TERMINATION OF PREGNANCY
AND MISCARRIAGE IN THE
SECOND TRIMESTER

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Note:
This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.
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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.
If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient’s medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.
This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:
• The use of interpreter services where necessary,
• Advising consumers of their choice and ensuring informed consent is obtained,
• Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
• Documenting all care in accordance with mandatory and local requirements

Explanation of the aboriginal artwork:
The aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant women. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.

Purpose and Scope of PPG

The purpose of this guideline is to provide clinicians with information on how to terminate pregnancy or induce labour following fetal demise in the second trimester using medical methods. It describes medical management based on a woman’s obstetric history, medical history and her personal preferences.

Australian Aboriginal Culture is the oldest living culture in the world yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2-5 times more likely to die in childbirth and their babies are 2-3 times more likely to be of low birth weight. The accumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that perinatal services prepare to respectively manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.
Termination of Pregnancy and Miscarriage in the Second Trimester

Flowchart: Medical induction methods in the second trimester

- **Previous uterine surgery**
  - **No**
    - Safe and acceptable to delay birth by 36-48 hours
      - **Yes**
        - 200 mg mifepristone
        - 36-48 hours later
      - **No**
        - OR
          - **Sublingual**
            - 400 micrograms misoprostol subling every 3 hours *
          - **Vaginal**
            - 800 micrograms misoprostol PV followed by 400 micrograms misoprostol PV every 3 hours *
          - **Sublingual or Vaginal**
            - 200 micrograms misoprostol subling or PV every 3 hours
              (max 800 microg in 24 hours)
  - **Yes**
    - Gestation ≤ 25 weeks and 6 days
      - Safe and acceptable to delay birth by 36-48 hours
        - **Yes**
          - 200 mg mifepristone
          - 36-48 hours later
        - **No**
          - OR
            - **Sublingual or Vaginal**
              - 200 micrograms misoprostol subling or PV every 3 hours
                (max 800 microg in 24 hours)
          - **Gestation 26 weeks – 27 weeks and 6 days**
            - Safe and acceptable to delay birth by 36-48 hours
              - **Yes**
                - 200 mg mifepristone
                - 36-48 hours later
              - **No**
                - OR
                  - **Sublingual or Vaginal**
                    - 200 micrograms misoprostol subling or PV every 3 hours
                      (max 800 microg in 24 hours)

*There is no recommended maximum dose of misoprostol, rather continued administration until products passed up to 24 hours following first misoprostol administration*. 
# Table: Medical induction methods in the second trimester

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<td>Misoprostol 400 microg PV every 3 hours until products passed for up to 24 hours</td>
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Termination of Pregnancy and Miscarriage in the Second Trimester

Table of Contents

Purpose and Scope of PPG ................................................................. 1
Flowchart: Medical induction methods in the second trimester .................. 2
Table: Medical induction methods in the second trimester .......................... 3
Summary of Practice Recommendations .................................................. 6
Abbreviations ...................................................................................... 6
Introduction .......................................................................................... 7
Parameters for late termination of pregnancy services ................................. 7
Medical methods ................................................................................. 7
Mifepristone ......................................................................................... 8
Indications ......................................................................................... 8
Contraindications .............................................................................. 8
Interactions ....................................................................................... 8
Side effects ........................................................................................ 8
Misoprostol .......................................................................................... 9
Advantages ........................................................................................ 9
Indications ....................................................................................... 9
Contraindications .............................................................................. 9
Precautions ........................................................................................ 9
Side effects ....................................................................................... 10
Seek medical review if: ........................................................................ 10
Misoprostol route of administration .......................................................... 10
Mifepristone and Misoprostol Regimen for second trimester TOP and Miscarriage........................................... 10
Mifepristone and misoprostol regimen ....................................................... 10
If safe and acceptable to delay birth by 36-48 hours and NO contraindications to mifepristone: .............................................................. 10
Where delaying labour is unacceptable to the woman, contraindications to mifepristone and/or considered unsafe (for example maternal sepsis): .................................................. 10
Misoprostol regimen ........................................................................... 11
WITH previous uterine scar AND gestational age of up to 25 weeks and 6 days 11
WITHOUT previous uterine scar AND gestational age up to 27 weeks and 6 days 11
WITH previous uterine scar AND gestational age of 26 weeks to 27 weeks and 6 days 11
If no products passed after 24 hours .................................................... 11
Additional information ...................................................................... 11
Gestational age of up to 26 weeks with previous uterine scar OR up to 28 weeks without previous uterine scar .................................................. 11
Gestational age of 26-28 weeks gestation with previous uterine scar ................ 11
Observations ...................................................................................... 12
Management of complications .............................................................. 12
Haemorrhage ................................................................................... 12
Retained products of conception ............................................................ 12
Infection ........................................................................................... 12
Rare complications ........................................................................... 12
References ....................................................................................... 13
Useful references .............................................................................. 13
Acknowledgements ........................................................................... 14
Summary of Practice Recommendations

Second trimester miscarriage and termination of pregnancy using mifepristone and misoprostol is effective and may be preferred to surgical methods of uterine evacuation by many women.

When delay of induction of labour is safe and acceptable to the patient, administration of a single dose of 200mg mifepristone orally 36-48 hours prior to commencing misoprostol is recommended.

Recommended misoprostol regimen depends on gestational age and the presence of previous uterine surgery.

Route of administration of misoprostol depends on the woman’s preference.

If no products passed after 24 hours of commencing misoprostol, consider:

> Repeating misoprostol regimen.
> Repeating mifepristone with misoprostol regimen commencing a further 36-48 hours later.
> Other methods of induction of labour (intravaginal gemeprost, extra-amniotic prostaglandins, oxytocin infusion) or surgical evacuation.

Perinatal service providers need cultural sensitivity within a non-judgemental environment when planning care for the Aboriginal woman.

Aboriginal women should be referred to an Aboriginal Health Professional to support their care.

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>ACOG</td>
<td>American College of Obstetrics and Gynaecology</td>
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<td>bpm</td>
<td>Beats per minute</td>
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<tr>
<td>et al</td>
<td>And others</td>
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<td>FDA</td>
<td>Food and Drug Administration (United States)</td>
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<td>g</td>
<td>Gram(s)</td>
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<td>Int</td>
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<td>IUGR</td>
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<td>Infectious Diseases</td>
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<td>Intravenous</td>
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<td>kg</td>
<td>Kilogram</td>
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<td>Milligram(s)</td>
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<td>microg</td>
<td>Microgram(s)</td>
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<td>Millilitre(s)</td>
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<td>NSAIDs</td>
<td>Non-steroidal anti-inflammatory drugs</td>
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<td>PO</td>
<td>Oral</td>
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<td>PPG</td>
<td>Perinatal Practice Guideline</td>
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<td>PV</td>
<td>Per vaginum</td>
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<tr>
<td>RANZCOG</td>
<td>The Royal Australian and New Zealand College of Obstetricians and Gynaecologists</td>
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<td>RCOG</td>
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<td>SAS</td>
<td>Special access scheme</td>
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<td>subling</td>
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<td>stat</td>
<td>immediately</td>
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<td>TGA</td>
<td>Therapeutic Goods Administration (Australian)</td>
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<td>TOP</td>
<td>Termination of pregnancy</td>
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<td>US</td>
<td>United States</td>
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Introduction

Women may prefer medical rather than surgical termination of pregnancy (TOP) depending on gestation, women’s preference and other clinical considerations. The medical officer counselling the pregnant woman should discuss the following to inform her choice:

- Does the woman wish to see and hold her baby and/or create mementos
- Is the experience of labour important to her?
- Time involved for different methods of termination
- The possibility that a surgical procedure may preclude viewing and handling of the fetus and may lead to some limitations with pathological examination?
- The possibility that the fetus may show signs of life following a medical TOP
- Any specific clinical circumstances (e.g. uterine scar) that may influence choice

For both TOP and second trimester miscarriage, the medical officer should discuss (and gain consent for) other possible investigations if indicated (e.g. amniocentesis, fetal tissue for chromosome analysis and/or DNA storage, histopathological investigation of the placenta) and autopsy.


Aboriginal people experience very high levels of grief and loss in their communities. Miscarriage demands diverse ceremonial acknowledgement. Discuss with the Aboriginal health professional.

Second trimester medical termination of pregnancy or management of miscarriage with mifepristone followed by a prostaglandin is effective and is associated with considerably shorter induction to delivery intervals than methods using prostaglandin alone or supplemented by oxytocin infusion.

Parameters for late termination of pregnancy services

It is important to note the following parameters in place within the institutions that provide late TOP services:

- TOP must commence on or by 22 weeks and 6 days gestation (22+6) at the Flinders Medical Centre, Lyell McEwin Hospital and the Women’s and Children’s Hospital.
- If a woman requests a TOP after this time, it may still be possible following agreement at case conferencing as per local policy (see Perinatal Loss PPG available at [www.sahealth.sa.gov.au/perinatal](http://www.sahealth.sa.gov.au/perinatal)).

Medical methods

Regimens for medical termination of pregnancy or management of miscarriage in the second trimester may include:

- mifepristone and misoprostol OR
- misoprostol alone
Mifepristone

In Australia, mifepristone is TGA approved for preparation for the action of registered prostaglandin analogues that are indicated for the termination of pregnancy for medical reasons beyond the first trimester. Mifepristone is a steroid derived from norethisterone that acts by blocking the effects of progesterone, a hormone necessary for the continuation of a pregnancy. Mifepristone is anti-progesterone, which sensitises the myometrium to prostaglandins, increases uterine contractility, and softens and dilates the cervix. It is not sufficient for medical termination of pregnancy when used on its own, but is effective when used synergistically with prostaglandins.

Medical practitioners wishing to prescribe mifepristone and misoprostol must be registered with and certified by MS Health via the secure healthcare professional website www.ms2step.com.au (for more information see Standards for the Management of Termination of Pregnancy in SA available at www.sahealth.sa.gov.au/perinatal).

Note: Registered medical practitioners with a Fellowship of the Royal Australian New Zealand College Obstetricians Gynaecologists will not have to complete the training but are still required to register with MS Health as part of the medical termination of pregnancy Risk Management Plan.

Indications

Mifepristone, in combination with a prostaglandin may be given for:

- Second trimester genetic termination of pregnancy
- Intrauterine fetal death (see Medical Management of Late IUFD PPG available at www.sahealth.sa.gov.au/perinatal)
- Late second trimester miscarriage

Contraindications

- Confirmed or suspected ectopic pregnancy
- Severe hepatic impairment
- Chronic adrenal failure
- Inherited porphyria
- Intrauterine device in situ
- Known hypersensitivity to mifepristone
- Concurrent long-term corticosteroid therapy.
- Bleeding conditions or concomitant administration of anticoagulants

Interactions

The following may interact with the action of mifepristone:

- Erythromycin, rifampicin
- Itraconazole
- Carbamazepine, phenytoin, phenobarbital
- St John’s Wort
- Grapefruit juice
- Non-steroidal anti-inflammatory medications (NSAIDs) – caution, theoretically NSAIDs/ aspirin could reduce the efficacy of mifepristone
- Corticosteroids – the efficacy of long-term corticosteroids (including inhaled corticosteroids) may be reduced by mifepristone due to its anti-glucocorticoid activity

Side effects

- Uterine bleeding
- Gastrointestinal (nausea, vomiting, diarrhoea)
Misoprostol

Misoprostol is a synthetic prostaglandin E1 analogue. Serum misoprostol peak levels occur at 34 and 80 minutes respectively for oral and vaginal routes of administration⁴.

Misoprostol is not approved for use during pregnancy because it causes miscarriage, vaginal bleeding and in continuing pregnancies, fetal malformations including the Mobius sequence (congenital facial paralysis, with or without limb defects)⁵. Misoprostol is approved by the Australian Therapeutic Goods Administration (TGA) in combination with mifepristone for the medical termination of pregnancy up to 63 days gestation. However, there is evidence and support for the off-label use of misoprostol for the management of miscarriage and termination of pregnancy in the second trimester⁶.

As an abortifacient in the second trimester, misoprostol, in combination with mifepristone has shown a success rate of 90% with a low recourse to surgical intervention for retained products⁷. A randomised study comparing misoprostol (800 micrograms vaginally followed by 400 micrograms orally every 3 hours) and gemeprost (1 mg vaginally every 6 hours) in combination with mifepristone reported similar complete abortion rates between the two regimens⁸.

In view of the significant saving and ease of storage associated with misoprostol, it is the preferred prostaglandin for second trimester termination of pregnancy².

Misoprostol, as a single agent has been found to have much higher failure rates in early pregnancy termination when compared to misoprostol in combination with mifepristone⁹ and is therefore not recommended as a single agent regimen. Exceptions to this are cases where delaying labour is unacceptable to the patient or considered unsafe (for example maternal sepsis).

Sublingual administration has a greater bioavailability than oral administration presumably because of the absence of a hepatic first pass effect, and a similar time to peak levels. Time to peak levels is longer after vaginal administration, but the effect may be more sustained after vaginal administration¹⁰.

A systematic review comparing vaginal and sublingual misoprostol for second trimester termination of pregnancy found the vaginal route more effective however was associated with more adverse effects and was less preferred by women compared to the sublingual route¹¹.

Advantages

> Inexpensive
> Stored at room temperature
> Few systemic side effects
> Rapidly absorbed orally or vaginally
> Effective in causing uterine contractions

Indications

> Second trimester genetic termination of pregnancy
> Second trimester miscarriage
> Intrauterine fetal death (see Medical Management of Late IUFD PPG available at www.sahealth.sa.gov.au/perinatal)

Ensure informed consent is signed before commencing treatment

Contraindications

Known hypersensitivity to misoprostol or other prostaglandin

Precautions

Bronchospasm and collapse are rare but may occur when prostaglandins are administered to asthmatics
Side effects
Although there are relatively few side effects, the following may occur:
> Pyrexia
> Vomiting
> Diarrhoea
> Flushing and shivering
> Headache

Administer antiemetics, antipyretics as indicated with medical order.

Seek medical review if:
> Abnormal abdominal pain or other symptoms of uterine rupture
> Dizziness
> Temperature > 38˚ Celsius (may be a prostaglandin E effect or an indication of chorioamnionitis)

Antipyretics such as paracetamol (1 g orally) can be administered

Misoprostol route of administration
Ensure that informed verbal consent is obtained and documented.
The two preferred routes for misoprostol administration in this setting are sublingual and vaginal.
The first vaginal misoprostol dose should be administered by a medical officer.

Mifepristone and Misoprostol Regimen for second trimester TOP and Miscarriage

Mifepristone and misoprostol regimen
If safe and acceptable to delay birth by 36-48 hours and NO contraindications to mifepristone:
Mifepristone single dose 200 mg PO STAT
PLUS
Misoprostol 36 to 48 hours later dictated by gestational age and the presence or absence of a previous uterine scar (see below)

Where delaying labour is unacceptable to the woman, contraindications to mifepristone and/or considered unsafe (for example maternal sepsis):
Do NOT give mifepristone
Give misoprostol ONLY as per regimen dictated by gestational age and the presence or absence of a previous uterine scar (see below).
Termination of Pregnancy and Miscarriage in the Second Trimester

Misoprostol regimen

**WITH previous uterine scar AND gestational age of up to 25 weeks and 6 days**

**OR**

**WITHOUT previous uterine scar AND gestational age up to 27 weeks and 6 days**

**Sublingual** (the route usually preferred by women)

Misoprostol 400 microg (200 microg x 2 tablets) subling every three hours until products passed for up to 24 hours

**OR**

**Vaginally**

Misoprostol 800 micrograms (200 microg x 4 tablets) stat PV followed by misoprostol 400 microg (200microg x 2 tablets) PV every three hours until products passed up to 24 hours.

There is no recommended maximum dose of misoprostol, rather continued administration until products passed or 24 hours following first misoprostol administration.

**WITH previous uterine scar AND gestational age of 26 weeks to 27 weeks and 6 days**

Sublingual or vaginally

200 microg misoprostol every three hours for a maximum of 800 microg every 24 hours

If no products passed after 24 hours

Consider repeating the same dose regimen or other method of induction. (e.g. intravaginal gemeprost, extra-amniotic prostaglandins, intravenous oxytocin or mechanical or osmotic cervical dilatation).

Mifepristone can be repeated 3 hours following the last dose of misoprostol, followed by the misoprostol regimen commencing 36-48 hours later.

Additional information

**Gestational age of up to 26 weeks with previous uterine scar OR up to 28 weeks without previous uterine scar**

The use of misoprostol in women with previous caesarean or transmural uterine scar has been debated because of concerns regarding an increased risk of uterine rupture. The International Federation of Obstetrics and Gynaecology (FIGO) released guidelines in 2017 for the use of misoprostol in pregnancy based on the evidence available. These guidelines included recommendations for women with previous caesarean sections and concluded that for pregnancies up to 26 weeks gestation, the rates of uterine rupture were extremely low and comparable to those of women with no previous uterine scar. Therefore, for gestations of up to 26 weeks, women with a previous caesarean scar are recommended the same misoprostol regimen that is used for women with no previous uterine surgery.

**Gestational age of 26-28 weeks gestation with previous uterine scar**

For gestational ages of 26-28 weeks there was insufficient evidence available to recommend a misoprostol regimen. However, a systematic review from 2004 found that misoprostol was safe for use in cases of previous caesarean section at up to 28 weeks. Therefore, for cases of previous caesarean section or transmural scar at gestations between 26-28 weeks, it is recommended that the lowest effective dose of misoprostol be used.
Observations

Perform the following observations before commencing procedure and every 4 hours following mifepristone administration and hourly after misoprostol administration (unless otherwise indicated)

> Temperature
> Pulse
> Respiration
> Uterine activity
> Vaginal loss
> Accurate fluid balance chart

Management of complications

Haemorrhage

Severe haemorrhage requires ready access to dilatation and curettage facilities.
Less heavy but persistent bleeding is better managed with further home medication with oral misoprostol and avoidance of surgery where possible.

Retained products of conception

The option of inpatient or outpatient medical management depends on the amount of bleeding, symptoms / signs of infection and the woman’s preference. Either:

> Medical management with further misoprostol (800 microg stat buccally followed by 400 microg buccally every 3 hours up to a maximum of 1600 microg i.e. 4 doses)

OR

> Surgical management with dilatation and curettage

Infection

If signs of infection, follow management for chorioamnionitis as per the Antibiotics in the Perinatal Period PPG available at www.sahealth.sa.gov.au/perinatal

Rare complications

> Uterine rupture
> Amniotic fluid embolus
References


Useful reference

Termination of Pregnancy and Miscarriage in the Second Trimester

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