Category: Best Practice Statement

The use of misoprostol in obstetrics and gynaecology

This statement has been updated in response to the Therapeutic Goods Administration (TGA) approval of misoprostol (oral 25ug) for Induction of Labour in women[1] and publication of the RANZCOG binational Clinical Guideline for Abortion Care. The interim update of this statement has been approved by the RANZCOG Women's Health Committee and RANZCOG 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 (Appendix B).

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 (Appendix C).

First endorsed by RANZCOG: November 2001
Current: March 2022 (updated March 2024)
Review due: March 2027

Objectives:	To provide advice on the use of misoprostol in obstetrics and gynaecology.
Target audience:	All health practitioners providing obstetrical and gynaecological care.
Background:	This statement was first developed by Women's Health Committee in November 2001 and reviewed in November 2019. The most recent interim update of this statement is to provide an update to regulatory information and signpost to recently updated College guidelines and statements. The statement draws on earlier evidence-based methodology (i.e. not GRADE methodology), for approval by the Women's Health Committee in February 2024 (Appendix B).
Funding:	The development and review of this statement was funded by RANZCOG.

[1] *RANZCOG currently uses the term 'woman' in its documents to include all individuals needing obstetric and gynaecological healthcare, regardless of their gender identity. The College is firmly committed to inclusion of all individuals needing O&G care, as well as all its members providing care, regardless of their gender identity.*

Contents

Purpose and scope

The purpose of this statement is to provide advice on the use of misoprostol in obstetrics and gynaecology, including the registration status of misoprostol in Australia and Aotearoa New Zealand. This statement covers the use of misoprostol for the medical management of miscarriage in the first and second trimesters. It also covers the administration of misoprostol in gynaecology prior to hysteroscopy.

Out of scope: Recommendations on abortion, the induction of labour, and the management of postpartum haemorrhage are out of scope for this statement, as these are provided in other relevant College statements and guidelines. For recommendations for misoprostol use in abortion, see the RANZCOG Clinical Guideline for Abortion Care. For recommendations for misoprostol use for the induction of labour, see the College statement Use of Prostaglandins for Induction of Labour (C-Obs 22). For recommendations on the management of postpartum haemorrhage, see the College statement Management of Postpartum Haemorrhage (C-Obs 43).

The statement draws on earlier evidence-based methodology (i.e., NHMRC methodology, that preceded the contemporary approaches to evidence synthesis using GRADE).

An interim partial update to the statement was undertaken in February 2024 to reflect updated regulatory information, and update evidence provided in the RANZCOG Clinical Guideline for Abortion Care and Use of Prostaglandins for Induction of Labour (C-Obs 22).

1. Plain language summary

Misoprostol is a medication that is available in Australia and Aotearoa New Zealand. It is used as part of the treatment for miscarriage (early pregnancy loss) and stillbirth, for abortion, induction of labour, and may also be used for the control of excessive bleeding after birth. When used in these settings, misoprostol is safe and effective, and can provide important benefits for women. These should be discussed with the doctor providing care.

2. Executive summary

This document discusses the use of misoprostol in Australia and Aotearoa New Zealand.

3. Table of recommendations

Recommendation 1	Grade
Misoprostol is appropriate for use, and demonstrates advantages over available alternatives, in the medical management of miscarriage.	Consensus-based recommendation
Good Practice Point	
The current Therapeutic Goods Administration (TGA) approved uses of misoprostol for obstetrics and gynaecology in Australia are induction of labour and abortion. There are no approved obstetrics and gynaecology indications in Aotearoa New Zealand, although it is widely used 'off-label' as outlined in this and other statements. Where practical any 'off-label' use should occur after obtaining and documenting informed consent from the woman.	
Recommendation 2	**Grade**
Misoprostol can be used in combination with mifepristone for management of some miscarriages.	Consensus-based recommendation

4. Introduction

There is considerable evidence in published studies about the use of misoprostol in obstetrics and gynaecology. There are in excess of 200 randomised controlled trials included in Cochrane Systematic Reviews, involving more than 35,000 women where misoprostol has been administered for obstetric or gynaecological indications.

5. Discussion and recommendations

Recommendation 1	Grade
Misoprostol is appropriate for use, and demonstrates advantages over available alternatives, in the medical management of miscarriage.	Consensus-based recommendation

5.1 Use in medical management of miscarriage

In general, the evidence demonstrates advantages of misoprostol over available alternatives for use in medical management of miscarriage. The advantages are that it is at least as effective as alternatives, has fewer side effects, is more practical to use and may be cheaper. Compared to surgical evacuation of the uterus, misoprostol is associated with a slightly higher rate of retained products of conception, vomiting and diarrhoea, but patient satisfaction is similar. There is no clear evidence that any route of administration or dosage regimen is superior to others[1].

5.2 Use in gynaecology

Misoprostol administration prior to hysteroscopy has been shown to reduce the need for mechanical dilatation and reduces the incidence of intra-operative complications (cervical laceration, false-track formation[2-4]). Vaginal administration, compared to oral, appears to reduce the time required for the priming to be effective and to reduce gastrointestinal side effects.[5]

5.3 Registration status of misoprostol

In Australia misoprostol is now registered for use in obstetrics through the use of a 25µg oral tablet of misoprostol for the induction of labour (at term), and gynaecology in a composite pack with mifepristone for the purpose of abortion up to 63 days gestation.

In 2012 misoprostol was registered in Australia for use orally or buccally in combination with mifepristone for abortion up to 49 days gestation. From February 2015 a composite pack containing both misoprostol and mifepristone was introduced with a new indication of abortion up to 63 days gestation. Whereas previously it was acceptable for misoprostol to be taken orally or buccally, the new indication for abortion up to 63 days requires misoprostol be administered buccally to maintain efficacy. This has been found to be effective and associated with few side-effects. For recommendations for misoprostol use in abortion, see the RANZCOG Clinical Guideline for Abortion Care.

In late 2022, the TGA listed the use of a 25µg oral tablet of misoprostol for the induction of labour (at term) in Australia. For recommendations for misoprostol use for the induction of labour, see the College statement Use of Prostaglandins for Induction of Labour (C-Obs 22).

The TGA approved product information and evidence based guidelines should be consulted for detailed information about appropriate regimens. [6, 7]

Misoprostol is included in the regimen for early medical abortion in the New Zealand Medsafe datasheet for mifepristone, but misoprostol itself is not registered for obstetric and gynaecological indications and its use is not an approved indication (unapproved medicine, 'off label').

The company that markets the widely used formulation of misoprostol which is registered for gastrointestinal indications has not researched, and does not support, its use in pregnancy, and has not expressed any intention to do so.

5.4 Use in clinical practice

Good Practice Point	
The current Therapeutic Goods Administration (TGA) approved uses of misoprostol for obstetrics and gynaecology in Australia are induction of labour and abortion. There are no approved obstetrics and gynaecology indications in Aotearoa New Zealand, although it is widely used 'off-label' as outlined in this and other statements. Where practical any 'off-label' use should occur after obtaining and documenting informed consent from the woman.	
Recommendation 2	**Grade**
Misoprostol can be used in combination with mifepristone for management of some miscarriages.	Consensus-based recommendation

6. Conclusion

There is reasonable evidence from peer reviewed literature attesting to the efficacy of misoprostol as a therapeutic agent in treating a number of conditions in Obstetrics and Gynaecology. Practitioners should be aware that when they prescribe it, they may be using it 'off-label' and, apart from in time-critical emergency settings, should only use it in clinical situations after obtaining and documenting informed consent from the woman.

The references which follow include information about dosage regimens evaluated.

7. References

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2. Al-Fozan H, Firwana B, Al Kadri H, Hassan S, Tulandi T. Preoperative ripening of the cervix before operative hysteroscopy. Cochrane Database of Systematic Reviews. 2015(4).
3. De Silva PM, Wilson L, Carnegy A, Smith PP, Clark TJ. Cervical dilatation and preparation prior to outpatient hysteroscopy: a systematic review and meta-analysis. BJOG : an international journal of obstetrics and gynaecology. 2021;128(7):1112-23.
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5. Abdelhakim AM, Gadallah AH, Abbas AM. Efficacy and safety of oral vs vaginal misoprostol for cervical priming before hysteroscopy: A systematic review and meta-analysis. European journal of obstetrics, gynecology, and reproductive biology. 2019;243:111-9.
6. TGA. GyMiso misoprostol 200 microgram oral tablet blister pack (188015) 2012. Available from: https://www.tga.gov.au/resources/artg/188015.
7. TGA. ANGUSTA (Norgine Pty Ltd) 2022. Available from: https://www.tga.gov.au/resources/prescription-medicines-registrations/angusta-norgine-pty-ltd.

8. Other suggested reading

National Consensus Guideline for Treatment of Postpartum Haemorrhage
http://www.health.govt.nz/publication/national-consensus-guideline-treatment-postpartum-haemorrhage

New Zealand Medicines and Medical Devices Safety Authority (MEDSAFE) Data Sheet – MIFEGYNE Mifepristone micronised 200 mg tablets. June 2012. Available at:
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Dodd JM, Crowther CA. Elective repeat caesarean section versus induction of labour for women with a previous caesarean birth. Review The Cochrane Database of Systematic Reviews 2006 Issue 4. Art. No.: CD004906. DOI: 10.1002/14651858.CD004906.

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Goldberg AB, Greenberg MB, Darney PD. Drug Therapy: Misoprostol and Pregnancy. New England Journal of Medicine 2001; 344: 38-47 (95 references).

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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: http://www.rcog.org.uk/files/rcog-corp/Abortion%20guideline_web_1.pdf

Weeks A, Fiala C, Safar P. Misoprostol and the debate over off-label (not an approved indication) drug use. BJOG 2005 Mar; 112 (3): 269-72.

9. Links to relevant College statements and guidelines

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

RANZCOG Clinical Guideline for Abortion Care

Birth after previous Caesarean Section (C-Obs 38)

Management of postpartum haemorrhage (C-Obs 43)

Use of Prostaglandins for Induction of Labour (C-Obs 22)

Appendices

Appendix A Women's Health Committee Membership

Name	Position on Committee
Dr Scott White	Chair
Dr Anna Clare	Deputy Chair (Gynaecology) and Councillor
Associate Professor Amanda Henry	Deputy Chair (Obstetrics) and Councillor
Dr Samantha Scherman	Member and Councillor
Dr Marilla Druitt	Member and Councillor
Dr Kasia Siwicki	Member and Councillor
A/Professor Jared Watts	Member and Councillor
Dr Victoria Carson	Member and Councillor
Dr Nisha Khot	Vice President and SIMG Representative
Dr Marilyn Clarke	Aboriginal and Torres Strait Islander Representative
Dr Angela Beard	He Hono Wahine representative
Dr Martina Mende	DRANZCOG representative
Dr Pallavi Desai	Specialist International Medical Graduate Representative
Professor Kirsten Black	Sexual & Reproductive Health Committee Representative
Dr Frank Clark	State representative - Tasmania
Dr Elizabeth Gallagher	Territory representative - ACT
Dr James Brown	State representative - VIC
Dr Kathy Saba	State representative - QLD
Adrienne Priday	Midwifery Representative, New Zealand
Dr Angela Brown	Midwifery Representative, Australia
Ms Leigh Toomey	Community Representative
Dr Steve Resnick	Co-opted member: Neonatalologist

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

i. 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. All members of the RANZCOG Guideline Development Group and 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.

ii. Steps in developing and updating this statement

This statement was originally developed in July 1992 and was most reviewed in November 2021. It was most recently reviewed by the Women's Health Committee in response to TGA approval of misoprostol (oral 25ug) for Induction of Labour and publication of the RANZCOG binational Clinical Guideline for Abortion Care. 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.
- In February 2024 the Women's Health Committee reviewed the updated statement out of session based on the available body of evidence in the clinical guideline, statement, and clinical expertise.

RANZCOG statements are developed according to the standards of the Australian 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 use of misoprostol 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 should be responsive to the needs of the individual person while using misoprostol and circumstances of each case.

Quality of information

The information available in Use of misoprostol in obstetrics and gynaecology (C-Obs 12) 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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Version	Date of Version	Pages revised / Brief Explanation of Revision
v1.1	Nov / 2001	Developed by WHC
v2.1	Nov / 2003	Reviewed by WHC
v3.1	Nov / 2005	Reviewed by Working party (WHC)
v4.1	Nov/2007	Reviewed by WHC
v5.1	Nov/2010	Reviewed by WHC
v6.1	Nov/2012	Reviewed by WHC
v7.1	Mar/2016	Reviewed by Sexual and Reproductive Health Advisory Group
V8.1	Mar/2022	Update approved by WHC, Council and Board
V8.2	Mar/2024	Interim update in response to TGA approval of misoprostol (oral 25ug) for Induction of Labour and publication of the RANZCOG binational Clinical Guideline for Abortion Care

Policy Version:	Version 8.2
Policy Owner:	Women's Health Committee
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