Depot Medroxyprogesterone Acetate

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.

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
Review due: November 2021
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1. **Patient 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**

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
<th>Recommendation 2</th>
<th>Grade</th>
<th>Recommendation 3</th>
<th>Grade</th>
<th>Recommendation 4</th>
<th>Grade</th>
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<tbody>
<tr>
<td>Women choosing DMPA for contraception should make an informed choice based on knowledge of its advantages and potential disadvantages.</td>
<td>Consensus-based recommendation</td>
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<tr>
<td>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.</td>
<td>Consensus-based recommendation</td>
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<tr>
<td>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.</td>
<td>Consensus-based recommendation</td>
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<tr>
<td>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.</td>
<td>Consensus-based recommendation</td>
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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. DMPA works by inhibiting ovulation, altering cervical mucus to limit sperm penetration and causing changes to the endometrium which are unfavourable for implantation. 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 Amenorrhea 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 dysmenorrhea 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 amenorrhea, 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≥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. DPMA 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. 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”.

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. Any possible small increase appears to decrease on discontinuation of DPMA.

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. 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.

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. 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.
7. **References**


15. World Health Organization. Cardiovascular disease and use of oral and injectable progestogen only contraceptives and combined injectable contraceptives. Results of an international, multicentre, case control study, Contraception. 1998;57:315–24


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


8. Other suggested reading


9. **Links to other College statements**


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

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](https://www.ranzcog.edu.au/Womens-Health/Patient-Information-Guides/Patient-Information-Pamphlets)
Appendices

Appendix A Women’s Health Committee Membership

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

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.

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

This information is intended to provide general advice to practitioners, 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 patient.

This information has been prepared having regard to general circumstances. It is the responsibility of each practitioner to have regard to the particular circumstances of each case. Clinical management should be responsive to the needs of the individual patient and the particular circumstances of each case.

This information has been prepared having regard to the information available at the time of its preparation, and each practitioner should have regard to relevant information, research or material which may have been published or become available subsequently.

Whilst the College endeavours 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.