Clinical Guideline
South Australian Perinatal Practice Guidelines – medical induction for 2nd trimester terminations of pregnancy and miscarriages

Policy developed by:  SA Maternal & Neonatal Clinical Network
Approved SA Health Safety & Quality Strategic Governance Committee on: 10 June 2014
Next review due: 31 July 2017

Summary
Clinical practice guideline for the management of the woman undergoing a medical induction for a second trimester termination of pregnancy, and those experiencing a miscarriage.

Keywords
induction, uterine surgery, sublingual, vaginal, mifepristone, misoprostol, gemeprost, syntocinon, surgical termination, second trimester, medical termination, Perinatal Practice Guidelines, medical induction for 2nd trimester terminations of pregnancy and miscarriages, clinical guideline

Policy history
Is this a new policy?  N
Does this policy amend or update an existing policy?  Y
Does this policy replace an existing policy?  Y
If so, which policies?
Medical induction for 2nd trimester terminations of pregnancy and miscarriages

Applies to
All SA Health Portfolio
All Department for Health and Ageing Divisions
All Health Networks
CALHN, SALHN, NALHN, CHSALHN, WCHN, SAAS
Other

Staff impact
All Clinical, Medical, Nursing, Allied Health, Emergency, Dental, Mental Health, Pathology

PDS reference  CG151

Version control and change history

<table>
<thead>
<tr>
<th>Version</th>
<th>Date from</th>
<th>Date to</th>
<th>Amendment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>18 Dec 2004</td>
<td>19 Mar 2007</td>
<td>Original version</td>
</tr>
<tr>
<td>2.0</td>
<td>19 Mar 2007</td>
<td>19 Sept 2011</td>
<td>Reviewed</td>
</tr>
<tr>
<td>3.0</td>
<td>19 Sept 2011</td>
<td>10 June 2014</td>
<td>Reviewed</td>
</tr>
<tr>
<td>4.0</td>
<td>10 June 2014</td>
<td>Current</td>
<td></td>
</tr>
</tbody>
</table>
South Australian Perinatal Practice Guidelines

medical induction for 2\textsuperscript{nd} trimester terminations of pregnancy and miscarriages

© Department of Health, Government of South Australia. All rights reserved.

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.

SA Health does not accept responsibility for the quality or accuracy of material on websites linked from this site and does not sponsor, approve or endorse materials on such links.

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.
Medical induction methods in the second trimester

<table>
<thead>
<tr>
<th>Induction – no previous uterine surgery</th>
<th>Misoprostol (misoprostol 200 micrograms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt; Misoprostol may be given sublingual or vaginally</td>
</tr>
<tr>
<td></td>
<td>Sublingual</td>
</tr>
<tr>
<td></td>
<td>&gt; 400 micrograms (i.e. 2 tablets) misoprostol every three hours for a total of 1600 micrograms of misoprostol or a total of 4 doses in 24 hours</td>
</tr>
<tr>
<td></td>
<td>Vaginal</td>
</tr>
<tr>
<td></td>
<td>&gt; 400 micrograms misoprostol tablets per vaginam every six hours for a total of four doses in 24 hours</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Misoprostone and mifepristone</td>
</tr>
<tr>
<td></td>
<td>&gt; Single dose 200 mg mifepristone</td>
</tr>
<tr>
<td></td>
<td>After 36-48 hours</td>
</tr>
<tr>
<td></td>
<td>&gt; Misoprostol may be given sublingual or vaginally</td>
</tr>
<tr>
<td></td>
<td>Sublingual</td>
</tr>
<tr>
<td></td>
<td>&gt; misoprostol 400 micrograms every 3 hours to a maximum of 4 doses in 24 hours</td>
</tr>
<tr>
<td></td>
<td>Vaginal</td>
</tr>
<tr>
<td></td>
<td>&gt; stat dose misoprostol 800 micrograms</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mifepristone and gemeprost</td>
</tr>
<tr>
<td></td>
<td>&gt; Single dose 200 mg mifepristone</td>
</tr>
<tr>
<td></td>
<td>After 36-48 hours</td>
</tr>
<tr>
<td></td>
<td>&gt; gemeprost 1 mg vaginally every 3 hours to a maximum of five pessaries in 24 hours</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oxytocin</td>
</tr>
<tr>
<td></td>
<td>&gt; The high dose infusion regimen may be considered when other methods of induction have failed</td>
</tr>
<tr>
<td></td>
<td>(see in <a href="#">Oxytocin high dose infusion regimen for IUFD</a>)</td>
</tr>
</tbody>
</table>

| Induction – previous uterine surgery | Discuss the dosage / regimen with the obstetrician / consultant if the woman has had previous uterine surgery |
Introduction

> Many women prefer medical rather than surgical termination of pregnancy when it is available and suitable for them.
> Second trimester medical termination 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.

Medical methods

> Regimens for medical termination of pregnancy in the second trimester may include a combination of:
  > mifepristone and misoprostol
  > mifepristone and gemeprost
  OR
  > misoprostol OR gemeprost alone
> The oxytocin high dose infusion regimen may be considered when other methods of induction have failed (see in oxytocin high dose infusion regimen for IUFD).

Care of women with a history of uterine surgery

> The method and/or dose of induction agent/s for second trimester induction of labour should take into account the clinical circumstances, availability of preparations and local guidelines and be determined in consultation with the obstetrician/consultant.
> Women with a single lower segment scar should be advised that, in general, induction of labour with prostaglandin is safe but not without risk.
> Women with two previous LSCS should be advised that, in general, the absolute risk of induction of labour with prostaglandin is only a little higher than for women with a single previous LSCS.
> Women with more than two LSCS deliveries or atypical scars should be advised that the safety of induction of labour is unknown.

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).
> 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)
And
> Is generally indicated for late second trimester miscarriage
> Ensure informed consent is signed before commencing treatment

Contraindications
> Confirmed or suspected ectopic pregnancy
> Renal or hepatic impairment
> Chronic adrenal failure
> Severe uncontrolled asthma
> Hereditary porphyria (disorder of enzymes in the haeme biosynthetic pathway that affects the skin, nervous system or both)

Precautions
> The following may interact with the action of mifepristone:
  > Erythromycin, rifampicin
  > Ketoconazole,
  > Carbamazepine, Phenytoin, phenobarbitol
  > Corticosteroids
  > NSAIDs (backup in Stockley’s Drug Interactions)
  > St John’s Wort
  > Grapefruit juice

Side effects
> Uterine bleeding and gastrointestinal (nausea, vomiting, diarrhoea)

Mifepristone and prostaglandin regimens

Mifepristone and misoprostol
> Give oral mifepristone 200 mg followed 36 to 48 hours later by sublingual misoprostol 400 micrograms every 3 hours to a maximum of 4 doses in 24 hours²
> Alternatively give oral mifepristone 200 mg followed 36 to 48 hours later by misoprostol 800 micrograms vaginally

Mifepristone and gemeprost
> Give oral mifepristone 200 mg followed 36 to 48 hours later by gemeprost 1 mg vaginally every 3 hours to a maximum of five pessaries in 24 hours²

Observations
> Perform the following observations before commencing procedure, then every 4 hc (unless otherwise indicated) until prostaglandin is commenced:
South Australian Perinatal Practice Guidelines

medical induction for 2nd trimester terminations of pregnancy and miscarriages

- Temperature
- Pulse
- Respirations
- Uterine activity
- Vaginal loss
- Record an accurate fluid balance chart
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 administration. 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). Misoprostol is not approved by the Australian Therapeutic Goods Administration (TGA) for use beyond the first trimester in pregnancy.

> As an abortifacient in the second trimester, the vaginal regimen of misoprostol has shown a success rate of 90% with a low recourse to surgical intervention for retained products.

> An Australian prospective randomised controlled trial by Dickinson et al., 1998, comparing intravaginal misoprostol 200 micrograms every 6 hours for 4 doses with gemeprost 1 mg every 3 hours for 5 doses, found no difference in induction to delivery interval or side effects apart from an increase in vomiting with misoprostol.

> In view of the significant saving and ease of storage associated with misoprostol, Dickinson et al., 1998 have recommended that misoprostol should be the preferred prostaglandin for second trimester termination of pregnancy.

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 administration.

Indications

> Second trimester genetic termination of pregnancy
> Second trimester miscarriage
> Intrauterine fetal death (see medical management of late IUFD)
> Ensure informed consent is signed before commencing treatment

Contraindications

> Known sensitivity to misoprostol or other prostaglandin

Advantages

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

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:

- Temperature > 38˚ Celsius (may be a prostaglandin E effect or an indication of chorioamnionitis)
- Chorioamnionitis (rising C-Reactive Protein, offensive / purulent vaginal discharge, maternal pulse > 100 bpm, uterine tenderness) requires antibiotic treatment. Give ampicillin 2 g IV initial dose, then 1g IV every 4 hours, gentamicin 5 mg / kg IV daily, metronidazole 500 mg IV every 12 hours, unless allergic to penicillin
- If allergic to penicillin, give lincomycin 600 mg IV in 100 mL over 1 hour every 8 hours OR clindamycin 450 mg IV in 50 – 100 mL over at least 20 minutes every 8 hours AND gentamicin 5 mg / kg IV daily until delivery
- Antipyretics such as Paracetamol (1 g rectally) can be administered
- Abnormal abdominal pain or other symptoms of uterine rupture
- Dizziness

Precaution

- Bronchospasm and collapse are rare but may occur when prostaglandins are administered to asthmatics

Dosage and administration

- Ensure that informed verbal consent is obtained and documented
- There are three possible routes of misoprostol administration:
  - Oral
  - Sublingual
  - Vaginal
- The first intravaginal misoprostol dose should be administered by a medical officer

Termination for genetic reasons and mid trimester miscarriage

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

- 400 micrograms (200 micrograms x 2 tablets) misoprostol every three hours for a total of 1600 micrograms of misoprostol or a total of 4 doses in 24 hours

**Vaginally**

- 400 micrograms misoprostol tablets per vaginam every six hours for a total of four doses in 24 hours

Second trimester intrauterine fetal death

- See [medical management of late IUFD](#) under misoprostol – dosage and administration – Before 34^{th} weeks of gestation

If no products passed after 24 hours

**Sublingual and per vaginam**

- Consider repeating the same dose regimen or other method of induction. (e.g. intravaginal gemeprost, extra-amniotic prostaglandins, intravenous oxytocin)
- **NB**: Intravenous oxytocin should not commence within 4 hours of the last intravaginal dose of misoprostol

* refer to individual hospital midwifery standard
medical induction for 2nd trimester terminations of pregnancy and miscarriages

Observations
> Perform the following observations before commencing procedure and hourly thereafter:
  > Temperature
  > Pulse
  > Respirations
  > Uterine activity
  > Vaginal loss
  > Record an accurate fluid balance chart
medical induction for 2nd trimester terminations of pregnancy and miscarriages

References


Useful references
medical induction for 2\textsuperscript{nd} trimester terminations of pregnancy and miscarriages


Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACOG</td>
<td>American College of Obstetrics and Gynecology</td>
</tr>
<tr>
<td>bpm</td>
<td>Beats per minute</td>
</tr>
<tr>
<td>et al</td>
<td>And others</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration (United States)</td>
</tr>
<tr>
<td>g</td>
<td>Gram(s)</td>
</tr>
<tr>
<td>Int</td>
<td>International</td>
</tr>
<tr>
<td>IV</td>
<td>Intravenous</td>
</tr>
<tr>
<td>J</td>
<td>Journal</td>
</tr>
<tr>
<td>kg</td>
<td>Kilogram</td>
</tr>
<tr>
<td>mg</td>
<td>Milligram(s)</td>
</tr>
<tr>
<td>mL</td>
<td>Millilitre(s)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Non-steroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>RANZCOG</td>
<td>The Royal Australian and New Zealand College of Obstetricians and Gynaecologists</td>
</tr>
<tr>
<td>RCOG</td>
<td>Royal College of Obstetricians and Gynaecologists</td>
</tr>
<tr>
<td>SAS</td>
<td>Special access scheme</td>
</tr>
<tr>
<td>TGA</td>
<td>Therapeutic Goods Administration (Australian)</td>
</tr>
<tr>
<td>US</td>
<td>United States</td>
</tr>
</tbody>
</table>

Version control and change history

**PDS reference**: OCE use only

<table>
<thead>
<tr>
<th>Version</th>
<th>Date from</th>
<th>Date to</th>
<th>Amendment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>18 Dec 2004</td>
<td>19 Mar 2007</td>
<td>Original version</td>
</tr>
<tr>
<td>2.0</td>
<td>19 Mar 2007</td>
<td>19 Sept 2011</td>
<td>Reviewed</td>
</tr>
<tr>
<td>3.0</td>
<td>19 Sept 2011</td>
<td>11 July 14</td>
<td>Reviewed</td>
</tr>
<tr>
<td>4.0</td>
<td>11 July 14</td>
<td>Current</td>
<td></td>
</tr>
</tbody>
</table>