Queensland Clinical Guidelines

Translating evidence into best clinical practice

Maternity and Neonatal **Clinical Guideline**

Preterm labour and birth

Queensland Government

Document title:	Preterm labour and birth
Publication date:	June 2020
Document number:	MN20.6-V10-R25
Document supplement:	The document supplement is integral to and should be read in conjunction with this guideline.
Amendments:	Full version history is supplied in the document supplement.
Amendment date:	December 2022
Replaces document:	MN20.6-V9-R25
Author:	Queensland Clinical Guidelines
Audience:	Health professionals in Queensland public and private maternity and neonatal services
Review date:	June 2025
Endorsed by:	Queensland Clinical Guidelines Steering Committee Statewide Maternity and Neonatal Clinical Network (Queensland)
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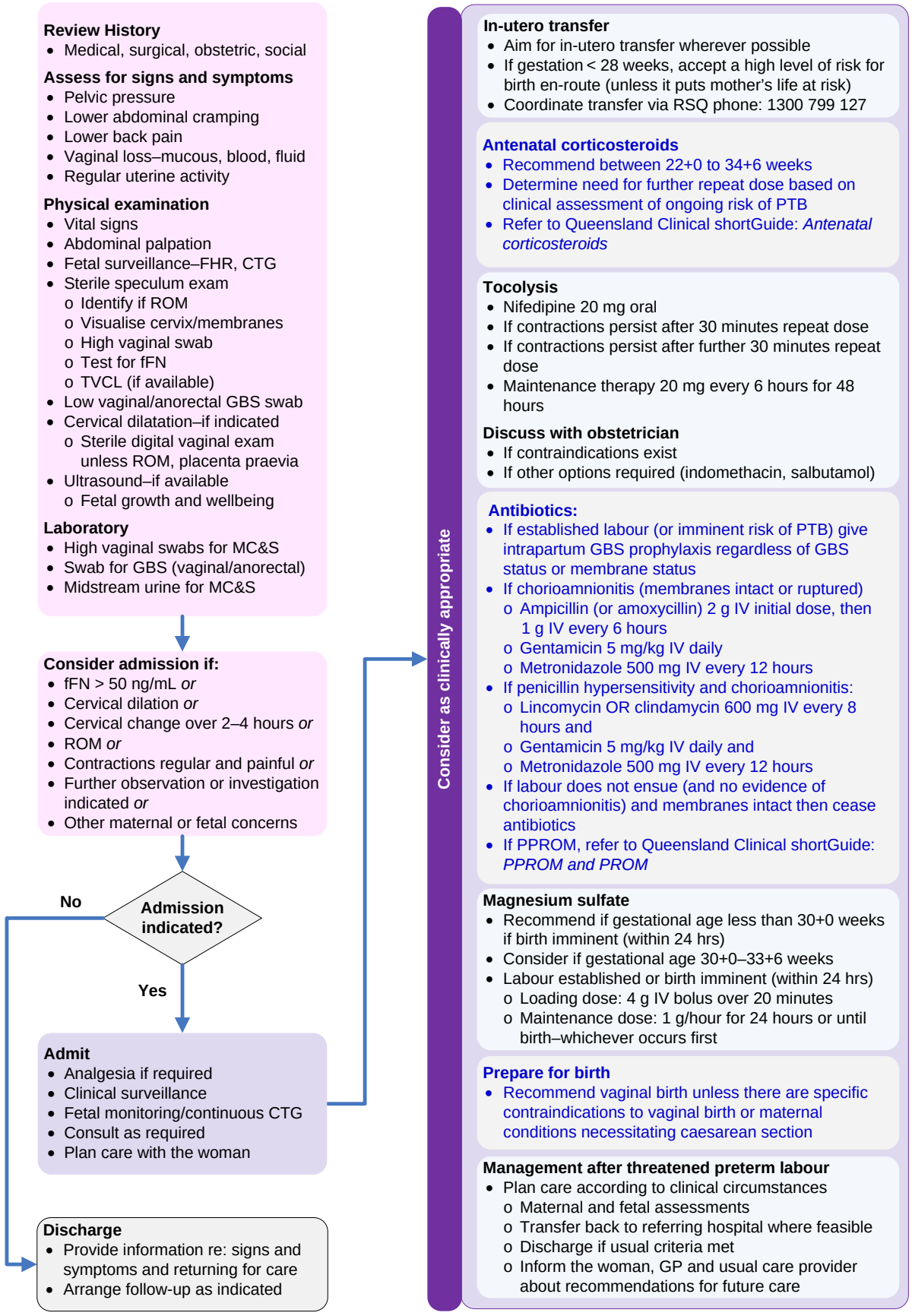
Cultural acknowledgement

The Department of Health acknowledges the Traditional Custodians of the lands, waters and seas across the State of Queensland on which we work and live. We also acknowledge First Nations peoples in Queensland are both Aboriginal Peoples and Torres Strait Islander Peoples and pay respect to the Aboriginal and Torres Strait Islander Elders past, present and emerging.

Recommended citation: Queensland Clinical Guidelines. Preterm labour and birth. Guideline No. MN20.6-V10-R25. Queensland Health. June 2020. Available from: http://www.health.qld.gov.au/qcg.

Flow Chart: Assessment and management of preterm labour (< 37 weeks)



Queensland Clinical Guidelines: Preterm labour and birth. Flowchart version: F20.6-1-V10-R25

CTG: Cardiotocograph, **EOGBSD:** early onset group B *Streptococcus* disease, **fFN**: Fetal fibronectin, **FHR:** Fetal heart rate, **g:** grams, **GBS:** Group B *Streptococcus*, **GP:** general physician, **hrs**: hours, **IM:** Intramuscular, **IV:** Intravenous, **kg:** kilogram, **MC&S:** microscopy, culture & sensitivity, **mg:** milligrams, **PROM:** Prelabour rupture of membranes, **PPROM:** Preterm prelabour rupture of membranes, **PTB:** Preterm birth, **RSQ:** Retrieval Services Queensland, **ROM:** Rupture of membranes, **TVCL:** Transvaginal cervical length, **>:** greater than, **<:** less than

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Abbreviations

aOR	Adjusted odds ratio
BP	Blood pressure
BV	Bacterial vaginosis
CI	Confidence interval
CS	Caesarean section
CTG	Cardiotocograph
fFN	Fetal fibronectin
FHR	Fetal heart rate
GBS	Group B *streptococcus*
GP	General practitioner
IM	Intramuscular
IV	Intravenous
MC&S	Microscopy, culture and sensitivity
OR	Odds ratio
PPROM	Preterm prelabour rupture of membranes
PROM	Prelabour rupture of membranes
PTB	Preterm birth
QH	Queensland Health
RR	Risk ratio
RSQ	Retrieval Services Queensland
TVCL	Transvaginal cervical length

Definition of terms

Cervical incompetence	In this guideline, cervical incompetence is defined as the inability to support a full term pregnancy due to a functional or structural defect of the cervix. This is often characterised by dilatation and shortening of the cervix prior to 37 weeks gestation.[1]
Fetal fibronectin	Fetal fibronectin (fFN) is a glycoprotein thought to promote adhesion between the fetal chorion and maternal decidua. • Normally present in low concentrations in the cervicovaginal secretions between 18 and 34–36 weeks gestation, rising as term approaches[2] Elevated levels of fFN (typically greater than 50 ng/mL) in cervicovaginal secretions after 22 weeks gestation are associated with an increased risk of preterm birth (PTB).
Health care providers	May include (but not limited to) obstetrician/gynaecologist, neonatologist, social worker, Aboriginal and Torres Strait Islander health worker, general practitioner, midwife, nurse, nurse practitioner, obstetrician, maternal-fetal medicine specialists, social worker pharmacy, anaesthetics.
Imminent risk of PTB	Substantial risk of birth within 24 hours as clinically determined by the woman's health care provider.
Preterm	Gestational age less than 37+0 completed weeks with subcategories of PTB based on weeks of gestational age[3]: • Late preterm (34+0–36+6 weeks) • Moderately preterm (32+0–33+6 weeks) • Very preterm (28+0–31+6 weeks) • Extremely preterm (less than 27+6 weeks) • Where gestational age is less than 25+6 weeks refer to the Queensland Clinical Guideline *Perinatal care at the threshold of viability*[4]
Short cervix	In this guideline, short cervix is defined as less than 25 mm in the second trimester of pregnancy.

1 Introduction

Preterm labour is a multifactorial condition associated with a high risk of neonatal morbidity and mortality, especially at lower gestational ages. The incidence of preterm birth (PTB) continues to rise world-wide. In Queensland in 2017, PTB (less than 37 weeks gestation) occurred in 9.4% of all pregnancies. In Australia in 2017, PTB accounted for[5]:

- 1 in 11 births
- 8.7% of all singleton births
- 66% of all twin births
- 14.2% of all the births to Aboriginal and/or Torres Strait Islander women
- 18.4% of all perinatal deaths

1.1 Background

Gestational age, along with individual circumstances and preferences may impact antenatal clinical management and neonatal outcomes.[6] Preterm is commonly defined as gestational age less than 37+0 completed weeks with subcategories of PTB based on weeks of gestational age[3]:

- Late preterm (34+0–36+6 weeks)
- Moderately preterm (32+0 to 33+6 weeks)
- Very preterm (28+0 to 31+6 weeks)
- Extremely preterm (less than 27+6 weeks)

Where gestational age is less than 25+6 weeks refer to the Queensland Clinical Guideline *Perinatal care at the threshold of viability.*[4]

1.2 Perinatal mental health

Early and unexpected labour, birth and the hospitalisation of a preterm baby can be distressing for mothers and families. Early recognition, referral and treatment (if required) of mental health issues may assist the woman with the often difficult decision making associated with preterm labour and birth.[7]

Table 1. Perinatal mental health

Aspect	Consideration
Context	• In Australia 10% of women experience antenatal anxiety and/or depression, increasing to 16% in the postnatal period[8] • Women, and families, experience significantly higher levels of stress, anxiety and depression when facing the diagnosis of preterm labour and/or birth compared with those who birth a baby at term[9]
Strategies	• Recommend screening women regularly throughout the pregnancy using validated tools[9] (e.g. Edinburgh Postnatal Depression Scale (EDPS)) • Offer referral to perinatal mental health support (e.g. social work, mental health teams, peer support groups)
Communication	• Share and discuss information with the woman and her family, in a manner that enables informed choice and supports woman centred care • Offer information to women and families based on individual circumstances o Refer to Queensland Clinical Guidelines parent information: ▪ *Preterm labour and birth*[10] ▪ *Transferring a sick or unwell baby*[11] • Adhere to usual/standard care recommendations (e.g. women centred care, respectful communication, consent and informed decision making) o Refer to Queensland Clinical Guidelines *Standard care*[12]
Model of care	• Support models of care that maximise continuity (e.g. midwifery continuity of care, case management, midwife navigator, social work, general practitioner (GP)) • A multidisciplinary healthcare approach to care is essential o Involve the relevant healthcare providers to support the woman's individual choice

2 Risk assessment

The cause of spontaneous preterm labour remains unidentified in up to half of all cases.[13] Although many factors have been associated with an increased risk of spontaneous PTB[3], there is a relative paucity of high level research.[13,14] The majority of women with traditional risk factors will not experience PTB and of those women who do, many have no identifiable risk factors. Whether or not some risk factors are markers for other conditions and/or other risk factors is unknown.

Table 2. Risk factors associated with preterm birth

Aspect	Consideration
Maternal characteristics	• Age of woman[3,5]: o Younger than 20 years o Older than 40 years • Women who smoke during pregnancy[5]: o 13.6% babies are born preterm compared to 8.1% of babies whose mothers did not smoke • Women residing in rural and remote areas[5]: o 13.5% babies are born preterm compared to 8.4% in major cities • Risk of PTB based on ethnicity compared to Caucasian women[15]: o African American women: increased (OR 2.0, 95% CI 1.8 to 2.2)[16] o East African women: increased (aOR 1.55, 95% CI 1.27 to 1.90)[17] o Asian or Hispanic women: no significant difference[17] • Women who identify as Aboriginal and/or Torres Strait Islander[5]: o 14.2% babies are born preterm compared to 8.5% of babies born to non-Indigenous women • Late or no antenatal care • Lack of continuity of care • Low socio-economic status • High or low body mass index (BMI)
Medical and pregnancy conditions	• Multiple birth[5]: o 66% of twins o 98.2% of all other multiples (triplets and higher order) • Presence of fetal fibronectin (fFN) in the vaginal secretions • Short cervical length[18]: o Previous PTB recurrence risk related to gestational age of prior PTB[19] o Approximately 30% of women who give birth prematurely in a prior pregnancy will give birth before 37 weeks in a subsequent pregnancy[6] ▪ Extremely preterm: 0.5%, aOR 2.0, (95% CI 1.6 to 2.3)[19] ▪ Very preterm: 6.8%, aOR 3.0, (95% CI 2.9 to 3.2)[19] ▪ Moderately preterm: 37.7%, aOR 2.2, (95% CI 2.2 to 2.3)[19] • Genital tract infections[1]: o Bacterial vaginosis[20] risk of PTB doubled • Urinary tract infections[21] • Vaginal bleeding[21] • Assisted reproduction[21] associated with two-fold risk of PTB • Preterm prelabour rupture of membranes (PPROM) • Surgical procedures involving the cervix[22] • Uterine anomalies[21] • Polyhydramnios/oligohydramnios • Chronic medical conditions • Acute medical conditions (e.g. preeclampsia, antepartum haemorrhage)

3 Risk reduction

Table 3. Risk reduction measures

Aspect	Consideration
Assessment and counselling	• Assess risk factors preconception • Perform a comprehensive review of all previous pregnancies because the most important historical risk factor is prior spontaneous PTB[13,23] • Counsel women, and refer to appropriate clinicians in the multidisciplinary team (as appropriate) about modifiable risk factors o Smoking cessation interventions reduce PTB rate by 18% (RR 0.86, 95% CI 0.74–0.98)[20] o Optimisation of control of underlying chronic diseases reduces risk[14] o Lifestyle (e.g. balanced diet, activity limitations, stress management) • Perform a psychosocial assessment and refer as appropriate for support (e.g. social work or mental health services, health worker, peer support) • Refer to Section 6 Perinatal mental health
Bacterial vaginosis (BV)	• Bacterial vaginosis (BV) has been associated with increased risk of PTB[20] • Women with previous PTB may benefit from routine screening and treatment of BV[20] o Routine screening and treatment for asymptomatic BV, in women with low risk pregnancies, is of minimal benefit • In women with abnormal vaginal flora, treatment with antibiotics may reduce the risk of PTB [refer to Section 5.5 Antibiotics]
Bacteriuria	• Asymptomatic bacteriuria has been associated with risk of PTB • Urinary tract infection is associated with threatened preterm labour • Screen and recommend treatment for urinary tract infections (asymptomatic bacteriuria, cystitis, pyelonephritis) with antibiotics
Cervical length measurement	• Recommend routine cervical length measurement to women during the mid-trimester morphology (18–20 weeks) ultrasound scan[18,24,25] o Support use of a consistent technique for accurate measurement of cervical length at all mid-trimester scans o Document cervical length in medical and hand-held records • Consider serial transvaginal cervical length (TVCL) measurement for high risk women with prior PTB[26] o The optimal frequency has not been established[27] o From 14–24 weeks gestation, serial TVCL every two[1] weeks may be appropriate[28] • Change in transvaginal sonographic cervical length over time is not a clinically useful test to predict PTB in women with singleton or twin pregnancies o A single cervical length measurement obtained at 18–24 weeks[22,29] gestation appears to be a better test to predict PTB than changes in cervical length over time[30] • Refer to section 3 Risk reduction

3.1 Progesterone therapy

Table 4. Progesterone therapy

Aspect	Consideration
Context	• Progesterone therapy is reported to reduce the risk of PTB before 34 weeks from 27.5% to 18.1% (RR 0.66; 95% CI:0.52 to 0.83) in women with short cervical length[31] • Limited evidence about the optimal regimen and longer term health effects • One meta-analysis showed no difference in effect between 90 mg, 100 mg and 200 mg progesterone pessaries for women with a short cervix[31] • Conflicting evidence for interventions for multiple pregnancies with a shortened cervix[18,32,33]—further research required
Recommendation	• For singleton pregnancies recommend vaginal progesterone [18,34,35] 200 mg nocte[24] from 16–36 weeks gestation[25,36] for women with: o An incidentally diagnosed shortened cervix[34] (less than or equal to 25 mm) on TVCL between 16–24 weeks[31] or o A prior spontaneous PTB between 20–34 weeks (with or without preterm prelabour rupture of membranes)[36]

*Refer to an Australian pharmacopoeia for complete drug information
^Support women at risk of PTB to have ready access to vaginal progesterone when indicated

3.2 Cervical cerclage

Table 5. Cervical cerclage

Aspect	Consideration
Context	• Compared with no treatment, cervical cerclage reduces the incidence of PTB in women at risk of recurrent PTB before 37 weeks gestation[37] • Consider individual clinical circumstances and the potentially serious risks associated with the procedure[35,37] • If cervical cerclage is offered, counsel women about the risk of uterine contractions, bleeding, ruptured membranes or infection[37]
Recommendation	• Offer cerclage where medically indicated including where the cervix continues to shorten despite the use of vaginal progesterone o Cared for, or in collaboration with, an expert practitioner • If cervical length less than or equal to 10 mm consider cervical cerclage[18], vaginal progesterone or a combination of both • Consider for women with history of[35]: o One or more prior spontaneous PTB and/or second-trimester loss related to painless/painful cervical dilation[38] and in the absence of labour or placental abruption *or* o Prior cerclage due to painless cervical dilation in second trimester[38] *or* o Cervical incompetence • Consider if TVCL less than 25 mm before 24 weeks if[22]: o PPROM in a previous pregnancy *or* o A history of cervical trauma/surgery *or* o Prior spontaneous PTB before 34 weeks gestation *and* o Current singleton pregnancy • Limited data about the effectiveness of rescue cerclage particularly beyond 24 weeks gestation, therefore individualise decisions[1] • Multiple dilation and evacuations or cervical surgery (e.g. cone biopsy, large loop excision of the transformation zone, laser ablation, diathermy) or other abnormalities (e.g. Mullerian anomaly) are not themselves an indication for cerclage • Not recommended for women with: o Funnelling of the cervix without cervical shortening of 25 mm or less[29] o An incidentally identified short cervix without a history of spontaneous PTB or second trimester loss[22] o Multiple pregnancy[39] • Emergency cerclage with cervical dilation more than 1 cm prior to neonatal viability may be considered based on clinical presentation[1] • If cervical cerclage, ensure a plan in place for removal of the suture[22]

4 Clinical assessment of preterm labour

Identifying and treating women with symptoms of preterm labour, provides the opportunity to utilise interventions to minimise the impact of PTB. Only around 10% of women who present with symptoms of preterm labour (contractions) will deliver preterm.[2]

Appropriate clinical diagnosis of preterm labour may reduce unnecessary interventions and hospitalisations.

Table 6. Clinical assessment

Aspect	Consideration
Review history	• Medical • Surgical • Obstetric • Psychosocial and lifestyle • Refer to Table 2. Risk factors associated with preterm birth
Signs and symptoms	• The most common sequence preceding PTB is cervical ripening (shortening of the cervix), followed by decidual membrane activation and then contractions[7] characterised by: o Cervical effacement/dilatation o Pelvic pressure o Lower abdominal cramping o Lower back pain o Vaginal loss (mucous, blood or fluid) o Regular uterine activity
Physical examination	• Vital signs • Abdominal palpation to assess uterine tone, contractions, fetal size and presentation • Sterile speculum examination to: o Confirm or exclude rupture of membranes o Assess liquor (e.g. clear, meconium stained, bloody) o Visualise cervix and membranes • Collect high vaginal swab for microscopy culture and sensitivity (MC&S) to test for BV • Perform test for the presence of fFN (if not contraindicated) o Refer to Section 4.2 Fetal fibronectin testing • If indicated, perform TVCL measurement o Refer to Section 4.1 Cervical length • Collect either a vaginal-rectal swab *or* a vaginal-perianal swab for *Group B streptococcus* (GBS) • Assess cervical dilatation by sterile digital vaginal examination unless contraindicated by: o Ruptured membranes o Suspected placenta praevia
Fetal surveillance	• Fetal heart rate (FHR) • Continuous CTG o Consider gestational age (interpret with caution if less than 28 weeks gestation) • Ultrasound examination for fetal growth and wellbeing o Fetal number, presentation, liquor volume and placenta localisation
Laboratory investigations	• High vaginal swabs for BV (MC&S) • Genital swab for GBS (vaginal-rectal *or* vaginal-perianal) • Midstream specimen of urine for bacteriology (MC&S)

4.1 Cervical length

Transvaginal ultrasound of cervical length (TVCL) can aid in assessing the risk of PTB.

- TVCL must be performed by a credentialed clinician
- Lack of local capability to perform TVCL is not a reason for transfer

4.1.1 Assessment of cervical length

Table 7. Cervical length assessment

Aspect	Consideration
Context	• To determine risk of PTB, various cervical lengths between 18–24 weeks of gestation, have been used (e.g. TVCL less than 25 mm, less than 20 mm or less than 15 mm)[18] • Short cervical length is associated with an increased risk of PTB o The shorter the cervical length, the greater the risk[18,22] o Refer to Table 8. Cervical length and risk of preterm birth • When performed by trained operators, transvaginal ultrasound is more reliable, reproducible and predictive for cervical length assessment compared to transabdominal ultrasound[29]
Recommendation	• Routinely recommend cervical length measurement to women during the mid-trimester (18–20 weeks) ultrasound scan[18,24,25] o Refer to Section 2 Risk assessment • Recommend therapeutic interventions when the TVCL is measured at less than 25 mm[18] o Refer to section 3 Risk reduction • fFN testing, alongside TVCL measurement, has been shown to increase the predictive quality of PTL risk o Consider fFN testing in conjunction with TVCL measurement in symptomatic and asymptomatic women with risk factors of PTL o Refer to Section 4.2 Fetal fibronectin testing[40]

4.1.2 Cervical length and risk of preterm birth

Table 8. Cervical length and risk of preterm birth

Cervical length (mm)	Likelihood ratio for birth at **X** weeks gestation[41]			
	< 28	28–30	31–33	34–36
< 2	745.29	74.29	44.22	99.36
5	119.19	36.81	24.26	18.10
7	62.08	27.80	19.08	11.15
10	26.79	18.24	13.31	6.53
12	16.29	13.77	10.47	4.93
15	8.26	9.04	7.30	3.47
18	4.45	5.93	5.09	2.60
20	3.03	4.48	4.01	2.20
22	2.10	3.38	3.15	1.89
25	1.25	2.22	2.20	1.53

4.2 Fetal fibronectin testing

In this guideline the quantitative fFN test is preferred because of its ability to provide a quantifiable test result that better informs management over and above other tests that only provide a 'positive' or 'negative' result (e.g. non-quantitative fFN/Quickcheck® or Actim Partus®).

Table 9. Fetal fibronectin testing

Aspect	Consideration
Context	• fFN is a glycoprotein thought to promote adhesion between the fetal chorion and maternal decidua o Normally present in low concentrations in the cervicovaginal secretions between 18 and 34–36 weeks gestation, rising as term approaches[2] • Elevated levels of fFN (typically greater than 50 ng/mL) in cervicovaginal secretions after 22 weeks gestation are associated with an increased risk of PTB[42] • A negative fFN is associated with a 99.5% negative predictive value for PTB within 7 days and 99.2% in the next 14 days[2] • Consider use of the QUIPP® app to assist with interpretation and management decisions
Indications	• Symptomatic women with threatened preterm labour: o Between 22+0 and 36+0 weeks gestation *and* o Intact membranes *and* o Cervical dilatation less than or equal to 3 cm *OR* • Asymptomatic women, greater than 22 weeks gestation, with a history of: o Cervical surgery/trauma[43] *or* o PTB in previous pregnancy *or* o Late miscarriage in previous pregnancy[44]
Contraindications	• Cervical dilatation more than 3 cm • Ruptured membranes • Cervical cerclage in situ • Presence of soaps, gels, lubricants or disinfectants
Relative contraindications	• Visual evidence of moderate or gross bleeding • Within 24 hours of vaginal intercourse • A negative fFN result of less than 10 ng/mL is still valid: o If a woman reports having intercourse in the previous 24 hours o In the presence of moderate or gross vaginal bleeding
Procedure	• Performed during sterile speculum examination prior to any examination of the cervix or vagina • Use only sterile water as a lubricant • Obtain the sample for testing from the posterior fornix of the vagina • Follow test kit instructions
Quantitative fFN testing	• Quantitative fFN testing may improve assessment of overall risk[45], reduce unnecessary transfer and ultimately reduce longer term costs[46] • Avoids unnecessary interventions • Identifies women for targeted interventions • Provides reassurance to health care providers and the woman

4.2.1 Fetal fibronectin results

Table 10. fFN results

Aspect	Consideration
fFN less than 50 ng/mL (negative)	• Low risk of birth within 7–14 days[2] • fFN less than 10 ng/mL o Higher negative predictive value for PTB (2.7%)[47] • False negative result may occur due to[48]: o Use of lubricant with speculum examination o Intravaginal disinfectants
fFN 50 ng/mL or more (positive)	• High risk of birth within 7–14 days • fFN greater than 200 ng/mL[43] o Higher positive predictive value for PTB (38%)[49] ▪ Provides reassurance to clinicians to provide immediate intervention and/or transfer • False positive may occur as a result of recent: o Vaginal intercourse o Digital vaginal examination o Transvaginal ultrasound o Bleeding

4.3 Assess need for admission

Use clinical judgement and appropriate consultation in assessing the need for admission. Consider the fFN result in the context of the overall clinical circumstances, the resources available and the service capability of the facility [refer to Section 5 Management of preterm labour]. If membranes are ruptured use alternate care pathways.

Table 11. Assessment of need for admission

Aspect	Assessment (assumes intact membranes)
Admission indicated	• Consider admission for reassessment and/or therapeutic interventions if any of the following[22]: o fFN test greater than or equal to 50 ng/mL ▪ Admission recommended if fFN test greater than 200 ng/mL o TVCL changes and/or less than 25 mm (if measured) o Cervical dilation (painless or painful) o Cervical change over 2–4 hours o Contractions regular and painful o Further observation or investigation indicated o Other maternal or fetal concerns • Refer to Table 12. Planning care • If membranes ruptured refer to Queensland Clinical Guidelines: *Preterm prelabour rupture of membranes*[50]
Admission not indicated	• If fFN less than 50 ng/mL and admission not otherwise indicated, discharge home if[22]: o Maternal vital signs within normal parameters o Normal fetal heart rate (FHR) and/or CTG relevant to gestational age o No signs of chorioamnionitis o Contractions infrequent/irregular o No/minimal cervical change • Inform woman about: o Signs and symptoms of preterm labour o Risk reduction measures appropriate to the circumstances ▪ Refer to Section 3 Risk reduction o When to seek clinical advice • Arrange follow-up: o If fFN 0–9 ng/mL routine follow-up as per usual model of care ▪ Less than 2% birth within two weeks ▪ Less than 2% birth before 34 weeks o If fFN 10–49 ng/mL return for medical review within 7 days ▪ Less than 2% birth within two weeks ▪ 5–15% birth before 34 weeks

5 Management of preterm labour

Tocolysis and steroids are the main strategies to manage preterm labour. Transfer to a centre with higher service capability may also be necessary. Management options will depend on:

- Gestational age and individual clinical circumstances
- Resource (equipment and human) availability to provide the required care (e.g. cardiotocograph (CTG), one to one midwifery care when indicated)
- Acuity level of the facility (care is provided in accordance with the Clinical Service Capability Framework (CSCF))[51]
- If necessary, refer to a service with higher level capability for further advice when access to services are unavailable/limited

There are current validated technologies (e.g. QUIPP® app) being utilised in some Queensland facilities. These may assist in diagnosing preterm labour using fFN and TVCL results and may help decision making.

5.1 Planning care

Use clinical judgement and appropriate consultation in planning care.

Table 12. Planning care

fFN ng/mL	Care considerations	% birthing within 2 weeks	% birthing before 34+0 weeks
All women requiring admission	• Develop local protocols that: o Are contextually and culturally appropriate o Consider in-utero transfer (as relevant to service capability) o Identify referral processes that support women accessing the most appropriate treatment in a timely way • Admit for observation • Offer analgesia • Administer corticosteroids if less than 35+0 weeks • [52]Measure TVCL if resources available • Communicate with multidisciplinary team as relevant to the circumstances (e.g. neonatology consultation, social worker referral, anaesthetic involvement) • Discuss plan for ongoing care with the woman in a manner that supports informed choice • Document plan of care in the health record • Clinical reassessment as required • If labour is established or birth appears imminent, and gestational age is less than 30 weeks, commence magnesium sulfate for neuroprotection of the fetus o Refer to Appendix A: Magnesium sulfate for fetal neuroprotection		
50–199	As for all women requiring admission *and* consider • Tocolysis if delay of birth indicated and no contraindications • All clinical circumstances including history of PTB	5–15	10–15
200-499	As for all women requiring admission *and* • Commence tocolysis if delay of birth indicated and no contraindications	30	30
≥ 500 or more	As for all women requiring admission *and* • Commence tocolysis if delay of birth indicated and no contraindications • Prepare for administration of magnesium sulfate (if gestational age less than or equal to 30 weeks)	50	75

5.2 In-utero transfer

Table 13. In-utero transfer

Aspect	Consideration
Context	• Neonatal outcomes are improved if PTB occurs in centres that manage high numbers of preterm babies[53-55] • If transfer required, contact Retrieval Services Queensland (RSQ) on 1300 799 127
Principles for transfer	• May accept a high level of risk of birth occurring en-route when gestational age is less than 28+0 weeks o Transfer discussions and decisions occur between senior clinicians o Use RSQ conference calls to facilitate involvement of all relevant clinicians in the most time efficient manner o Discuss with RSQ medical co-ordinator the tasking of a second aeromedical clinician to accompany the flight nurse • Transfer decisions involve *both* obstetric and neonatal clinicians, particularly at the receiving site and the RSQ medical co-ordinator from an aeromedical asset allocation perspective • Recognise that retrieval platforms may not be immediately available (e.g. due to pilot and crew hours, weather or aircraft service needs) • Decisions about transfer may be escalated within RSQ by receiving or transferring clinicians, or by the flight nurse as required • RSQ will co-ordinate a combined services audit of births less than 28+0 weeks gestational age occurring outside a level 6 neonatal unit
Clinical assessment	• If birth is considered a possibility en-route: o Perform clinical assessment of the woman by the transferring consultant or equivalent ▪ Refer to Section 4.3 Assess need for admission • Reassess the woman after initial stabilisation to review timelines around transfer decisions, particularly if there are delays in transfer or transfer is not immediately feasible • If clinically appropriate, use tocolysis to allow in-utero transfer
Accountability and responsibilities	• Accountability and responsibility for transfer decisions and their outcomes reside with the transferring and receiving consultants o Accountability and responsibility for transfer decisions and outcomes does not reside with the flight nurse • The transferring consultant (or equivalent) is responsible for: o Discussing risks and benefits of in-utero transfer with the woman/partner/family including the limited resuscitation that will be provided should birth occur en-route o Ensuring comprehensive documentation in the health record and transfer documents of ▪ Discussions that have occurred with woman and family ▪ Clinical assessment of the woman and the assessed risk of PTB ▪ Discussions between receiving and transferring clinicians about the planned transfer
If birth occurs en-route	• Contact RSQ to task a neonatal retrieval team to meet the aircraft • Intubation and/or full resuscitation is not generally feasible within the aircraft environment o Neonatal resuscitation measures (should birth occur en-route) may include (but are not necessarily limited to) keeping baby warm, administering oxygen, providing continuous positive airway pressure (CPAP) via bag and mask)
Recommendation	• If preterm birth is very likely and life sustaining interventions are planned or may be a possibility, recommend in-utero transfer • In-utero transfer not indicated if palliative care planned o Refer to Queensland Clinical Guideline *Perinatal care at the threshold of viability*[4] • If life sustaining interventions are to be initiated only if a specific gestational age achieved (e.g. interventions only if gestation reaches 24 weeks) then arrange transfer prior to the specified gestation (i.e. don't wait until 24 weeks+0 days) • If gestational age uncertain, then discuss with the receiving neonatal and obstetric unit • Inform the family that transfer does not oblige or necessarily equate to a final decision for life sustaining interventions

5.3 Tocolysis

Table 14. Tocolysis

Aspect	Consideration
Context	• Tocolytic drugs may delay birth and allow[22]: o Administration of corticosteroids o Administration of magnesium sulfate for neuroprotection o In-utero transfer to an appropriate level facility • Tocolysis not associated with a clear reduction in perinatal mortality or serious neonatal morbidity • No evidence to support the use of prophylactic tocolytic therapy after contractions have ceased • Recommend when a 48 hour delay in birth will benefit the newborn
PPROM	• There is limited evidence about the use of tocolytics in the setting of PPROM[56] • Gestational age is a major determinant for management • Tocolysis in women with PPROM before 34+0 weeks associated with[56]: o A lower risk of birth within 48 hours o An increased risk of chorioamnionitis without significant maternal or neonatal benefit • Tocolysis before viability not generally recommended[56]
Contraindications	• Maternal contraindications to tocolysis (agent specific) • Any condition where prolongation of pregnancy is contraindicated including but not limited to: o In-utero fetal death/lethal fetal anomalies o Suspected fetal compromise o Maternal bleeding with hemodynamic instability o Severe pre-eclampsia o Placental abruption o Chorioamnionitis

5.3.1 Nifedipine

Table 15. Nifedipine

Aspect	Consideration
Context	• Nifedipine is a calcium channel blocker that relaxes smooth muscle • Nifedipine is the tocolytic of choice[57,58] • Do not use sustained release formulation o Immediate release formulation available with special scheme access (SAS) authority
Cautions*	• If there are contraindications to nifedipine, liaise with an obstetrician to determine alternate tocolysis[59] • Contraindications include: o Maternal hypotension or cardiac disease (risk of fluid overload) o Previous adverse reaction to calcium channel blockers • Use cautiously with magnesium sulfate o Concomitant use may increase effects of magnesium sulfate and the risk of hypotension
Administration*	• Nifedipine 20 mg oral stat[59] • If contractions persist after 30 minutes repeat nifedipine 20 mg oral • If contractions persist after a further 30 minutes repeat nifedipine 20 mg oral
Maintenance*	• If blood pressure (BP) stable: nifedipine 20 mg oral every 6 hours for 48 hours—maximum dose is 160 mg/day[59] • Further maintenance therapy is ineffective[60]
Observations	• CTG until contractions cease (relative to gestation) • BP, pulse and respiratory rate o Every thirty minutes for first hour, then hourly for four hours o Review frequency in accordance with clinical circumstances • Temperature every four hours

*Refer to an Australian pharmacopoeia for complete drug information

5.3.2 Other tocolytics

Table 16. Other tocolytics

Aspect	Consideration
Betamimetics (salbutamol, terbutaline)*	• Compared to placebo, betamimetics are effective tocolytic agents[61,62], but significant adverse side effects including maternal death from pulmonary oedema have been reported[62] • No evidence to support oral betamimetics for maintenance after threatened preterm labour[63] • Not recommended unless there are contraindications to other tocolytics
Inhibitors of prostaglandin synthesis (indomethacin)*	• Potent inhibitor of uterine contractility by inhibiting cyclo-oxygenase (COX) enzyme[61] but limited high level evidence with few adequate trials[64,65] • Risks for the fetus and neonate include[64,66]: o Constriction of the fetal ductus arteriosus (increased risk with advancing gestational age; the effects are transient and reversible with short term administration; longer administration may lead to pulmonary hypertension in the fetus and neonate) o Alteration of fetal (especially cerebral) blood flow o Reduced renal function (may result in oligohydramnios) o Necrotising enterocolitis • Because of the potential adverse fetal and neonatal effects, consider use of indomethacin only where: o Gestational age is less than 28+0 weeks o There is failure to achieve tocolysis with other tocolytic regimens o Contraindications to other tocolytics exist (e.g. cardiac disease) • With indomethacin administration, ensure close monitoring of fetal wellbeing

*Refer to an Australian pharmacopoeia for complete drug information

5.4 Antenatal corticosteroids

Table 17. Antenatal corticosteroids

Aspect	Consideration
Context	• Administration of antenatal corticosteroids before PTB is an important intervention that improves outcomes for preterm babies and may provide: o Significant reduction in rates of neonatal death, respiratory distress syndrome and intraventricular haemorrhage (IVH)[67] o Reduction in necrotising enterocolitis, respiratory support, intensive care admissions and systemic infections in the first 48 hours of life compared with no treatment or treatment with placebo[67] • Beneficial effect demonstrated regardless of membrane status[67] • If the risk of PTB persists seven or more days after initial course, repeat dose(s) are associated with[68]: o Less respiratory distress and fewer serious health problems in the first few weeks after birth o Small reduction in size at birth
Recommendation	• Recommend antenatal corticosteroids to women with a viable fetus who are at increased risk of PTB[67] between 22+0 to 34+6 weeks gestational age[67,69] • Determine the need for further weekly repeat dose(s) based on clinical assessment of the ongoing risk of PTB o If the risk of PTB persists seven or more days after initial course, consider a repeat dose of corticosteroids[68] o Seek expert obstetric/neonatal advice if uncertainty exists about continued risk of PTB o If there is maternal diabetes, monitor blood glucose levels • Refer to Queensland Clinical Guideline *Antenatal corticosteroids*[52]

*Refer to an Australian pharmacopoeia for complete drug information

5.5 Antibiotics

Table 18. Antibiotics

Aspect	Consideration
Preterm labour (or imminent risk of PTB) without evidence of chorioamnionitis*	• If preterm labour ensues *or* there is imminent risk of PTB, give intrapartum antibiotic prophylaxis for prevention of early onset *Group B streptococcal* disease irrespective of GBS status or membrane status • Refer to Queensland Clinical Guideline: *Early onset Group B streptococcal disease*[70]
Signs of chorioamnionitis (intact or ruptured membranes)*	• Signs of chorioamnionitis include[71]: o Maternal fever greater than 38 °C (present in 95–100% of cases) o Maternal tachycardia greater than 100 beats per minute (bpm) (present in 50–80% of cases) o Fetal tachycardia greater than 160 bpm (present in 40–70% of cases) o Uterine tenderness o Offensive smelling vaginal discharge o Increased white cell count (greater than $15x10^9$/L) o Elevated C-reactive protein (CRP)
Management of chorioamnionitis	• Do not inhibit labour, but consider hastening birth under broad spectrum intravenous antibiotic cover • Suspect chorioamnionitis in women with PPROM if labour ensues • Optimal antibiotic regimen not established—if no local protocols exist suggested regimen[72]: o Ampicillin (or amoxycillin) 2 g IV initial dose, then 1 g IV every 6 hours o Gentamicin 5 mg/kg IV daily o Metronidazole 500 mg IV every 12 hours • If allergic to penicillin: o Lincomycin 600 mg IV in 100 mL over 1 hour every 8 hours OR clindamycin 600 mg IV in 50–100 mL over at least 20 minutes every 8 hours o Gentamicin 5 mg/kg IV daily o Metronidazole 500 mg IV every 12 hours • Continue antibiotic treatment after birth • Consider oral antibiotics once woman is afebrile and tolerating oral medication
Woman not in preterm labour	• Routine administration of prophylactic antibiotics to women in threatened preterm labour with intact membranes and without evidence of infection is not recommended[69,73] • If preterm labour does not commence and no other indications: o If intact membranes, cease antibiotics o Refer to Queensland Clinical Guideline: *Early onset Group B streptococcal disease*[70] • If PPROM refer to Queensland Clinical Guideline: *Preterm prelabour rupture of membranes–preterm (PPROM)*[50]

*Refer to an Australian pharmacopoeia for complete drug information

5.6 Magnesium sulfate for neuroprotection

Table 19. Magnesium sulfate for neuroprotection

Aspect	Consideration
Context	• Magnesium sulfate administered shortly before birth may assist in reducing the risk of cerebral palsy and protect gross motor function in those babies born preterm[22,69] o Number needed to treat (NNT): 63 babies for one baby to avoid cerebral palsy (95% CI 44–155)[74] o Number needed to treat to benefit (NNTB): 42 babies for combined death or cerebral palsy (95% CI 24–346)[74] o The effect may be greatest at early gestations and is not associated with adverse long-term fetal or maternal outcome[75] • In one follow-up randomised controlled trial, magnesium sulfate was not associated with improved neurological, cognitive, behavioural, growth or functional outcomes in school age children although mortality advantage could not be excluded[76]
Recommendation *	• Recommend magnesium sulfate to women with a viable fetus before 30+0 weeks gestation [22,75] where birth is expected or planned within 24 hours[22] o Consider magnesium sulfate for women between 30+0 and 33+6 weeks gestation[22] • If birth is planned, commence administration as close to four hours prior to birth as possible[75] • Best effect when given for at least four hours within the six hours prior to birth • If birth is expected to occur within four hours, commence magnesium sulfate immediately, as there may still be benefit from administration[75] • In situations where urgent birth is necessary, do not delay birth to administer magnesium sulfate[75] • If birth does not occur after giving magnesium sulfate and PTB (less than 30 weeks gestation) again appears imminent (planned or expected within 24 hours), a repeat dose of magnesium sulfate may be considered at the discretion of the obstetrician[75] • Refer to Appendix A: Magnesium sulfate for fetal neuroprotection

*Refer to an Australian pharmacopoeia for complete drug information

5.7 Mode of preterm birth

Table 20. Mode of preterm birth

Aspect	Consideration
Context	• There is insufficient high quality evidence about whether mode of birth affects neonatal morbidity and outcomes[77,78] • Preterm caesarean section (CS) is usually technically more difficult to perform and is not without risk to the baby as the lower segment is usually not well formed[79] o A classical incision may be required with risks to future pregnancies including scar dehiscence, uterine rupture, placental adherence and maternal death o Discuss implications of decision with the woman • Early consultation with anaesthetic team required
Singleton vertex presentation	• Recommend vaginal birth unless there are specific contraindications to vaginal birth or maternal conditions necessitating CS[77]
Breech presentation 26+0 weeks or more gestation	• The evidence regarding optimal mode of birth for preterm breech is conflicting and unclear due to a lack of high quality studies • Base decisions on individual circumstances and maternal preferences • CS is not generally recommended where vaginal birth is imminent[77]
25+6 weeks or less gestation (vertex or breech)	• CS for fetal indications alone not generally recommended at less than 25+0 weeks gestation[4] • Refer to Queensland Clinical Guideline: *Perinatal care at the threshold of viability*[4]

6 Management after threatened preterm labour

When PTB does not occur following admission for threatened preterm labour, co-ordinate care and discharge planning with the family, relevant health care professionals and the referring hospital (as required).

Table 21. Management of threatened preterm labour

Aspect	Consideration
Prolonged admission	• Plan care relevant to the underlying clinical circumstances • Use clinical judgement and as clinically appropriate consider: o Consultation/referral/transfer o Serial TVCL o Progesterone o Fetal assessments o Maternal investigations and assessments o Repeat fFN testing o Planning for PTB • Frequency of clinical observations (e.g. temperature, blood pressure)
Back transfer	• If discharge home is not considered an option, transfer back to the referring hospital where feasible • Consider: o Individual clinical circumstances and likelihood of PTB o Gestational age, and maternity and neonatal clinical service capability of the receiving hospital o Access to required ongoing monitoring and clinical surveillance o Preferences of the woman and her family • Retrieval logistics and aircraft availability
Discharge	• Consider usual discharge criteria including: o Maternal vital signs o Signs of chorioamnionitis o Membrane status o If contractions infrequent/irregular o Cervical change/TVCL (if measured) o Normal CTG relevant to gestational age o fFN test result • Inform woman of: o Signs and symptoms of preterm labour o Risk reduction measures appropriate to the circumstances ▪ Refer to Section 3 Risk reduction o When to seek clinical advice o Refer to Queensland Clinical Guidelines *Preterm labour and birth*[10] parent information • Determine follow-up and on-going clinical surveillance requirements
Referral and follow-up	• Inform the woman, the usual health care provider and/or referring hospital about the recommendations for follow-up and ongoing clinical surveillance (e.g. GP, birth centre, private midwife) • Offer social worker referral as indicated

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Appendix A: Magnesium sulfate for fetal neuroprotection

In the absence of local monitoring protocols, the following guidance is provided.

Aspect	Consideration
Resources	• One to one midwifery care in birth suite or high dependency unit for the duration of therapy • Resuscitation and ventilator support immediately available • Calcium Gluconate 1 g available in case of respiratory depression
Contraindications	• Maternal cardiac conduction defects (heart block) • Hypermagnesaemia • Maternal myasthenia gravis–use cautiously and monitor closely • Concomitant nifedipine use cautiously and monitor closely • Reduced renal function monitor plasma magnesium level/urine output
Route	• IV infusion via controlled infusion device
Loading dose	• 4 g IV bolus over 20 minutes
Maintenance dose	• 1 g/hour for 24 hours or until birth, whichever occurs first
Side effects	• Related to hypermagnesaemia • Common (more than 1%): nausea and vomiting, flushing • Infrequent (0.1–1%): headache, dizziness
Baseline observations	• Vital signs: BP, pulse, respiratory rate • Oxygen saturation (SpO_2) • Patellar reflex • Abdominal palpation • Monitor contractions for 10 minutes • Fetal heart rate (FHR)/CTG
Monitoring during loading dose	• BP, pulse, and RR every 5minutes (for minimum 20 minutes) until stable • SpO_2 continuously • Contractions for 10 minutes every 30 minutes • If greater than or equal to 24 weeks gestation continuous CTG o Interpret CTG relevant to gestational age if less than 28 weeks o If CTG not able to be performed document reason • If less than 24 weeks gestation • Observe for side effects auscultate FHR every 15–30 minutes • Check deep tendon reflexes (patellar or, if epidural insitu, biceps) after completion of loading dose o If absent and do not commence maintenance dose–notify obstetrician
Monitoring during maintenance dose	• BP, pulse, temperature, respiratory rate, and SpO_2 every 30 minutes • Contractions for 10 minutes every 30 minutes • If greater than or equal to 24 weeks gestation continuous CTG o If less than 28 weeks interpret CTG relevant to gestational age • If less than 24 weeks gestation auscultate FHR every15–30 minutes • Strict fluid balance monitoring and documentation o If urine output less than 25 mL/hour, notify medical officer • Deep tendon reflexes hourly o Record as A=Absent, N=Normal, B=Brisk
Monitoring post infusion	• Repeat baseline observations/vital signs • Minimum 4 hourly or more frequently as clinically indicated • If renal function normal serum magnesium monitoring not usually required o Therapeutic serum magnesium levels are 1.7–3.5 mmol/L
Discontinuation and urgent medical review	• Respiratory rate less than 12 breaths/minute or more than 4 breaths/minute below baseline • Diastolic BP decreases more than 15 mmHg below baseline • Absent deep tendon reflexes • Urine output less than 25 mL/hour or less than 100 mL over 4 hours • Magnesium serum levels greater than 3.5 mmol/L

Adapted from: The Antenatal Magnesium Sulphate for Neuroprotection Guideline Development Panel. Antenatal magnesium sulphate prior to preterm birth for neuroprotection of the fetus, infant and child: national clinical practice guidelines. The University of Adelaide. 2010 [cited 2019, October 09]. Available from: www.nhmrc.gov.au.

Acknowledgements

Queensland Clinical Guidelines gratefully acknowledge the contribution of Queensland clinicians and other stakeholders who participated throughout the guideline development process particularly:

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Funding
This clinical guideline was funded by Healthcare Improvement Unit, Queensland Health