTEE

Clinical Effectiveness Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Faculty of Family Planning and Reproductive Health Care Web site.

Print copies: Available from the Faculty of Family Planning and Reproductive Health Care, 27 Sussex Place, Regent's Park, London NW1 4RG

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on August 16, 2005.

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Date Modified: 9/22/2008