

Category: Best Practice Statement

Depot Medroxyprogesterone Acetate

This statement has been developed and reviewed by the Women's Health Committee and approved by the RANZCOG Board and Council.

A list of Women's Health Committee Members can be found in [Appendix A](#).

Disclosure statements have been received from all members of this committee.

Disclaimer This information is intended to provide general advice to practitioners. This information should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The document has been prepared having regard to general circumstances.

First endorsed by RANZCOG: July 1994

Current: November 2018

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Objectives: To provide advice regarding the use of Depot Medroxyprogesterone acetate (Depot Provera).

Target audience: Health professionals providing women's health care, and patients.

Values: The evidence was reviewed by the Women's Health Committee (RANZCOG), and applied to local factors relating to Australia and New Zealand.

Background: This statement was first developed by Women's Health Committee in July 1994.

Funding: The development and review of this statement was funded by RANZCOG.

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1. Plain language summary

Depot medroxyprogesterone acetate (DMPA) is a progesterone-only long-acting hormonal contraceptive administered as an injection.

DMPA is regarded as a very effective and safe method of contraception if given at 12 weekly intervals. Advantages include only needing to take a contraceptive measure every 12 weeks, absence of vaginal bleeding for many women and reduction of pelvic pain associated with periods or endometriosis. Disadvantages include an unpredictable effect on menstrual pattern with some experiencing irregular or prolonged vaginal bleeding, a delay in the return of fertility after cessation of use, and weight gain for some women.

2. Summary of Recommendations

Recommendation 1	Grade
Women choosing DMPA for contraception should make an informed choice based on knowledge of its advantages and potential disadvantages.	Consensus-based recommendation
Recommendation 2	Grade
DMPA is not recommended for women who are pregnant or wish to become pregnant in the near future, who have undiagnosed abnormal vaginal bleeding, or those who have a history of breast cancer, stroke, ischaemic heart disease or severely impaired liver function.	Consensus-based recommendation
Recommendation 3	Grade
DMPA is not recommended for women over 50 years of age, those considered at particular risk of osteoporosis or as a first line option for women under 18 years of age who are yet to reach peak bone mass.	Consensus-based recommendation
Recommendation 4	Grade
Women using DMPA who wish to continue use should be reviewed every two years to assess their individual circumstance and to discuss benefits, potential risks and ongoing suitability.	Consensus-based recommendation

3. Introduction

DMPA is an effective and safe contraceptive for medically eligible women who are making an informed choice based on its particular advantages and disadvantages. It was given full approval by the regulatory authorities for its use as a contraceptive agent in Australia in 1994. DMPA is a reversible method of contraception which is less user dependent than oral contraceptive pills. In Australia the injection is given intramuscularly. In some countries a subcutaneous preparation is available. DMPA has a number of social and medical advantages that have led to its approval in 100 countries and current usage by over 47 million women worldwide.

DMPA demonstrates dose-related teratogenicity and toxicity in animals. Although contraindicated in human pregnancy, inadvertent exposure to therapeutic doses of DMPA does not appear to represent a significant risk of structural defects.

Safety aspects have been reviewed thoroughly by several independent international bodies which have supported its use for contraception.¹

DMPA works by inhibiting ovulation, altering cervical mucus to limit sperm penetration and causing changes to the endometrium which are unfavourable for implantation². No other contraceptive measures are required if given in the first 5 days of the menstrual cycle; additional contraceptive measures are required if given later in the menstrual cycle.^{3,4}

4. Advantages

DMPA provides highly effective contraception with a 'perfect use' failure rate in the first year of use of approximately 0.2% which increases to 6% in 'typical use' (includes incorrect or inconsistent use), due to the need to return for repeat injections.² This typical use failure rate is higher than those observed with the long acting reversible methods (LARC), the progesterone only subdermal implant and the levonorgestrel intrauterine system.²

An advantage of DMPA over other hormonal contraceptive methods is that it is unaffected by concurrent liver enzyme-inducing medications, such as some anticonvulsant therapies.⁵ Amenorrhoea has been reported to occur in 47% of DMPA users after one year of use, many women regard this as a benefit particularly if they had been having menstrual problems.⁶ DMPA has been found to improve dysmenorrhoea and may be useful in the management of endometriosis.⁶⁻⁸ There is increasing evidence for protection against endometrial cancer, ovarian cancer and acute episodes of pelvic inflammatory disease.^{9,10}

5. Disadvantages

Disadvantages of DMPA include a variable change in the menstrual cycle during treatment, usually with infrequent bleeding or amenorrhoea, but sometimes with troublesome and irregular bleeding, especially in the first few months of use. An unpredictable but temporary delay in return of fertility of up to one year usually follows after stopping treatment.¹¹ There is an association between DMPA use and weight gain, particularly in adolescents with a BMI \geq 30. The available evidence suggests that women who gain more than 5% of their baseline body weight in the first six months of DMPA use are likely to continue to experience weight gain.² It appears that obese women are more likely to gain more weight during DMPA use, while thin women do not.¹² This weight gain in obese women is accompanied by disturbances of insulin and glucose regulation.

The association of DMPA and bone density has been controversial in the past and current evidence points to a small decrease of bone mineral density (BMD) which is usually recovered on discontinuation.²

Lower body mass index, low calcium intake and greater alcohol use, were associated with greater BMD loss in adolescents using DMPA. DMPA is generally not recommended as a first line option in women under 18 years who are yet to obtain their peak bone mass.^{2,13} Follow-up of previous long-term DMPA users at age of menopause showed no difference in BMD compared with non-users, however women may

be advised to switch to an alternative method of contraception at 50 years of age.^{2, 14} Alternative methods of contraception should be considered in women at particular risk of osteoporosis.²

6. Health Issues which are not as well defined

6.1 Venous Thromboembolism (VTE)

In the number of small studies carried out there has been no causal association found with venous thromboembolic disease and DMPA use. In a case controlled study WHO reported a small but not statistically significant increase in the incidence of venous thrombosis amongst a small number of users of DMPA.¹⁵ A meta-analysis of five case control and three retrospective cohorts reported a statistically significant increased risk of VTE in users of progestin-only injectable contraception.¹⁶ More research is required before a causal relationship can be confirmed or excluded. The UKMEC (UK Medical Eligibility Criteria for Contraceptive use) classify VTE and known thrombotic mutations as category 2 for DPMA; that is conditions where “the advantages of using the method generally outweigh the theoretical or proven risks”.¹⁷

6.2 Breast and Cervical Cancer

Controversy about a subtle influence on risk of detection of breast and cervical cancer is very similar to that pertaining to the combined oral contraceptive pill.^{18, 19} Any possible small increase appears to decrease on discontinuation of DPMA.²

6.3 HIV Acquisition

DMPA does not offer protection against sexually transmitted infections including HIV and at risk women should be advised on the concurrent use of condoms. Recent controversy about the use of DMPA by women at high risk of HIV in sub-Saharan African countries has been fuelled by some studies showing an increase in the risk of acquisition amongst DMPA users while others do not.^{2, 20, 21} WHO advise that while DMPA may be used by women at high risk of HIV, this should be with the additional use of condoms.

6.4 Ischaemic Heart Disease and Stroke

There is insufficient evidence to exclude or confirm an association between DMPA and stroke and ischaemic heart disease, but current or previous arterial disease is a strong relative contraindication to its use.^{2, 15, 17}

6.5 Mood Change, Libido and Headache

Reliable data relating to other adverse effects of DMPA are scarce but do not support a causal relationship between DMPA and mood change, libido or headache.^{2, 22} Indeed, DMPA is perceived by users as being associated with an improvement in physical health, with no apparent adverse effects on mental health and sexual function.²³

7. References

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4. Family Planning SA (Shine SA). Injectable Contraception 2015. Available from: <http://www.shinesa.org.au/health-information/contraception/injectable-contraception/>.
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8. Other suggested reading

Progesterone-only Injectable Contraception (2015) Faculty of Sexual & Reproductive Healthcare Clinical Guidance. <http://www.fsrh.org/pdfs/CEUGuidanceProgestogenOnlyInjectables.pdf>

RCOG Faculty of Sexual & Reproductive Healthcare: UK Medical Eligibility Criteria for Healthcare (2009) <http://www.fsrh.org/pdfs/UKMEC2009.pdf>

RCOG Faculty of Sexual & Reproductive Healthcare: Depot Medroxyprogesterone Acetate (DMPA, Depo-provera) and the Risk of HIV Acquisition (January 2015)

<https://www.fsrh.org/standards-and-guidance/documents/cec-ceu-statement-dmpa-hiv-jan-2015/cec-ceu-statement-dmpa-hiv-jan-2015.pdf>

9. Links to other College statements

[Consent and the Provision of Information to Patients in Australia regarding Proposed Treatment \(C-Gen 02a\) \[https://www.ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical%20-%20General/Consent-and-provision-of-information-to-patients-in-Australia-\\(C-Gen-2a\\)-Review-July-2016.pdf?ext=.pdf\]\(https://www.ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical%20-%20General/Consent-and-provision-of-information-to-patients-in-Australia-\(C-Gen-2a\)-Review-July-2016.pdf?ext=.pdf\)](https://www.ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical%20-%20General/Consent-and-provision-of-information-to-patients-in-Australia-(C-Gen-2a)-Review-July-2016.pdf?ext=.pdf)

[Consent and Provision of Information to Patients in New Zealand regarding Proposed Treatment \(C-Gen 02b\) \[https://www.ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical%20-%20General/Consent-and-provision-of-information-NZ-\\(C-Gen-2b\\)-Review-March-2016.pdf?ext=.pdf\]\(https://www.ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical%20-%20General/Consent-and-provision-of-information-NZ-\(C-Gen-2b\)-Review-March-2016.pdf?ext=.pdf\)](https://www.ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical%20-%20General/Consent-and-provision-of-information-NZ-(C-Gen-2b)-Review-March-2016.pdf?ext=.pdf)

Evidence-based Medicine, Obstetrics and Gynaecology (C-Gen 15)

[https://www.ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical%20-%20General/Evidence-based-medicine,-Obstetrics-and-Gynaecology-\(C-Gen-15\)-Review-March-2016.pdf?ext=.pdf](https://www.ranzcog.edu.au/RANZCOG_SITE/media/RANZCOG-MEDIA/Women%27s%20Health/Statement%20and%20guidelines/Clinical%20-%20General/Evidence-based-medicine,-Obstetrics-and-Gynaecology-(C-Gen-15)-Review-March-2016.pdf?ext=.pdf)

10. Patient information

A range of RANZCOG Patient Information Pamphlets can be ordered via:

<https://www.ranzcog.edu.au/Womens-Health/Patient-Information-Guides/Patient-Information-Pamphlets>

Appendices

Appendix A Women's Health Committee Membership

Name	Position on Committee
Professor Yee Leung	Chair
Dr Joseph Sgroi	Deputy Chair, Gynaecology
Associate Professor Lisa Hui	Member
Associate Professor Ian Pettigrew	EAC Representative
Dr Tal Jacobson	Member
Dr Ian Page	Member
Dr John Regan	Member
Dr Craig Skidmore	Member
Associate Professor Janet Vaughan	Member
Dr Bernadette White	Member
Dr Scott White	Member
Associate Professor Kirsten Black	Member
Dr Greg Fox	College Medical Officer
Dr Marilyn Clarke	Chair of the ATSI WHC
Dr Martin Byrne	GPOAC Representative
Ms Catherine Whitby	Community Representative
Ms Sherryn Elworthy	Midwifery Representative
Dr Amelia Ryan	Trainee Representative

Appendix B Overview of the development and review process for this statement

i. Steps in developing and updating this statement

This statement was originally developed in July 1994 and was most recently updated in November 2018. The Women's Health Committee carried out the following steps in reviewing this statement:

- Declarations of interest were sought from all members prior to reviewing this statement.
- Structured clinical questions were developed and agreed upon.
- An updated literature search to answer the clinical questions was undertaken.
- At the July 2018 face-to-face committee meeting, the existing consensus-based recommendations were reviewed and updated (where appropriate) based on the available body of evidence and clinical expertise. Recommendations were graded as set out below in Appendix B part iii)

ii. Declaration of interest process and management

Declaring interests is essential in order to prevent any potential conflict between the private interests of members, and their duties as part of the Women's Health Committee.

A declaration of interest form specific to guidelines and statements was developed by RANZCOG and approved by the RANZCOG Board in September 2012. The Women’s Health Committee members were required to declare their relevant interests in writing on this form prior to participating in the review of this statement.

Members were required to update their information as soon as they become aware of any changes to their interests and there was also a standing agenda item at each meeting where declarations of interest were called for and recorded as part of the meeting minutes.

There were no significant real or perceived conflicts of interest that required management during the process of updating this statement.

iii. Grading of recommendations

Each recommendation in this College statement is given an overall grade as per the table below, based on the National Health and Medical Research Council (NHMRC) Levels of Evidence and Grades of Recommendations for Developers of Guidelines. Where no robust evidence was available but there was sufficient consensus within the Women’s Health Committee, consensus-based recommendations were developed or existing ones updated and are identifiable as such. Consensus-based recommendations were agreed to by the entire committee. Good Practice Notes are highlighted throughout and provide practical guidance to facilitate implementation. These were also developed through consensus of the entire committee.

Recommendation category	Description
Evidence-based	A Body of evidence can be trusted to guide practice
	B Body of evidence can be trusted to guide practice in most situations
	C Body of evidence provides some support for recommendation(s) but care should be taken in its application
	D The body of evidence is weak and the recommendation must be applied with caution
Consensus-based	Recommendation based on clinical opinion and expertise as insufficient evidence available
Good Practice Note	Practical advice and information based on clinical opinion and expertise

Appendix C Full Disclaimer

Purpose

This Statement has been developed to provide general advice to practitioners about women's health issues concerning Depot Medroxyprogesterone Acetate and should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any person. It is the responsibility of each practitioner to have regard to the particular circumstances of each case. Clinical management Depot Medroxyprogesterone Acetate and the particular circumstances of each case.

Quality of information

The information available in Depot Medroxyprogesterone Acetate (C-Gyn 4) is intended as a guide and provided for information purposes only. The information is based on the Australian/New Zealand context using the best available evidence and information at the time of preparation. While the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) had endeavoured to ensure that information is accurate and current at the time of preparation, it takes no responsibility for matters arising from changed circumstances or information or material that may have become subsequently available. The use of this information is entirely at your own risk and responsibility.

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These terms and conditions will be constructed according to and are governed by the laws of Victoria, Australia.

Version	Date of Version
v1.1	Nov / 1990
v2.1	Jul / 1994
v3.1	Oct / 1997
V4.1	Oct / 1999
V5.1	Nov / 2001
V6.1	Nov / 2003
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