

Faculty of Sexual & Reproductive Healthcare Clinical Guidance



Progestogen-only Injectable Contraception

Clinical Effectiveness Unit
November 2008
(Updated June 2009)

DETAILS OF CHANGES TO ORIGINAL GUIDANCE DOCUMENT

The print version of this CEU Guidance Document (issued in November 2008) contained some inconsistencies that the CEU has corrected in this version. These corrections are to Table 1: UK Medical Eligibility for Contraceptive Use for progestogen-only injectable use (page 2), Timing of repeat injections (page 6), and to Table 3: Summary of indications for emergency contraception following late progestogen-only injections (page 7).

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FSRH Guidance (November 2008) Progestogen-only Injectable Contraception

(Date of planned revision 2013)

Purpose and scope

This Guidance document provides evidence-based recommendations and good practice points for clinicians on the use of progestogen-only injectable contraception. The Guidance will refer to the most commonly used injectable in the UK, depot medroxyprogesterone acetate¹ (DMPA), unless otherwise stated. The other progestogen-only injectable contraceptive available in the UK is norethisterone enantate (NET-EN).² The rarely used NET-EN is only licensed for short-term use (e.g. for women whose partners have undergone vasectomy, until vasectomy is effective). Information on NET-EN will be included where relevant. A subcutaneous preparation of DMPA has been developed for self-administration. A UK licence was authorised in October 2005 but it is not yet currently available.

Recommendations from the National Institute for Health and Clinical Excellence (NICE) Guidance on long-acting reversible contraception (LARC) published in 2005 are reproduced in this Guidance.³

This document is not intended to serve alone as a standard of medical care, as this should be determined individually, based on available clinical information. This Guidance has been systematically developed using the standard methodology outlined in the Appendix.

Background

The Office for National Statistics collects information about contraceptive use in Great Britain from the Omnibus Survey.⁴ In 2006/2007 the survey included a stratified random sample of 3025 respondents (1696 men aged 16–69 years and 1329 women aged 16–49 years). Injectable contraception was used by 3% of women overall aged 16–49 years but the majority of users were young women in the 18–19-year age range.

Which women are eligible to use progestogen-only injectable contraception?

UK Medical Eligibility Criteria

The *UK Medical Eligibility Criteria for Contraceptive Use* (UKMEC)⁵ provides evidence-based recommendations to allow couples to select the most appropriate method of contraception without imposing unnecessary restrictions. Definitions for the UKMEC categories are given in Table 1. For most women, progestogen-only injectable contraception (DMPA and NET-EN) is a safe option. There are few circumstances where UKMEC recommends that

the theoretical or proven risks usually outweigh the advantages of using the method (UKMEC 3) or use of the method represents an unacceptable health risk (UKMEC 4) (Table 1). The only UKMEC Category 4 is current breast cancer.⁵

1 Health professionals should be familiar with the UK Medical Eligibility Criteria for progestogen-only injectable contraceptive use. (Good Practice Point)

What should clinicians assess when a woman is considering progestogen-only injectable contraception?

Clinical assessment

In order to advise on eligibility for progestogen-only injectable contraceptive use, clinicians should take a medical history (see Box 1 on page 6) and refer to the recommendations in the UKMEC (reproduced in Table 1).⁵ An individual assessment of the risk of sexually transmitted infections (STIs) will inform decisions about the need for additional barrier methods and appropriate testing for STIs.

2 A medical history (including sexual history), together with consideration of the UKMEC recommendations, should be used to assess the appropriateness of progestogen-only injectable contraception. (Good Practice Point)

What information should be given to women considering progestogen-only injectable contraception?

All women choosing a contraceptive method should be given oral and written information (e.g. fpa leaflet) as part of routine counselling. The clinician should discuss the points outlined below.

Mode of action

Progestogen-only injectable contraception works primarily by inhibiting ovulation.^{1,6} There is thickening of cervical mucus inhibiting sperm penetration into the upper reproductive tract. In addition, changes to the endometrium make it an unfavourable environment for implantation.^{6–8}

3 Women should be informed that progestogen-only injectable contraception acts primarily by inhibition of ovulation. (Grade C)

Table 1 UK Medical Eligibility Criteria for Contraceptive Use for progestogen-only injectable use⁵

UKMEC 1 (A condition for which there is <i>no restriction</i> for the use of the contraceptive method)	UKMEC 2 (A condition for which the <i>advantages of using the method generally outweigh the theoretical or proven risks</i>)
<p>Age 18–45 years Parity nulliparous and parous Breastfeeding ≥6 weeks postpartum Postpartum (in non-breastfeeding women) Post-abortion Past ectopic pregnancy History of pelvic surgery Smoking Obesity Hypertension consistently elevated blood pressure levels (properly taken measurements) systolic >140–159 mmHg or diastolic >90–94 mmHg; history of high blood pressure during pregnancy (where current blood pressure is normal) Venous thromboembolism (VTE) family history of VTE in first-degree relative of any age; major surgery without prolonged immobilisation; minor surgery without immobilisation; immobility (unrelated to surgery) (e.g. wheelchair use, debilitating illness) Superficial venous thrombosis Valvular and congenital heart disease Headaches non-migrainous (mild or severe) [Initiation and Continuation] Epilepsy Depressive disorders Endometriosis Benign ovarian tumours (including cysts) Severe dysmenorrhoea Gestational trophoblastic neoplasia (GTN) (includes hydatidiform mole, invasive mole, placental site trophoblastic tumour) hCG normal Cervical ectropion Breast disease benign breast disease or family history of breast cancer Endometrial cancer Ovarian cancer Uterine fibroids Pelvic inflammatory disease (PID) Sexually transmitted infections (STIs) High risk of HIV HIV infected (not using anti-retroviral therapy) Schistosomiasis Tuberculosis Malaria Diabetes history of gestational disease Thyroid disorders Cholestasis pregnancy-related Viral hepatitis carrier Inflammatory bowel disease Thalassaemia Sickle cell disease Iron-deficiency anaemia Raynaud's disease primary; secondary without lupus anticoagulant Drugs which affect liver enzymes Non-liver enzyme-inducing antibiotics</p>	<p>Age menarche to <18 years or >45 years Breastfeeding <6 weeks postpartum Hypertension adequately controlled hypertension; consistently elevated blood pressure levels (properly taken measurements) systolic >160 mmHg or diastolic >95 mmHg Venous thromboembolism (VTE) history of VTE; major surgery with prolonged immobilisation Known thrombogenic mutations (e.g. factor V Leiden; prothrombin mutation; protein S, protein C and antithrombin deficiencies) Known hyperlipidaemias Headaches migraine without aura at any age; with aura, at any age [Initiation only]; past history of migraine with aura at any age Vaginal bleeding pattern Cervical intraepithelial neoplasia (CIN) Cervical cancer (awaiting treatment) Breast disease undiagnosed mass; carriers of known genetic mutations associated with breast cancer (e.g. BRCA1) AIDS and using HAART Diabetes non-vascular disease Gallbladder disease History of cholestasis past COC-related Cirrhosis mild (compensated) Raynaud's disease with lupus anticoagulant Highly active antiretroviral therapy (HAART)</p> <hr/> <p>UKMEC 3 (A condition where the theoretical or proven risks usually outweigh the advantages of using the method)</p> <p>Significant multiple risk factors for arterial cardiovascular disease Vascular disease Venous thromboembolism (VTE) current VTE (on anticoagulants) Ischaemic heart disease Stroke (history of cerebrovascular accident) Headaches migraine with aura, at any age [Continuation] Unexplained vaginal bleeding (suspicious for serious underlying condition) before evaluation Gestational trophoblastic neoplasia (GTN) (includes hydatidiform mole, invasive mole, placental site trophoblastic tumour) hCG abnormal Breast cancer past and no evidence of current disease for 5 years Diabetes nephropathy/retinopathy/neuropathy; other vascular disease or diabetes of >20 years' duration Viral hepatitis active Cirrhosis severe (decompensated) Liver tumours</p> <hr/> <p>UKMEC 4 (A condition which represents an unacceptable health risk if the contraceptive is used)</p> <p>Breast cancer current (within the last 5 years)</p>

Initiation = Starting a method of contraception by a woman with a specific medical condition.

Continuation = Continuation with a method already being used by a woman who develops a new medical condition.

^aThe provision of a method to a woman with a condition given a UKMEC Category 3 requires expert clinical judgement and/or referral to a specialist contraceptive provider since use of the method is not usually recommended unless other methods are not available or not acceptable.

Contraceptive efficacy

In a multi-national randomised controlled trial (RCT) cumulative pregnancy rates for DMPA users were 0.7% at 1 year of use.⁹ Similar results were reported in two cohort studies (0.4%¹⁰ and 0.3%¹¹) at 1 year of use. An RCT that compared pregnancy rates for NET-EN and DMPA users found 1-year cumulative pregnancy rates of 0.4% (NET-EN) and 0.1% (DMPA). At 2 years, cumulative pregnancy rates were <0.4% (<4 in 1000).⁹

4 Women should be advised that the failure rate with the progestogen-only injectable given within license every 12 weeks is very low (<4 in 1000 over 2 years). (Grade A)

Duration of use

No maximum duration of use for DMPA is suggested. Women who wish to continue to use DMPA should be

reviewed every 2 years. Specific enquiry should be made about the individual clinical situation and the balance between the benefits and potential risks discussed. Women may choose to continue use. [NB. See additional information in section on bone mineral density.] Women can continue to use DMPA to age 50 years, at which time an alternative contraceptive method is advised.¹²

Return of fertility

There is a *delay in the return* of fertility following discontinuation of the progestogen-only injectable but *no evidence of reduced fertility* long term.³ The delay in return of fertility for DMPA is greater than for NET-EN.¹³ Non-comparative studies have reported evidence of ovulation within 6 months after the last DMPA injection.^{13–19} Although a large cohort study identified a median delay from discontinuation of DMPA to conception of 5.5 months [compared to 4.5 months for intrauterine device (IUD) users], there were no significant

differences in cumulative pregnancy rates with the two methods.²⁰

5 Women should be advised that there can be a delay of up to 1 year in the return of fertility after discontinuation of progestogen-only injectable contraception. (Grade C)

6 Women who do not wish to conceive should be advised to start another contraceptive method before or at the time of the next scheduled injection even if amenorrhoeic. (Good Practice Point)

Side effects

Bleeding changes

Eighty percent of women in a large cohort study experienced changes in the bleeding pattern with DMPA use over 3 years. Amenorrhoea (14.4%), infrequent bleeding (24.2%), spotting (27.9%) and prolonged bleeding (33.5%) were all reported.²¹

Some women may find amenorrhoea more acceptable than prolonged or infrequent bleeding.²² Amenorrhoea is more likely as duration of use increases²³ and indeed 34–35% of women are amenorrhoeic at 3 months use and 70.3% by 12 months.²⁴

7 Women should be informed about the altered bleeding patterns that usually occur with the use of a progestogen-only injectable contraceptive. (Good Practice Point)

8 Up to 70% of DMPA users are amenorrhoeic at 1 year of use. (Grade B)

Weight change

In women of reproductive age minor weight fluctuation is common. A Cochrane Review found that progestogen-only injectable contraceptive users had a mean weight gain of approximately 3 kg at 2 years use.²⁵ Average weight gain among women using DMPA is between 2 and 6.1 kg.^{26–33} A baseline assessment of body mass index (BMI) may predict weight gain expected with DMPA use.^{27,29} A prospective cohort found that after 18 months of use women with a BMI ≥ 30 had a significantly higher mean weight increase (9.45 kg) compared to women with a BMI < 25 (4.04 kg).³³

9 Women should be advised that there is an association between DMPA use and weight gain. (Grade C)

Mood change, libido and headache

Cohort studies provide no evidence of a causal association between DMPA use and mood change.^{34–36}

No studies have reported the effect of progestogen-only injectable contraceptives on libido.

Headache is a common symptom in the general population and a causal relationship with progestogen-only injectable contraceptive use has not been demonstrated. In cohort studies the reported rates of headache in DMPA users ranges between 5% and 25%.^{21,28} Young women (aged 11–20 years) reported no significant differences in symptoms of headache between DMPA and combined oral contraceptive (COC) use (26% DMPA and 21% COC users) over the first 6 months of use.³⁵

10 Women should be advised that there is no evidence of a causal association between the use of progestogen-only injectable contraceptives and mood change, libido or headache. (Grade C)

Discontinuation

An RCT found that women who had repeated, structured information about DMPA were less likely to discontinue the method by 12 months (OR 0.27; 95% CI 0.16–0.44) than women who had routine counselling.²⁴ Non-comparative studies report widely different discontinuation rates for DMPA (36–77%).^{21,37–41} The main reasons cited for discontinuation were bleeding problems (8–51%)^{21,38–41} and weight gain (2–24%).^{38,39,41,42} A randomised trial reported a 20% discontinuation rate for DMPA and 3% for the copper-containing IUD at 12 months. It is unclear if this difference was statistically significant.⁴³ A large cohort study found no significant differences in discontinuation rates between DMPA, IUD and COC users at 24 months.⁴⁴ Cohort studies comparing DMPA with other contraceptive methods have reported varying results.^{45,46}

11 Women should be informed that up to 50% of progestogen-only injectable contraceptive users will discontinue by 1 year, and that the most common reason for discontinuation is changes to bleeding pattern. (Grade B)

12 Women should be informed about the main reasons for discontinuation of progestogen-only injectable contraception and be given appropriate oral and written advice. (Grade A)

Health concerns

Cardiovascular disease

Progestogen-only injectable contraceptive use does not appear to be associated with an increased risk of stroke, venous thromboembolism (VTE) or myocardial infarction (MI). An international hospital-based case-control study⁴⁷ comparing progestogen-only injectable users and non-users reported that current use did not affect risk of combined cardiovascular disease, risk of stroke, VTE or MI. A cohort study comparing users of copper-containing IUDs with DMPA users found no significant differences between the two groups at 120 months with respect to systolic and diastolic blood pressure.⁴⁸

Bone mineral density

Inhibition of follicular development can lead to a decrease in estradiol concentrations and endometrial atrophy. For most women, however, estradiol concentrations are similar to those seen in the early phase of the menstrual cycle.

Concerns have been raised about the potential detrimental effects of the progestogen-only injectable contraceptive DMPA on bone mineral density (BMD). There has been particular concern about use of DMPA in women aged < 18 years (who have not yet attained their peak bone mass) and among older women (who are approaching the menopause when bone loss will occur).³ In a systematic review conducted as part of the NICE LARC Guidelines,³ several studies investigated the effects of progestogen-only injectable contraception on BMD.^{13,49–76}

No studies were identified that evaluated fracture risk in current or past users of progestogen-only injectable contraception. The review concluded that there was conflicting evidence that DMPA reduced BMD, which may be reversible on discontinuation.

Since the publication of the NICE LARC Guidelines, several other studies have been conducted investigating the effects of DMPA on BMD.^{77–81} The conclusions in NICE are not altered by this new data.

A prospective matched cohort study,⁷⁷ a cross sectional study⁷⁸ and a cohort study⁷⁹ reported significant reductions in mean BMD. However, BMD recovered after discontinuation of use.⁷⁷ A longer duration of use of DMPA was associated with more loss and less complete recovery.⁷⁸ When used for less than 1 year, the reduction in BMD identified did not differ significantly from non-users ($p = 0.90$). Recovery of BMD occurred following discontinuation of DMPA.⁸⁰

A recent study investigated the effects of DMPA use in relation to BMD in young women aged 12–18 years.⁸¹ Overall, BMD decreased in DMPA users ($n = 29$) with a mean percentage change of -1.4% (95% CI -2.73 to 0.10) in the lumbar spine and -2.2% (95% CI -3.95 to -0.39) in the femoral neck. Women not using any contraception ($n = 107$) had BMD increases in lumbar spine and femoral neck measurements of $+3.8\%$ (95% CI 3.11 – 4.57) and $+2.3\%$ (95% CI 1.29 – 3.27), respectively ($p < 0.001$). Women using oral contraception had increases in BMD in both femoral neck and lumbar spine measurements, however these increases were significantly smaller in comparison to the controls ($p = 0.03$) for both measurements. No long-term follow-up after discontinuation of use in women aged < 18 years has been identified.

The Department of Health Medicines and Healthcare products Regulatory Agency (MHRA) issued guidance⁷⁶ that was endorsed by the Faculty of Sexual and Reproductive Healthcare (FSRH)⁸² on the use of DMPA as follows:

- In women aged under 18 years DMPA may be used as first-line contraception after all options have been discussed and considered unsuitable or unacceptable.
- A re-evaluation of the risks and benefits of treatment for all women should be carried out every 2 years in those who wish to continue use.
- For women with significant lifestyle and/or medical risk factors for osteoporosis other methods of contraception should be considered.

13 Women should be informed that progestogen-only injectable contraceptive use is associated with a small loss of BMD, which is usually recovered after discontinuation. (Grade B)

14 Women should be advised that there is no available evidence on the effect of DMPA on long-term fracture risk. (Good Practice Point)

15 In women aged under 18 years DMPA can be used as first-line contraception after consideration of other methods. (Grade C)

16 Women using DMPA who wish to continue use should be reviewed every 2 years to assess individual situations and discuss the benefits and potential risks, and be supported in their choice of whether or not to continue. Use may continue to age 50 years. (Good Practice Point)

Drug interactions

The clearance of DMPA is approximately equal to the rate of hepatic blood flow. Drugs which induce liver enzymes *do not* reduce the contraceptive efficacy of DMPA and NET-EN.¹ The usual injection intervals do not need to be reduced. The efficacy of DMPA is unaffected by the use of non-liver enzyme-inducing antibiotics.⁸³

17 Women should be informed that the efficacy of progestogen-only injectable contraception is not reduced with concurrent use of medication (including antibiotics and liver enzyme-inducing drugs) and the injection intervals do not need to be reduced. (Grade C)

Non-contraceptive benefits

The NICE LARC Guidelines do highlight specific non-contraceptive benefits associated with the use of progestogen-only injectable contraception.³ In common with other methods that suppress ovulation, a progestogen-only injectable contraceptive may improve dysmenorrhoea⁸⁴ and the symptoms of endometriosis. A proportion of women may become amenorrhoeic, which may be perceived as a benefit.

Symptoms requiring medical attention

Women should be advised to seek advice if symptoms of migraine *with aura* develop as investigation may be indicated.⁵ The continued use of progestogen-only injectable contraception in women with new symptoms of migraine *with aura* can be considered (UKMEC 3). As with any intramuscular injection there is a risk of abscess formation at the site of injection.¹ Women should be advised to return if they experience any reaction to the progestogen-only injection that may suggest infection (e.g. redness, swelling, pain or rash).

18 Women should be advised to return if they experience any signs or symptoms of infection at the site of injection. (Good Practice Point)

Pregnancy

There is little relationship between DMPA use during pregnancy and effects on the fetus. The UKMEC⁵ and NICE LARC Guidelines³ recommend that if a pregnancy occurs while using progestogen-only injectable contraception then women should be advised that there is no evidence of harm to the pregnancy or the fetus.

The Summary of Product Characteristics (SPC) for DMPA¹ is more cautious if conception occurs within 2 months of an injection, however pregnancies in women using DMPA are rare.

When can progestogen-only injectable contraceptives be started?

Recommendations for routinely starting a progestogen-only injectable are given in Table 2.

Table 2 Recommendations for timing of initiation of a progestogen-only injectable

Circumstances when progestogen-only injectable can be initiated	Recommendations for timing of initiation
General initiation	Ideally, first injection should occur between Days 1–5 (inclusive) of a normal menstrual cycle. No additional contraception is required. Injections may also be initiated at any other time in the menstrual cycle if the clinician is reasonably certain that the woman is not pregnant and that there is no risk of conception. Additional contraception (barrier method or abstinence) should be advised for 7 days after initiation. If the woman is amenorrhoeic, the clinician must be reasonably certain that the woman is not pregnant and there is no risk of conception. Additional contraception should be used for 7 days.
Postpartum	Progestogen-only injectables may be initiated up to Day 21 postpartum with immediate contraceptive cover. If initiated after Day 21 then condoms or abstinence is advised for 7 days.
Following miscarriage or abortion	Initiate on day of surgical or second part of medical abortion or immediately following miscarriage: no additional contraception is required. If started >5 days after abortion or miscarriage, additional contraception is required for 7 days.
Switching from another contraceptive	
Combined hormonal contraception (CHC)	Can be initiated immediately if CHC has been used consistently and correctly or if the clinician is reasonably certain that the woman is not pregnant and that there has been no risk of conception. No additional contraception is needed.
Progestogen-only pill (POP)	Can be initiated immediately if POP has been used consistently and correctly or if the clinician is reasonably certain that the woman is not pregnant and that there has been no risk of conception. No additional contraception is needed.
Progestogen-only implant	Can be initiated immediately if implant has been used consistently and correctly or if the clinician is reasonably certain that the woman is not pregnant and that there has been no risk of conception. No additional contraception is needed.
Progestogen-only injectable	If the woman's previous method was another injectable, she should have the injection before or at the time the next injection was due. No additional contraception is needed.
Levonorgestrel-releasing intrauterine system (LNG-IUS)	Can be initiated immediately if the LNG-IUS was used consistently and correctly or if the clinician is reasonably sure that the woman is not pregnant. As bleeding with the LNG-IUS may not reflect ovarian activity, the LNG-IUS should be continued for at least 7 days.
Copper-bearing intrauterine device (IUD)	Can be initiated immediately if the IUD was used consistently and correctly or if the clinician is reasonably sure that the woman is not pregnant. The IUD should be continued for at least 7 days unless the first injection occurs between Days 1–5 (inclusive) of a normal menstrual cycle.
Barrier method (male condom, female condom, cap or diaphragm)	Can be initiated immediately if barrier method has been used consistently and correctly or if the clinician is reasonably certain that the woman is not pregnant and that there is no risk of conception. If the woman is amenorrhoeic or it has been more than 5 days since menstrual bleeding started, additional contraception should be continued for 7 days.

Initiation of progestogen-only injectable contraceptives in special circumstances

Postpartum

The SPC for DMPA recommends that initiation of the method should be within the first 5 days postpartum if not breastfeeding.¹ Women who are postpartum (vaginal or operative delivery) and bottle feeding may use the progestogen-only injectable without restriction (UKMEC 1).⁵

The SPC for DMPA recommends the first injection should be delayed until at least 6 weeks postpartum if women are breastfeeding.¹ The majority of studies show no adverse effects of progestogen-only injectables on breast milk, volume of breast milk, infant growth or development.^{85–91} Most of the concerns about the use of a progestogen-only injectable in the first 6 weeks postpartum relate to the theoretical risks of sex steroids being transferred via breast milk to an infant with immature organs, central nervous system or liver. A follow-up study of infants whose mothers were using a progestogen-only injectable whilst breastfeeding showed no problems.⁹² The benefits of using a progestogen-only injectable by breastfeeding women under 6 weeks postpartum outweigh any risks (UKMEC 2).⁵

Use of progestogen-only injectable contraception in

breastfeeding women is unrestricted after 6 weeks postpartum (UKMEC 1).⁵

19 Women can start a progestogen-only injectable contraceptive up to Day 21 postpartum to provide immediate contraceptive protection. If started after that time another method of contraception or abstinence is required for 7 days. (Grade C)

20 Progestogen-only injectable contraception can be safely used by women who are breastfeeding. (Grade B)

Following abortion or miscarriage

The UKMEC⁵ suggests that the use of the progestogen-only injectable immediately after a surgical abortion or after the second part of a medical abortion is unrestricted (UKMEC 1). The Royal College of Obstetricians and Gynaecologists (RCOG) Guidelines⁹³ recommend immediate initiation of contraception after abortion. NICE LARC³ Guidelines similarly recommend that a progestogen-only injectable may be initiated immediately after abortion in any trimester. In keeping with advice on starting progestogen-only injectable contraception, if administered within 5 days of an abortion or miscarriage additional contraception or abstinence is not required.

Box 1: Appropriate information to document when giving progestogen-only injectables (adapted from *Service Standards for Record Keeping*)⁹⁵

DOCUMENTATION REQUIRED WHEN INITIATING THE PROGESTOGEN-ONLY INJECTABLE

Medical history and clinical assessment

- Age
- Previous contraception used
- Duration of use of the progestogen-only injectable to date
- Medical history including cardiovascular disease/liver disease
- Past gynaecological history/other serious illness
- Menstrual history including date of last menstrual period (LMP)
- Coital history
- Medication – prescribed/non-prescribed/complementary
- Allergies
- Risk factors for osteoporosis (e.g. family history, smoking, corticosteroids, excessive alcohol, anorexia nervosa, coeliac disease)

Information advice and counselling

- Contraceptive choices discussed
- Risks/benefits/uncertainties discussed
- How it works/efficacy
- Side effects
- Explanation of injection procedure
- Leaflet given – including manufacturer's leaflet
- Date for next injection
- Follow-up arrangements

Prescribing and administration

- Record prescription
- Site of injection
- Batch number and expiry date (according to local protocol)
- Special instructions if any (e.g. additional contraception for 7 days, 'off licence' prescribing)

DOCUMENTATION REQUIRED WHEN CONTINUING THE PROGESTOGEN-ONLY INJECTABLE

- Any change in history or medication since last attendance should be recorded
- Date of last injection or number of weeks since last injection
- Reassessment of risk factors for osteoporosis (after 2 years)

21 Progestogen-only injectable contraception may be given following surgical abortion (or second part of) medical abortion or miscarriage. If administered within 5 days after the abortion or miscarriage then additional contraceptive protection or abstinence is not required. (Grade C)

Practical procedures for administering a progestogen-only injectable contraception

DMPA is an aqueous suspension usually in a pre-filled syringe that should be stored at room temperature and in a horizontal position. Syringes should be shaken vigorously before use to ensure complete suspension of the contents.³ The solution should be administered using the pre-packed needle. NET-EN is a thick, oily fluid that is drawn up into a syringe; the ampoule should be immersed in warm water before use to reduce the viscosity.

Both methods should ideally be given as a deep intramuscular injection administered to the upper outer quadrant of the buttock (gluteus maximus). The deltoid may be used as an alternative site if this facilitates the injection being given intramuscularly.^{1,2}

Emergency equipment for administering progestogen-only injectable contraceptives

The FSRH *Service Standards for Resuscitation in Sexual Health Services*⁹⁴ recommend training and regular updates in resuscitation for all staff dealing with emergencies (such as anaphylaxis) that may arise during contraceptive procedures.

22 Emergency resuscitation equipment must be available in all settings where progestogen-only injectable contraception is administered and local referral protocols must be in place for women who require further medical input. (Grade C)

Documentation

Recommendations from the FSRH for record keeping specific to progestogen-only injectable contraception are summarised in Box 1.⁹⁵

Ongoing use and follow-up of progestogen-injectable contraception and follow-up

Timing of repeat injections

Repeat injections of DMPA should be planned at 12-week intervals.¹ NET-EN should be given every 8 weeks.² The SPC suggests that DMPA can be given up to 12 weeks and 5 days since the last injection (licensed use).¹

Recommendations from the World Health Organization (WHO), supported by the FSRH, suggest that women can have a repeat injection up to *2 weeks early* (i.e. every 10 weeks for DMPA or 6 weeks for NET-EN) or *up to 2 weeks late* (i.e. 14 weeks for DMPA and 10 weeks for NET-EN) (Table 3).^{96,97}

It is likely that if DMPA is given up to 14 weeks since the last injection then the risk of ovulation is low and additional contraceptive use is not required. However, there are no large clinical trials to support this supposition. A small study observed serum medroxyprogesterone concentrations and ovarian activity (measured with serum progesterone and luteinising hormone) following a single intramuscular injection.⁹⁸ Concentrations of medroxyprogesterone gradually declined and remained relatively constant at 1 ng/ml for 2–3 months following an injection. Serum estradiol concentrations remained equivalent to those expected in the early to mid-follicular phase of the menstrual cycle for 4–6 months after the injection. The serum concentration of medroxyprogesterone fell by the 6th month (to 0.2 ng/ml) and by 7–9 months was undetectable. Estradiol concentrations increased to ovulatory concentrations only when serum medroxyprogesterone concentrations had declined to below 0.25–0.5 ng/ml. In some women medroxyprogesterone acetate can be identified in serum for as long as 9 months after an injection.⁹⁹

If more than 2 weeks have elapsed since her last injection of DMPA or NET-EN was scheduled a woman may have the injection if she has had no unprotected sex since the injection ceased to provide contraceptive protection (i.e. since 14 weeks + 1 day or more since the last DMPA injection or 10 weeks + 1 day or more since the last NET-EN injection). If the injection is administered then the woman should be advised to use additional contraception or avoid sex for the next 7 days.^{96,97} The need for emergency contraception should be assessed individually (Table 3).

If the timing of her previous DMPA injection is unknown, a woman can have the injection if it is reasonably certain that she is not pregnant. She will need to abstain from sex or use additional contraceptive protection for the next 7 days.⁹⁷

23 Women should be advised to return every 12 weeks for a repeat injection of DMPA (or every 8 weeks for NET-EN). (Grade C)

Table 3 Summary of indications for emergency contraception following late progestogen-only injectable injections

Timing of injection	Has unprotected sex occurred?	Can the injection be given?	Is emergency contraception indicated? ^a	Is additional contraception or abstinence advised?	Should a pregnancy test be performed?
<ul style="list-style-type: none"> ● Up to 14 weeks since last IM DMPA injection ● Up to 10 weeks since last NET-EN injection 	Not applicable, as long as next injection is given 14 weeks since last IM DMPA injection or 10 weeks since last NET-EN injection or before	YES	NO	NO	NO
When an injection is overdue, e.g. <ul style="list-style-type: none"> ● 14 weeks +1 day or more since last IM DMPA injection ● 10 weeks +1 day or more since last NET-EN injection 	NO (abstained or used barrier methods)	YES	NO	YES, for the next 7 days	NO, if abstained YES, if used barrier methods but at least 21 days later
	YES, but only in the last 3 days ^b	YES	YES, should offer progestogen-only EC or a copper IUD	YES, for the next 7 days	YES, at least 21 days later
	YES, but only in the last 4–5 days ^b	YES	YES, should offer a copper IUD	NO, if opts for copper IUD	YES, at least 21 days later
	YES, more than 5 days ago ^b	NO	NO	YES, for 21 days until a pregnancy test is confirmed negative and for a further 7 days after giving progestogen-only injectable	YES, at the initial presentation and at least 21 days later

^aIf EC is refused, decisions about ongoing use of DMPA should be tailored to the individual woman. Alternative methods if required should then be considered.

^bNot applicable if unprotected sex occurred within 14 weeks of last DMPA injection or 10 weeks of last NET-EN injection.

DMPA, depot medroxyprogesterone acetate; EC, emergency contraception; IM, intramuscular; IUD, intrauterine device; NET-EN, norethisterone enantate.

24 If necessary, a repeat progestogen-only injectable contraceptive can be given up to 2 weeks early (i.e. 10 weeks for DMPA and 6 weeks for NET-EN). (Grade C)

25 A repeat injection of progestogen-only injectable contraception can be given up to 2 weeks late (i.e. 14 weeks since the last DMPA and 10 weeks for NET-EN) without additional contraception (unlicensed). (Grade C)

26 The decision to provide a further DMPA injection and advice regarding the need for additional contraception should be considered individually, assessing the risk of pregnancy, the duration of use and the method (e.g. one previous injection or using DMPA for the last 5 years). (Good Practice Point)

Managing common problems associated with DMPA use

Unacceptable bleeding

Sexually transmitted infections (STIs) can be a common cause of irregular bleeding in women of reproductive age. Clinicians should consider a woman's risk of STIs (in particular *Chlamydia trachomatis*) if she presents with unscheduled bleeding. Women should be investigated for gynaecological pathology if clinically indicated.^{96,97}

The UK Selected Practice Recommendations for Contraceptive Use⁹⁷ and the 2005 WHO version⁹⁶ provide recommendations on the management of women with bleeding abnormalities whilst using progestogen-only injectable contraceptives.

If a woman experiences amenorrhoea during use this does not require any medical treatment.

Counselling is sufficient. If the woman still finds this unacceptable then the injectable should be discontinued and she should be helped to choose another contraceptive method.⁹⁷

Spotting or light bleeding is common during progestogen-only injectable use, particularly in the first injection cycle. If a woman does not wish treatment or if treatment fails then the progestogen-only injectable should be discontinued and another contraceptive method discussed.⁹⁷

Current guidance suggests that ethinylestradiol (given as a COC pill) and mefenamic acid may be effective in the management of unacceptable bleeding associated with progestogen-only injectable use.^{100,101}

27 Clinicians managing women who experience unacceptable bleeding while using a progestogen-only injectable contraceptive should take a sexual history, establish risk of STIs and consider possible gynaecological pathology. (Grade C)

28 Women using progestogen-only injectable contraception who have unacceptable bleeding but wish to continue with this method may consider the use of a COC pill (if appropriate) as a short-term treatment. (Grade C)

Cost-effectiveness of DMPA

Evidence suggests that amongst LARC methods, IUDs and intrauterine systems are the most cost-effective method; however, progestogen-only injectables are more cost-effective than the COC pill even after 1 year of use.

Increasing the uptake of long-acting reversible methods such as the progestogen-only injectable can reduce the number of unintended pregnancies.³

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APPENDIX: DEVELOPMENT OF CEU GUIDANCE

This Guidance was developed by the Clinical Effectiveness Unit (CEU): **Dr Gillian Penney** (Acting Chairperson for Expert Group), **Dr Susan Brechin** (Unit Director), **Ms Lisa Allerton** (Research Assistant) and **Ms Gillian Stephen** (Former research Assistant) on behalf of the Faculty of Sexual and Reproductive Healthcare (FSRH) with a multidisciplinary group of health professionals comprising: **Dr Alison Black** (Associate Specialist in Rheumatology, Grampian Osteoporosis Service, Woolmanhill Hospital, Aberdeen); **Dr Audrey Brown** (Consultant in Family Planning, The Sandyford Initiative, Glasgow/Chair of Clinical Effectiveness Committee); **Dr Joan Burnett** (General Practitioner, Links Medical Practice, City Hospital, Aberdeen); **Dr Lucy Caird** (Consultant in Gynaecology, Raigmore Hospital, Inverness); **Dr Babatunde Gbolade** (Consultant Gynaecologist and Director of Fertility Control Unit, Department of Obstetrics, Gynaecology and Reproductive Medicine, St James's University Hospital, Leeds); **Dr Louise Massey** (Consultant in Public Health, Wolverhampton); **Ms Shelley Mehigan** (Nurse Specialist, Margaret Pyke Centre, Camden Primary Care Trust, London); **Mrs Pat Murray** (NHS Quality Improvement Scotland Representative/User Representative); **Ms Nancy Robson** (NHS Quality Improvement Scotland Representative/User Representative, Elgin). Written feedback was received from: **Ms Toni Belfield** (Former Director of Information, fpa, London); **Professor Anna Glasier** (Consultant in Sexual and Reproductive Health, Lothian Primary Care/Director of Sexual and Reproductive Health, University of Edinburgh, Edinburgh) and **Dr Poornima Prabhu** (Consultant in Family Planning, Contraception, Sexual and Reproductive Health, Britannia Court, Worcester). In addition, this Guidance document was independently peer reviewed by **Professor Martha Hickey** (Clinical Psychologist and Obstetrician Gynaecologist, School of Women's and Infants' Health, University of Western Australia) and **Professor Daniel R Mishell Jr** (Lyle G McNiele Professor, Department of Obstetrics and Gynecology, Keck School of Medicine, University of Southern California). No competing interests were noted by members of the multidisciplinary group. Administrative support to the CEU is provided by **Mrs Jane Carmichael**.

CEU Guidance is developed in collaboration with the Clinical Effectiveness Committee (CEC) of the FSRH. The CEU Guidance development process uses 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 clinicians working in family planning, sexual and reproductive healthcare, general practice, other allied specialities, and user representation. In addition, the aim is to include a representative from the FSRH CEC, the FSRH Education Committee 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) (1996–2008); EMBASE (1996–2008); PubMed (1996–2008); The Cochrane Library (to 2008) 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 systematic reviews, meta-analyses and controlled trials relevant to progestogen-only injectables. 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 below, 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. Feedback on Guidance documents should be directed to the CEU via e-mail (ceu.members@ggc.scot.nhs.uk).

Level of evidence	Evidence
Ia	Evidence obtained from meta-analysis of randomised trials
Ib	Evidence obtained from at least one randomised controlled trial
IIa	Evidence obtained from at least one well-designed controlled study, without randomisation
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study
III	Evidence obtained from well-designed non-experimental descriptive studies, correlation studies and case studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

Grades 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

SUMMARY POINTS: PROGESTOGEN-ONLY INJECTABLES

CLINICAL ASSESSMENT

- Health professionals should be familiar with the UK Medical Eligibility Criteria for progestogen-only injectable use. (Good Practice Point)
- A medical history (including sexual history), together with consideration of the UKMEC recommendations, should be used to assess appropriateness of progestogen-only injectables.

WHAT INFORMATION SHOULD BE GIVEN TO WOMEN WHEN CONSIDERING A PROGESTOGEN-ONLY INJECTABLE?

Mode of action and efficacy

- The progestogen-only injectable acts primarily by inhibition of ovulation.
- The pregnancy rate with progestogen-only injectables is <4 in 1000 over 2 years.
- The efficacy of progestogen-only injectables is not reduced by antibiotics or liver enzyme-inducing drugs and injections can be continued at the usual intervals.
- Women should be informed about the possible bleeding patterns that may occur with a progestogen-only injectable, in particular up to 70% of users are amenorrhoeic in the first year of use. *[Around 50% of users have discontinued by 1 year, the main reason for discontinuation being changes to bleeding patterns.]*

Potential harms

- The use of progestogen-only injectables is associated with weight gain. *[There is no evidence of an association with depressive mood or headache.]*
- There can be a delay in return to fertility of up to 1 year after discontinuation but no reduction in fertility.
- Use of progestogen-only injectables is associated with a small loss of bone mineral density, which is usually recovered after discontinuation. There is no evidence of an increased risk of fracture. *[Progestogen-only injectables may be used as first-line contraception for women under the age of 18 years after other methods have been considered.]*

STARTING PROGESTOGEN-ONLY INJECTABLES

- In order to provide immediate contraceptive protection a progestogen-only injectable can be given:
 - up to and including Day 5 of the menstrual cycle
 - within 21 days of delivery (vaginal or operative)
 - within 5 days of a surgical abortion, the second part of a medical abortion, or after a spontaneous pregnancy loss (first- or second-trimester or immediate post-septic abortion).

If started at other times an additional method of contraception such as condoms is required for 7 days.

- Emergency equipment must be available in all settings where progestogen-only injectables are administered and local referral protocols must be in place for women who require further medical input.

ONGOING USE AND FOLLOW-UP

- For women who wish to continue using a progestogen-only injectable a discussion about the risks and benefits should be carried out every 2 years. Women with significant lifestyle and/or medical risk factors for osteoporosis may need to consider other methods of contraception.
- Women should be advised to attend for repeat injections of DMPA every 12 weeks. When necessary a repeat injection can be given up to 2 weeks late (14 weeks since the last injection) *without* the need for additional contraceptives. *[NB. This use is unlicensed.]*
- Women who experience unacceptable bleeding whilst using progestogen-only injectables should be assessed for STI risk (in particular *Chlamydia trachomatis*) and consideration given to the possibility of gynaecological pathology.
- If bleeding is unacceptable and the woman wishes to continue with this method of contraception, mefenamic acid or ethinylestradiol (as combined oral contraception) may be indicated as a short-term treatment if there are no contraindications to use.

INDICATIONS FOR EMERGENCY CONTRACEPTION FOLLOWING LATE PROGESTOGEN-ONLY INJECTABLE INJECTIONS

- These are summarised in Table 3.

Discussion Points for Progestogen-only Injectable Contraception

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

Discussion Points

- 1 A 15-year-old girl wishes to consider depot medroxyprogesterone acetate (DMPA). What would you specifically counsel her about at her age?
- 2 Discuss the management of a 45-year-old smoker who wished to continue with DMPA in the foreseeable future.
- 3 How would you assess a woman who appears 4 weeks late for her next DMPA injection and is requesting a further injection?

Questions for Progestogen-only Injectable Contraception

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

Indicate your answer by ticking the appropriate box for each question

	<i>True</i>	<i>False</i>
1 Progestogen-only injectable contraception works primarily by thickening cervical mucus and making it hostile to sperm penetration.	<input type="checkbox"/>	<input type="checkbox"/>
2 The maximum duration of use of injectable progestogen-only contraception is 5 years.	<input type="checkbox"/>	<input type="checkbox"/>
3 The upper age limit for use of injectable progestogen-only contraception is 50 years.	<input type="checkbox"/>	<input type="checkbox"/>
4 When long-term users discontinue DMPA they do not need to use another method of contraception for 6 months because of the delay in return of fertility.	<input type="checkbox"/>	<input type="checkbox"/>
5 Average weight gain with DMPA after 2 years of use is 3 kg.	<input type="checkbox"/>	<input type="checkbox"/>
6 Women receiving liver enzyme-inducing drugs should have their DMPA injections at 10-weekly intervals.	<input type="checkbox"/>	<input type="checkbox"/>
7 DMPA can be safely given to non-breastfeeding mothers within the first 5 days after delivery.	<input type="checkbox"/>	<input type="checkbox"/>
8 There is no evidence that DMPA is associated with a higher risk of depression.	<input type="checkbox"/>	<input type="checkbox"/>
9 DMPA pre-filled syringes must be kept refrigerated.	<input type="checkbox"/>	<input type="checkbox"/>
10 DMPA can be used in the management of endometriosis.	<input type="checkbox"/>	<input type="checkbox"/>

Answers

10 True
5 True

9 False
4 False

8 True
3 True

7 True
2 False

6 False
1 False

STEPS INVOLVED IN THE DEVELOPMENT OF CEU GUIDANCE

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 researchers.</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 and errors or where the text is incomprehensible.</p>
<p>Multidisciplinary Group Meeting comprising stakeholders and including service user representation, representation from the Faculty of Sexual and Reproductive Healthcare (FSRH) Education Committee and, where possible, representation from the FSRH Clinical Effectiveness Committee (CEC) and FSRH Council.</p>	<p>A one-day meeting held in Glasgow with the Multidisciplinary Group to discuss the Draft One Guidance document.</p>
<p>Preparation of Draft Two Guidance document based on discussion at the Multidisciplinary Group.</p>	<p>The Multidisciplinary Group meeting is held at least 2 months before the Guidance deadline to allow time for development of further drafts.</p>
<p>Peer Review of Draft Two Guidance document by the Multidisciplinary Group and the FSRH CEC.</p>	
<p>All written feedback on the Draft Two Guidance document is tabulated and the CEU response to these comments outlined.</p>	
<p>Draft Three Guidance document is prepared based on written feedback and is sent to the Multidisciplinary Group and the FSRH CEC. In addition, two independent peer reviewers are identified by the CEC to provide feedback at this stage.</p>	<p>Only minor comments can be accepted at this stage.</p>
<p>The Final Guidance document is published by the FSRH.</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. A pdf version of the Guidance is 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) via e-mail (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] 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, after review by the Clinical Effectiveness Committee, will be posted on the Faculty website (www.fsrh.org).