The Royal Australian and New Zealand College of Obstetricians and Gynaecologists
Excellence in Women's Health

The use of mifepristone for medical abortion

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: November 2007
Current: March 2019
Review due: March 2022

Objectives: To provide advice on the use of mifepristone for medical abortion.

Target audience: All health professionals providing gynaecological 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 November 2007 and reviewed in March 2019.

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

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1. Summary of recommendations

Recommendation 1	Grade
Mifepristone, (a synthetic anti progesterone) in combination with misoprostol (a prostaglandin analogue) is the best available regimen for medical abortion. Alternative regimens are reported but are generally less effective and take longer to work.	Consensus-based recommendation
Recommendation 2	**Grade**
Abortion by any method should be conducted in accordance with the legal and regulatory requirements of the jurisdiction within which it occurs. Clinicians should be familiar with local requirements, which in some jurisdictions determine where the relevant drugs may be administered and by whom, and may preclude home administration of misoprostol.	Consensus-based recommendations
Recommendation 3	**Grade**
Where early medical abortion is offered suitable emergency care (in a service accepting this responsibility) should be available.	Consensus-based recommendations
Recommendation 4	**Grade**
For gestations above 63 days (9+0 weeks) both mifepristone and prostaglandin should be administered within the treating facility, where it is expected that the conceptus will be passed.	Consensus-based recommendations

2. Introduction

Medical, rather than surgical, abortion is an alternative method which may be offered to women when it is available and suitable for them. Mifepristone (a synthetic anti progesterone) in combination with misoprostol (a prostaglandin analogue) is the best available regimen for medical abortion. Alternative regimens are reported but are generally less effective and take longer to work.

For around 95% of women up to 9 weeks gestation, mifepristone with a suitable misoprostol regimen results in complete expulsion of the products of conception within a few hours of the administration of the misoprostol, but up to around 5% of women will need surgical evacuation of the uterus for heavy or prolonged bleeding or for continuing pregnancy. Complication rates are comparable to surgical abortion. There is also good evidence for effective regimens for medical abortion beyond 9 weeks and in the second trimester of pregnancy. The Mifepristone dose is well established, but optimal misoprostol regimens continue to be researched and the evidence is likely to continue to evolve regarding dosage, frequency and route of administration at different gestations.

3. Discussion

3.1 Access to mifepristone

Until quite recently surgical abortion was the only method available. Greater access to medical abortion was possible when mifepristone was registered in Australia in 2012. Initially this medication was approved for use in sequential combination with the prostaglandin analogue, misoprostol, for pregnancies up to 49 days gestation. From February 2015, a composite pack has been available containing both mifepristone and misoprostol with a new indication of abortion up to 63 days gestation.

This regimen comprises mifepristone 200mg followed by misoprostol 800micograms generally taken buccally within 48 hours. The oral route is no longer an approved route of administration because it has been shown to be less effective at gestations above 49 days. Mifepristone single pack will continue to be available for the abortion for medical reasons beyond the first trimester, which is primarily a hospital based specialist use.

The Therapeutic Goods Administration (TGA) requires that both practitioners and pharmacies are registered with the sponsoring company, before mifepristone is supplied. Holders of FRANZCOG or Advanced DRANZCOG will need to provide evidence of this qualification or complete the online training, offered by the sponsoring company in order to register.

In New Zealand, Mifepristone was approved by the New Zealand Medicine and Medical Device Safety Authority (MEDSAFE) on 30 August 2001. Current approved indications are:

1. As a medical alternative to surgical termination of intra-uterine pregnancy.
2. Softening and dilatation of the cervix uteri prior to surgical pregnancy termination.
3. Preparation for the action of prostaglandin analogues in the abortion for medical reasons.
4. Labour induction for the expulsion of a dead fetus (fetal death in utero).

In New Zealand the drug is not available through pharmacies but on a restricted basis to institutions licensed to carry out abortion. It is not available for use as a post-coital contraceptive. Within these limitations and subject to legal and regulatory constraints specific to pregnancy termination mifepristone may be prescribed by any medical practitioner.

Any use outside the indications listed above for each country is “off label”.

Mifepristone was first registered in France and China in 1988, the United Kingdom in 1991 and has been registered in much of Western Europe and the United States of America for one to two decades. There is an extensive body of literature to support its use.

3.2 Mifepristone use in medical abortion

Abortion by any method should be conducted in accordance with the legal and regulatory requirements of the jurisdiction within which it occurs. Clinicians should be familiar with local requirements, which in some jurisdictions determine where the relevant drugs may be administered and by whom, and may preclude home administration of misoprostol.

Clinicians should be familiar with the TGA approved product information (Australia) or MedSafe data sheet (New Zealand).

3.3 Staff and facilities for early medication abortion (up to 63 days or 9+0 weeks)

- The prescribing practitioner must supervise and take responsibility for arrangements for the entire process of abortion from administration of mifepristone through to confirmation of abortion and completion of follow-up including implementation of a contraceptive plan.

- These arrangements must include 24 hour access to specific telephone advice and support and to provision of surgical uterine evacuation or other interventions required for the management of complications, for example through on call arrangements or in an emergency department resourced to respond to women's health needs (such as required for miscarriage care).

- Elements of clinical care may be delivered by another suitably qualified and experienced clinician or service; where more than one service or facility is involved there must be clearly understood pathways and mechanisms for sharing of relevant clinical information and for the provision of care which may be necessary, possibly with shared protocols.

- There is abundant evidence to support the option of misoprostol being self-administered at home by women at less than 63 days gestation who prefer this; the woman must be advised to have an accompanying support person present at least until the conceptus is passed, who should be able to assist in contacting and accessing support and/or emergency care if needed.

- Prescribing practitioners should have appropriate training plus adequate experience in caring for women undergoing abortion and/or experiencing spontaneous miscarriage.

- For women in rural and remote areas telemedicine medical abortion service may enhance access and has been found to be safe and effective.

- Credentialing arrangements should be established by each service for practitioners who prescribe mifepristone for medication abortion.

- Where early medical abortion is offered suitable emergency care (in a service accepting this responsibility) should be available.

3.4 Staff and facilities for medication abortion (after 63 days or 9+0 weeks)

For gestations above 63 days (9+0 weeks) both mifepristone and prostaglandin should be administered within the treating facility, where it is expected that the conceptus will be passed.

Credentialing arrangements and access to follow-up and emergency care should apply as for earlier medication abortion; in general more specific staff experience and expertise will be needed.

Abortion after 9 weeks gestation must take place in a hospital with access to all necessary clinical and psychological support.

3.5 General considerations prior to pregnancy termination

- All women should be given accurate information and appropriate counselling should be available.

- Clinical assessment should be undertaken including medical history and examination.

- Clinicians should consider any contraindications to mifepristone or misoprostol, any co morbidities, surgical risk factors and the woman's preference in choosing a method of abortion.

- Accurate gestational assessment is essential to selecting optimal treatment options and regimens. Ultrasound examination is mandatory prior to abortion to confirm gestation and exclude ectopic

pregnancy; a diagnosis of ectopic pregnancy can be very difficult after attempted medical or surgical abortion.

- Consideration should be given to screening for STIs and/or antibiotic prophylaxis in accordance with published guidelines and considering local prevalences.
- Blood group and Rh (D) status should be assessed if not known and anti-D given to non-sensitised Rh negative women within 72 hours of the termination in accordance with current local guidelines.
- Products of conception should be treated in accordance with local and legislative protocols.
- A plan for future contraception should be made prior to undertaking abortion and arrangements made to implement this.

3.6 Clinical protocols

- Protocols should be consistent with established clinical evidence, such as those published in the RCOG Evidence-based Clinical Guidelines and in accordance with institutional guidelines.
- There should be written clinical protocols including dosage, administration, timing and follow up care, including diagnosis and management of failed attempted abortion; the latter should include the option of a repeat course of treatment. Protocols should have distinct provisions for early abortion (intra-uterine pregnancy of less than 63 days gestation), late first trimester abortion and second trimester abortion.
- There should be written information for women about treatment and follow up.
- Written consent should be obtained prior to the commencement of treatment.
- In New Zealand mifepristone must be administered by a health professional in a licensed premise.
- When a woman is discharged from the treatment facility, whether before or after completion of the abortion, she should be given clear written instructions as to how to access advice on a 24 hour basis and help in an emergency, as well as information about what to expect and follow-up arrangements. She should be accompanied by a support person who has been adequately informed about what to expect, until the abortion process is complete.
- Follow-up should be undertaken to ensure the abortion is complete. Local protocols should be developed which include clinical assessment and if indicated HCG estimations and/or ultrasound examination. Follow-up should also confirm ongoing access to and use of effective contraception.

4. Other suggested reading

RANZCOG Online Learning Module 'Abortion'
https://www.climate.edu.au/course/view.php?id=201

Hyland P, Raymond EG, Chong E. A direct-to-patient telemedicine abortion service in Australia: Retrospective analysis of the first 18 months. ANZJOG; 58 (3): 335-340.

Goldstone P, Walker C, Hawtin K. Effficacy and safety of mifepristone-buccal misoprostol for early medical abortion in an Australian clinical setting. ANZJOG 2017; 57: 366–371

Therapeutic Goods Administration 2012: Media Release: Registration of Mifepristone Linepharma (RU 486) and GyMiso (misoprostol), 30 August.
Available at: https://www.tga.gov.au/behind-news/registration-mifepristone-linepharma-ru-486-and-gymiso-misoprostol

Therapeutic Goods Administration (TGA) Product Information – MS-2 Step. Version 24 December 2014.
Available at https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2014-PI-01965-1

Therapeutic Goods Administration (TGA) Product Information. Mifepristone Linepharma 200 mg Tablet. Version 12-05-2015. Available at
https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2012-PI-02513-1

Australian Public Assessment Report for mifepristone/misoprostol.
Available at https://www.tga.gov.au/auspar/auspar-mifepristone-misoprostol

Swannel C. Medical abortion access extended. MJA. 27th Jan 2015
Available at: https://www.mja.com.au/insight/2015/2/medical-abortion-access-extended

New Zealand Medicines and Medical Devices Safety Authority (MEDSAFE) Data Sheet – MIFEGYNE Mifepristone micronised 200 mg tablets. June 2012.
Available at: http://www.medsafe.govt.nz/profs/datasheet/m/Mifegynetab.pdf

MS Health website
http://www.mshealth.com.au/

Royal College of Obstetricians and Gynaecologists. The Care of Women Requesting Induced Abortion. Evidence-based Clinical Guideline Number 7. RCOG Press November 2011. Available at:
https://www.rcog.org.uk/en/guidelines-research-services/guidelines/the-care-of-women-requesting-induced-abortion/

Shand C, Irvine H, Iyengar V. Guidelines for the use of mifepristone medical abortion in New Zealand: Abortion Supervisory Committee; 2004.

For more detail relevant to clinical treatment regimens, clinicians are referred to the RCOG guideline, the references it reviews, relevant Cochrane reviews and other peer-reviewed publications in this evolving literature.

Reports of Australian and New Zealand experience

de Costa CM. Use of mifepristone for medical abortion in Australia, 2006-2009. The Medical Journal Of Australia 2011; 194 (4): 206-7.

de Costa CM, Russell DB, de Costa NR, Carrette M, McNamee HM. Early medical abortion in Cairns, Queensland: July 2006 - April 2007. The Medical Journal Of Australia 2007; 187 (3): 171-3.

de Costa CM, Russell DB, de Costa NR, Carrette M, McNamee HM. Introducing early medical abortion in Australia: there is a need to update abortion laws. Sexual Health 2007; 4 (4): 223-6.

Dickinson JE, Brownell P, McGinnis K, Nathan EA. Mifepristone and second trimester pregnancy termination for fetal abnormality in Western Australia: Worth the effort. The Australian & New Zealand Journal Of Obstetrics & Gynaecology 2010; 50 (1): 60-4.

Goodyear-Smith F, Knowles A. Choosing medical or surgical terminations of pregnancy in the first trimester: what is the difference? The Australian & New Zealand Journal Of Obstetrics & Gynaecology 2009; 49 (2): 211-5.

Goodyear-Smith F, Knowles A, Masters J. First trimester medical termination of pregnancy: an alternative for New Zealand women. The Australian & New Zealand Journal Of Obstetrics & Gynaecology 2006; 46 (3), pp. 193-8.

Mamers PM, Lavelle AL, Evans AJ, Bell SM, Rusden JR, Healy DL. Women's satisfaction with medical abortion with RU486. The Medical Journal Of Australia 1997; 167 (6): 316-7.

Mulligan E, Messenger H. Mifepristone in South Australia - the first 1343 tablets. Australian Family Physician 2011; 40 (5): 342-5.

Petersen K. Abortion laws and medical developments: a medico-legal anomaly in Queensland. Journal Of Law And Medicine 2011; 18 (3): 594-600.

Petersen KA. Early medical abortion: legal and medical developments in Australia. The Medical Journal Of Australia 2010; 193 (1): 26-9.

Rose SB, Shand C, Simmons A. Mifepristone- and misoprostol-induced mid-trimester termination of pregnancy: a review of 272 cases. The Australian & New Zealand Journal Of Obstetrics & Gynaecology 2006; 46 (6): 479-85.

Shand C, Rose SB, Simmons A, Sparrow MJ. Introduction of early medical abortion in New Zealand: an audit of the first 67 cases. The Australian & New Zealand Journal Of Obstetrics & Gynaecology 2005; 45 (4): 316-20.

Sparrow M. Introducing Mifepristone into New Zealand. O&G 2004; 6 (2): 141-144.

5. Links to other College statements

Emergency contraception (C-Gyn 11)

Abortion (C-Gyn 17)

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

6. 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 and Board Member
Dr Gillian Gibson	Deputy Chair, Gynaecology
Dr Scott White	Deputy Chair, Obstetrics and Subspecialties Representative
Associate Professor Ian Pettigrew	Member and EAC Representative
Dr Kristy Milward	Member and Councillor
Dr Will Milford	Member and Councillor
Dr Frank O'Keeffe	Member and Councillor
Professor Sue Walker	Member
Dr Roy Watson	Member and Councillor
Dr Susan Fleming	Member and Councillor
Dr Sue Belgrave	Member and Councillor
Dr Marilyn Clarke	ATSI Representative
Associate Professor Kirsten Black	Member
Dr Thangeswaran Rudra	Member
Dr Nisha Khot	Member and SIMG Representative
Dr Judith Gardiner	Diplomate Representative
Dr Angela Brown	Midwifery Representative
Ms Ann Jorgensen	Community Representative
Dr Rebecca Mackenzie-Proctor	Trainee Representative
Prof Caroline De Costa	Co-opted member (ANZJOG member)
Dr Christine Sammartino	Observer

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 November 2007 and was most recently reviewed in March 2019.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 November 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

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.