

Standardised Maternal Guideline for Induction of Labour with Misoprostol



A Western Cape Provincial Reference Group compiled this guideline for use in the Western Cape Province of South Africa with contributions from staff of the health facilities and academic institutions in the province. It was accredited by the Western Cape Clinical Guidelines Advisory Committee, established by the Provincial Government to advise on matters related to the development of clinical guidelines that deal with interventions provided at all levels of care, and to accredit those guidelines that meet pre-specified standards or criteria. Professor J Volmink, the director of the South African Cochrane Centre, chairs the advisory group.

For the purpose of this guideline, induction of labour is defined as an intervention designed to artificially initiate uterine contractions leading to progressive dilatation of the cervix and delivery of the baby, from 28 weeks of gestation onwards (the legal gestational age of fetal viability). This will include induction of labour in women with intact membranes and women with spontaneous rupture of membranes but who are not in labour. Induction of labour is only indicated when it is agreed that the mother or fetus will benefit from a higher probability of a healthy outcome than if the birth is delayed.

Background

This guideline is a priority and was identified as such by the Maternal Guidelines Committee after publication of the 2002 and 2006 Saving Mothers Report (Confidential Enquiry into Maternal Mortality in South Africa). The off-label use of misoprostol as alternative to the much more expensive registered drugs for induction of labour caused concern as there is no single provincial guideline ensuring safe use of the drug, even though there is extensive published evidence available. About 20% of

pregnant women will require induction of labour, which usually requires more than one intervention and will present challenges to clinicians, health care workers and mothers. As most mothers requiring induction of labour have an underlying medical problem, safe delivery in the appropriate setting is a priority.

Target group

These guidelines are mainly intended for use by midwives and doctors conducting deliveries at level 1

The Maternal, Child and Women's Health (MCWH) sub-directorate of the Western Cape established the Maternal Guidelines Reference Group after the publication of the first Saving Mothers Report. The reference group consists of the rural MCWH co-ordinators, clinicians from both academic and secondary hospitals in the province and personnel involved in nursing training. The mandate was to address the recommendations of the Saving Mothers report with a specific aim to produce evidence-based but user-friendly guidelines on key conditions, and to plan implementation and monitor usage of these guidelines.

To ensure uniformity, the Clinical Guidelines Advisory Committee was established by the Provincial Government of the Western Cape's Health Department in July 2003.

This committee advises on matters related to the development of clinical guidelines in all disciplines and at all levels of care and accredits those guidelines that meet pre-specified standards or criteria. The guidelines are appraised using the AGREE¹ (Appraisal of Guidelines Research & Evaluation) tool.

Once the guideline advisory committee is satisfied that a guideline fulfils all these criteria, it is accredited for use and distributed throughout the province as a policy document. It is hoped that the wider circulation of these documents may help reduce the burden of maternal mortality.

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1. The AGREE Collaboration. Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument 2001. www.agreecollaboration.org (last accessed 10 October 2007).

(district hospital) and level 2 (secondary hospital) of care in the Western Cape province of South Africa. Although tertiary care requires more individualised treatment, the guidelines can also be used at tertiary level of care under the discretion of the managing clinician.

Local protocol development

This provincial guideline can be used as a basis to develop local protocols for use in all facilities able to provide obstetric services.

Guideline development

This guideline is a local adaptation of Evidence Based Clinical Guideline No. 9 (Induction of Labour) of the Royal College of Obstetricians and Gynaecologists of the UK, and additionally incorporates an extensive review on the use of misoprostol in a South African setting using current world literature (up to October 2006) as well as the Cochrane Library up to issue 1 of 2007. It was developed over a period of 12 months through a process of review by

- The Maternal Guidelines Reference Group
- External review by experts from both academic hospitals and secondary hospitals in the Western Cape province.

Additionally the guideline was sent for peer review to 3 general obstetrics and gynaecology specialists at secondary level hospitals, 8 medical officers working in obstetrics at district level, 4 midwives at all levels of care, the pharmaceutical coding committee for the Western Cape, 3 anaesthetists, an emergency services representative, the provincial spokesperson on medico-legal concerns and 2 patient representatives.

Implementation

The guideline is based on the current regimen of induction of labour as was used at Tygerberg Hospital, Mowbray Maternity Hospital and Paarl and Worcester Secondary Hospitals over the past 3 years, and as such it has been extensively piloted. Implementation of this guideline requires fetal heart rate monitoring, preferably with cardiotocography, as well as the ability to do a safe caesarean section within 1 hour of decision.

Levels of evidence

- Ia** Evidence obtained from a systematic review of meta-analysis of randomised controlled trials
- Ib** Evidence obtained from at least one randomised controlled trial
- IIa** Evidence obtained from at least one well-designed controlled study without randomisation
- IIb** Evidence obtained from at least one other type of

well-designed quasi-experimental study

- III** Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies
- IV** Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

Grading of recommendations

- A** Evidence level Ia and Ib
- B** Evidence level IIa, IIb or III
- C** Evidence level IV.

Induction of labour according to level of care

The following patients can be safely induced at **district (level 1) hospitals**

- Post-term pregnancy in an otherwise healthy mother with no complications and no previous uterine surgery (including caesarean section)
- Prelabour rupture of membranes (confirmed) ≥ 34 weeks' gestation in an otherwise healthy mother with no complications or previous uterine surgery (including caesarean section)
- Intrauterine fetal death (uncomplicated)
- Logistic factors (e.g. history of precipitous labour and large distance from hospital)
- Mild to moderate pre-eclampsia at gestation of 36 weeks or more.

The following patients can be safely induced at **level 2 (secondary) hospitals** (with specialist cover) or **district hospitals with level 2 beds** (must be discussed with the consultant at the level 2 hospital first)

- Gestational hypertension with proteinuria (≥ 34 weeks)
- Prelabour rupture of membranes ≥ 32 weeks
- Gestation > 41 weeks (accurate gestational age)
- Gestation > 41 weeks (unsure dates, with amniotic fluid index of < 5)
- Intrauterine growth restriction (≥ 34 weeks)
- Previous history of intrauterine death > 28 weeks gestation, of unknown cause (induce at 38 weeks)
- Chorioamnionitis
- Logistic factors (e.g. history of precipitous labour and large distance from hospital)
- One previous abruptio placentae (induce at 38 weeks)

Summary: recommendations from the RCOG guideline

Place of induction of labour

- C** Healthy women with an otherwise uncomplicated pregnancy: induction of labour can be conducted in the antenatal ward
- C** Induction of labour for women with recognised risk factors including suspected fetal growth compromise, high parity or previous caesarean section should preferably be induced in labour ward or special induction suite

Fetal surveillance and induction of labour

- C** Facilities should be available for continuous uterine and fetal heart rate monitoring wherever induction of labour occurs
- C** Fetal wellbeing should be established immediately prior to induction of labour
- B** Following induction of labour with misoprostol, fetal wellbeing should be established within 30 minutes. Continuous monitoring should be done for 45 minutes
- C** When oxytocin is used for induction or augmentation of labour, continuous fetal heart rate monitoring should be used

Uterine hypercontractility

- B** In cases of uterine hypercontractility and suspicious or pathological CTG secondary to oxytocin infusion, the oxytocin infusion should be discontinued or decreased
- A** In the presence of abnormal fetal heart rate patterns and uterine hypercontractility, tocolysis should be considered
- B** In cases of suspected or acute fetal compromise, delivery should be accomplished as soon as possible, taking clinical considerations into account. The accepted standard is, ideally, within 30 minutes
- C** When undertaking induction of labour in women with recognised risk factors (including suspected fetal growth compromise, previous caesarean section, high parity), the clinical decision should be undertaken at consultant level

Prolonged pregnancy

- A** An ultrasound scan to confirm gestational age should ideally be offered to all women before 20 weeks of gestation as this reduces the need for induction of perceived post-term pregnancy
- A** Women with uncomplicated pregnancies should be offered induction of labour beyond 41 weeks

Diabetes in pregnancy

- C** Women who have pregnancies complicated by diabetes should be offered induction of labour prior to the estimated date for delivery

Prelabour rupture of membranes

- A** Women with prelabour rupture of membranes at term (beyond 37 weeks) should be offered a choice of immediate induction of labour or expectant management.
- A** Expected management should not exceed 96 hours following membrane rupture

Methods of induction

- A** Prostaglandins should be used in preference to oxytocin when induction is undertaken in women with intact membranes, regardless of cervical favourability
- A** Either prostaglandins or oxytocin may be used for induction of labour in women with rupture of membranes, regardless of cervical status, as they are equally effective
- C** Oxytocin should not be started within 6 hours following administration of cervical prostaglandins
- C** Amniotomy should be performed where feasible prior to oxytocin administration
- C** Oxytocin administration should start at a low dose of 1 - 2 mU per minute and increased at 30-minute intervals or more

Contraindications to labour induction

Malpresentation (e.g. transverse lie, footling breech)
Absolute cephalopelvic disproportion
Placenta praevia
Previous major uterine surgery or classic caesarean section
Cord presentation
Active genital herpes
Maternal convenience
Any gynaecological, obstetric or medical condition that precludes vaginal delivery

- Medical conditions: diabetes in pregnancy after 38 weeks
- Patients with one previous caesarean section who require induction for valid indications (misoprostol not indicated, use Prepidil® gel)
- Induction of labour for other reasons but with breech

presentation (try external cephalic version first)

- Women with high parity (5 or more previous deliveries) (misoprostol not indicated, use Prepidil® gel)
- Any woman with a body mass index (BMI) $\geq 40 - 50$ who needs induction of labour for other reasons must be evaluated by the anaesthetist on call before induction is started.

The following patients will need referral to a **tertiary (level 3) hospital for evaluation for induction of labour**, presuming that they have had antenatal care at level 2. Discuss with the level 3 hospital before referral.

- Medical conditions: diabetes with extensive end-organ damage, maternal cardiac lesions especially stenotic lesions, auto-immune disease
- Any induction <32 weeks' gestation, for fetal proximity to a neonatal ICU

- Any underlying maternal condition that may require level 3 anaesthetic care (e.g. BMI >50)
- Eclampsia complicated by organ failure.

A. Induction of labour with misoprostol

Background

The synthetic prostaglandin E₁ analogue, misoprostol (Cytotec®), was developed as a treatment for NSAID-induced ulcers, but has been widely used in obstetrics and gynaecology, even though it has never been registered for this use. Its advantages over prostaglandin E₂/dinoprostone (Prepidil gel® or Prandin®) are cost (R4.05/200 µg tablet v. R222.64/1 mg tube in 2006) and the fact that it is stable at room temperature and therefore does not need to be kept refrigerated. It is a highly effective stimulator of uterine contractions, and it is this that makes its use potentially dangerous – uterine hyperstimulation and rupture are well-documented complications, and these may be life threatening. Confusion as to the correct dose is also possible, as the dose used in gynaecology for inducing first-trimester abortion is massively more than the dose appropriate to third-trimester induction of labour. It is therefore vital that its use in the induction of labour be kept within the constraints of clear guidelines, and with very careful monitoring of both mother and fetus. **(Ia)**

Pharmacodynamics

Misoprostol shows different dynamics according to the route of administration. This will clearly influence the frequency of dosage. Oral misoprostol is rapidly absorbed (peak concentration at 12 minutes) and has a half-life of 30 - 40 minutes; rectal or vaginal misoprostol has a much slower absorption, with a bioavailability of 4 - 6 hours. The sublingual route has rapid onset, prolonged action and a total bioavailability many times greater than the oral route. For this reason, the sublingual route should NOT be used for induction of labour in the third trimester. Misoprostol deteriorates in solution, and solutions should therefore be dated, and discarded after 24 hours. **(Ia)**

Other constraints

The vaginal route is not recommended in the presence of ruptured membranes, as it washes out, and there is an increased risk of infection. **(IV)**

Before induction of labour, the condition of the baby must be assessed as being reassuring. **(Ia)** This is done ideally by cardiotocographic (CTG) monitoring (normal baseline, good variability, no decelerations). **(IV)**

During induction of labour, a CTG must be started within 30 minutes of administering the dose to exclude fetal heart changes, or the presence of tachysystole (>5 contractions in 10 minutes) or hypertonus (contraction lasting >2 minutes). Monitoring should be continued for

45 minutes after each dose. Induction of labour without electronic monitoring is not ideal, and in that case patients should preferably be referred to hospitals where electronic monitoring is available. **(III)**

Assess the dilatation of the cervix and descent of the head 4-hourly during the latent phase, and 4-hourly in the active phase of labour, and enter the findings on the partogram. **(IV)**

If the woman is not in labour within 24 hours of starting induction, reassess the situation. The options are any of the following

1. Stop the induction, wait a day and start again (for non-urgent indications)
2. Choose another method of induction of labour:
 - EASI (extra-amniotic saline infusion)* or
 - Amniotomy followed by oxytocin 1 hour later
3. Proceed to caesarean section (CS) (EASI unsuccessful or amniotomy not possible or not indicated).

The use of misoprostol induction is contraindicated in the following circumstances:

- Previous uterine surgery (CS, myomectomy, hysterotomy) **(III)**
- Grand multiparity (para 5 or more) **(IIa)**
- Intrauterine growth impairment/placental insufficiency **(IIa)**
- Any other circumstances where induction of labour in general is contraindicated.

Regimen for pregnancies 26 weeks' gestation or more

Do a full abdominal examination, cervical assessment and 10-minute CTG to exclude fetal distress. If the cervix is favourable (Bishop score 8 or more – see table on p. 47) and there is no contraindication to rupture of membranes (HIV test negative) and no fetal distress, do a sterile rupture of membranes followed by oxytocin administration 1 hour later, if no adequate contractions by then. Try to do rupture of membranes early in the morning so that progress can be assessed during office hours when there are more senior personnel on duty.

If the cervix is unfavourable (Bishop score <8) or the patient is HIV positive, and there is no fetal distress,

*Protocol for EASI (Ib)

Pass a speculum. After cleaning the cervix and fornices thoroughly with Betadine/Hibitane, using sterile technique place a F18-30 Foley's catheter with a 30 - 45 ml bulb through the cervix to beyond the internal cervical os. Fill the bulb with 40 - 50 ml of water. Tape the catheter under light tension to the thigh. Attach an infusion set with room temperature normal saline to the catheter port of the Foley and infuse at 40 ml per hour and continue until the catheter is removed or expelled. Start with oxytocin if necessary after expulsion of the catheter.

Bishop score	0	1	2	3
Station	3	-2	-1/0	Engaged
Position	Posterior	Mid cavity	Anterior	
Effacement	>4cm	3 - 4 cm	1 - 2 cm	<1 cm
Dilatation	<1cm	1 - 2 cm	3 - 4 cm	>4 cm
Consistency	Firm	Medium	Soft	

start with oral induction with misoprostol as follows (oral dose of 50 µg):

Dissolve one tablet (200 µg) of misoprostol in 200 ml water. This gives a concentration of 1 µg/ml. The binder does not dissolve, and leaves a chalky deposit in the cup. Shake the solution well before each administration. Unused solution must be discarded after 24 hours. Alternatively one tablet of 200 µg can be cut (with a scalpel blade) or broken into 4 even sized pieces (of 50 µg each).

Fifty ml (50 µg) is given orally. Do a CTG within 30 minutes after administration; this CTG must run for at least 45 minutes. Repeat this procedure (that is: 10 minute CTG to exclude fetal distress, followed by a 50 µg misoprostol dose, followed by a 45-minute CTG) every 4 hours orally until contractions start. An alternative regime is 25 ml/25 µg every 2 hours for 24 hours.

Should oxytocin be necessary, it should be delayed till at least 6 hours after the last dose of oral misoprostol, to avoid hyperstimulation. **(III)**

It is not necessary to wait these periods before rupturing membranes, should this be indicated (Bishop score >8).

Do not continue with the misoprostol once regular adequate contractions have started (i.e. two or more moderate contractions in 10 minutes) because of the danger of uterine hyperstimulation. **(Ia)**

If uterine tachysystole or hypertonus occurs, give salbutamol (Ventolin®) 250 - 500 µg intravenously slowly, diluted in 10 ml water for injection, or nifedipine (Adalat®) 20 mg orally should be given, if there are no contraindications to these drugs. **(Ia)**

If fetal distress develops at any time during induction, do intrauterine resuscitation (turn mother on left side, give 40% oxygen with face or nasal mask, stop any oxytocin administration, give a 200 ml fluid bolus intravenously and suppress contractions as above with salbutamol or nifedipine).

Regimen for pregnancies less than 26 weeks

Should it be necessary to terminate a pregnancy before 26 weeks, e.g. with an intrauterine death or a severe fetal abnormality, it is generally necessary to use bigger doses of misoprostol.

24 - 26 weeks: Oral misoprostol 100 µg (i.e. ½ tablet), repeated 2 hourly x 2. If no response, give 200 µg (1 tablet) 2-hourly per os x 2. **(III)**

<24 weeks: Oral misoprostol 200 µg 2-hourly x 2, thereafter 400 µg orally 2-hourly x 2 if necessary. **(Ia)**

Failure to induce labour could suggest that the pregnancy is extrauterine.

Special cases: Induction of labour (for obstetric reasons) in HIV-positive patients (or patient who declined HIV testing)

- Do not rupture membranes unless it is inevitable.
- Follow the same guidelines as for misoprostol.
- If labour does not start after 24 hours of misoprostol, and mother has been on a prevention of mother-to-child transmission (PMTCT) programme of drug treatment with AZT since 28 weeks, or in the case of good adherence to HAART therapy, do a sterile rupture of membranes and follow with oxytocin as above.
- If not on good antiretroviral cover, induce labour with oxytocin, for a maximum of 8 hours - if no effect, do a CS for failed induction of labour (if maternal condition allows for anaesthetic).
- If the maternal condition is not favourable for anaesthetic (advanced HIV disease), do a sterile rupture of membranes and try to deliver the baby as soon as possible to minimise risk of HIV transfer.

B. Induction of labour with Prepidil® or Prandin® gel

Vaginal prostaglandins in the form of commercially available intracervical or intravaginal prostaglandin E₂ gel preparations should be used when misoprostol is contraindicated or not recommended, according to the dose recommended by the manufacturers. There is no difference in the outcome between the use of intracervical or intravaginal gel. **(Ia)**

Typical scenarios would include:

- Induction of labour with one previous caesarean section
- Induction of labour with fetal intrauterine growth restriction or severe pre-eclampsia
- Fetal compromise.

C. Suggested dose of oxytocin for induction of labour (after rupture of membranes) (IV)

- Put ten units (10 IU) oxytocin in one litre (1 l) normal saline (0.9%)
- Rinse infusion set after oxytocin has been added
- Administer as side infusion with infusion pump
- Increase dose every 30 minutes until there are adequate contractions.

Dose	60 drops per milliliter (dpm) set	20 dpm set
12 ml/h (2 mU/min)	12 dpm	4 dpm
24 ml/h (4 mU/min)	24 dpm	8 dpm
36 ml/h (6 mU/min)	36 dpm	12 dpm
48 ml/h (8 mU/min)	48 dpm	16 dpm
60 ml/h (10 mU/min)	60 dpm	20 dpm
72 ml/h (12 mU/min)	72 dpm	24 dpm

Precautions

- Stop or decrease oxytocin if there are more than 4 contractions in 10 minutes or if the uterus does not relax between contractions.
- Do continuous CTG during oxytocin administration
- Monitor contractions by hand if electronic monitoring is not satisfactory, for at least 10 minutes every half hour
- Stop oxytocin with any signs of fetal distress.

Suggested further reading

- ACOG Committee on Obstetric Practice. Committee opinion. Induction of labour for vaginal birth after cesarean delivery. *Obstet Gynecol* 2002; 99(4): 679-680.
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