

Preterm Labour - Management of Threatened and Active Preterm Labour

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1. Purpose of guideline

This guideline outlines the expected management of women presenting with threatened or active (established) preterm labour (PTL) within Auckland District Health Board (Auckland DHB) or referred to Auckland DHB at gestations $\geq 24^{+0}$ weeks and $< 37^{+0}$ weeks. Between 23^{+0} and 23^{+6} weeks gestation it may be appropriate to follow the pathway outlined in this guideline. However, this should **only be done after reviewing Section 13** (Threatened and active PTL at $< 24^{+0}$ weeks), and after discussion with both an obstetric specialist (and Maternal Fetal Medicine (MFM) when available) and neonatal specialist.

2. Management principles

Preterm birth is the leading cause of neonatal death and major morbidity. It imposes additional risks on infant, child and life-long health of the off-spring. The rate of preterm birth ranges from 5% to 18% of babies born worldwide and at Auckland City Hospital (ACH) it is 9 - 10%. Approximately half of preterm births within the Auckland DHB unit are due to spontaneous labour or preterm pre-labour rupture of membranes (PPROM).

Current therapeutic strategies are unlikely to prevent preterm birth in women presenting with symptoms of preterm labour (PTL) (threatened PTL). However, we do have an opportunity to identify those at most risk of going onto preterm birth so interventions that reduce neonatal morbidity and mortality can be targeted appropriately.

Of women presenting with symptoms of PTL, 60 - 70% do not deliver until term and only 5% deliver within one week of presentation and therefore, clinical assessments of threatened PTL alone is a relatively poor predictor of preterm birth. The use of adjunct tests including vaginal biomarkers such as fetal fibronectin (fFN) or transvaginal ultrasound measurement of cervical length with strong negative predictive values allows us to rule out the risk of preterm birth in many women and limit the use of unnecessary antenatal admissions and interventions. Those interventions proven to be of value in improving neonatal outcomes include antenatal corticosteroids $\leq 34^{+6}$ weeks, magnesium sulfate $< 30^{+0}$ weeks, delayed cord clamping and delivery within a unit with level three neonatal intensive care unit (NICU) facilities available. Tocolysis therapy has only been shown to have limited effects on outcome, however, it has been demonstrated to delay delivery > 48 hours therefore its use should be considered in women receiving a first course of antenatal corticosteroids at $\leq 34^{+6}$ weeks, magnesium sulfate at $< 30^{+0}$ weeks or if antenatal transfer is required to access appropriate NICU facilities.

3. Definition and risk factors

Preterm labour (PTL)

- Refers to the onset of labour $< 37^{+0}$ weeks gestation (and the fetus is deemed viable).
- Clinically it is determined by regular uterine contractions with accompanied significant cervical dilatation of ≥ 3 cm.

Threatened PTL

- Defined as uterine contractions but with no or limited evidence of cervical change at < 37⁺⁰ weeks gestation (and the fetus is deemed viable).
- Clinically it is difficult to differentiate those with threatened PTL who will go onto PTL and birth and those that will not.

Risk factors for PTL

Many cases of threatened PTL and PTL are not associated with any identifiable risk factors; however, there are certain conditions which may increase the risk:

- Previous PTL
- Preterm PPROM
- Previous second trimester loss
- History of cervical surgery (cone biopsy, large loop excision of the transformation zone (LLETZ) with depth ≥ 10 mm)
- History of ≥ one surgical termination of pregnancy or evacuation of retained products of conception after miscarriage
- History of caesarean section at full cervical dilatation
- Congenital uterine and/or cervical anomalies
- Multiple pregnancy
- Polyhydramnios
- Recurrent bleeding in first trimester (≥ five days)
- Placental abruption/anteartum haemorrhage
- Smoking, alcohol or illicit drug use.

4. Diagnosis of preterm labour

4.1 History taking

- Review history for symptoms of labour or other diagnosis which may present with similar symptoms (e.g. antepartum haemorrhage (APH), urinary tract infection (UTI), constipation) and review risk factors.
- Confirm gestational age.

4.2 Physical examination

- Examine for signs of PTL or other diagnosis which may present with similar symptoms
- Vital signs (temperature, pulse and blood pressure).
- Abdominal palpation to detect uterine activity (frequency, duration and strength), assess fetal size and presentation.
- Sterile speculum examination
- Avoid gel to allow fetal fibronectin (fFN) testing if indicated (see [below](#))
- Look for pooling of liquor, discharge, cervical dilatation and length
- If pooling of liquor present, rupture of membrane is confirmed, refer to *Rupture of Membranes in Pregnancy* guideline (see [Associated documents](#)).
- Digital vaginal examination
- Assess using Bishops score if cervix < 3cm dilated

- Computed tomography of gestation (CTG) – fetal heart rate (FHR) pattern and evidence of uterine activity.

4.3 Investigations

- Mid stream urine (MSU)
- High vaginal swab for culture
- Consider use of fFN (see [below](#)) if $\leq 34^{+6}$ weeks
- If fFN is not available and $\leq 34^{+6}$ weeks, consider transvaginal ultrasound of cervical length.

Cervical length	Management
$\geq 30\text{mm}$	Treat as fFN 0 - 49 ng/mL
15 - 30mm	Assess clinical situation and discuss with specialist obstetrician on-call
$\leq 15\text{mm}$	Treat as fFN > 200 ng/mL

4.4 Fetal Fibronectin (fFN)

Fetal fibronectin is one of several commercially available vaginal biomarker tests for the prediction of preterm birth in women presenting with symptoms of PTL. To date fFN is the most extensively tested with data on predictive value in several thousand symptomatic women.

It is a glycoprotein found in amniotic fluid and extracts of placental tissue that can be thought of as ‘trophoblast glue’ promoting cellular adhesion at the utero-placental and decidual-fetal membrane interfaces. It is rarely detected at elevated levels in cervico-vaginal fluid in normal pregnancy during the second and third trimesters. However, it is released through mechanical or inflammatory mediated damage to the membranes or placenta before birth, and is therefore, found at elevated levels in the cervico-vaginal fluid of women between 22 and 36 weeks gestation who have an increased risk of PTL.

Fetal fibronectin should be used to identify women at most risk of PTL within the next seven days (when use of hospital admission, tocolysis and antenatal corticosteroids are being considered). Its greatest value lies in its negative predictive value.

The test uses an enzyme linked immunosorbent assay (ELISA) containing FDC-6 monoclonal antibody to detect fFN. Both a qualitative analyser (positive or negative result) and a quantitative analyser (absolute value 0 - 500 ng/mL) are commercially available. If using a qualitative analyser it has been established that the best threshold to define a positive/negative test result is 50 ng/mL. A negative result < 50 ng/mL has a strong negative predictive value for delivery within the next seven days (98 - 100%) i.e. women presenting with symptoms of PTL and a negative fFN are very unlikely ($< 2\%$) to deliver within a time-frame where current hospital admission and corticosteroid use will be of benefit. Women with a positive test ≥ 50 ng/mL have a higher risk of delivery within the next seven days (positive predictive value 15 - 50%). However, the majority of women will still not deliver within a time-frame where current hospital admission and other interventions may be of benefit.

Use of the quantitative analyser to obtain an absolute value of fFN is better able to identify those at highest risk and more appropriately tailor care to each individual women ensuring antenatal care is not compromised to the detriment of mother and their babies who do go on to deliver preterm but reducing unnecessary interventions for all others. Using data including local Auckland

DHB data obtained in the Biomarkers for Preterm Birth Study the following thresholds for care have been set:

fFn result	Care plan
fFn 0 - 49 ng/mL	The women should be discharged home with no acute intervention if no other diagnosis is considered to be the cause of their symptoms.
fFn 50 - 200 ng/mL	The women should be considered for corticosteroids if $\leq 34^{+6}$ weeks and these should be administered in Women's Assessment Unit (WAU) with women then discharged home (if no other diagnosis is considered to be the cause of their symptoms). Women should be reviewed in WAU/Day Assessment Unit (DAU) the following day for administration of second dose of corticosteroid. Women should be clearly informed of signs and symptoms that should precipitate an early return to hospital. Review in an obstetric clinic one week later should be arranged. The women should be advised that they are at an increased risk of early birth but are still more likely to continue their pregnancy to term.
fFn > 200 ng/mL	The women should be admitted to hospital and considered for tocolysis therapy and corticosteroids if $\leq 34^{+6}$ weeks. Discussion with neonatology service should occur to ensure an appropriate neonatal cot is available in event of birth (and consider <i>in-utero</i> transfer if not available). The women should be advised that they are at an increased risk of early birth but may still continue their pregnancy to term.

Indications for fFN testing:

Inclusion criteria	Exclusion criteria *
<ul style="list-style-type: none"> Fetus is alive and viable 24⁺⁰ - 34⁺⁶ weeks gestation 23⁺⁰ - 23⁺⁶ weeks gestation if active intervention is being considered** Membranes are intact Cervix is < 3cm dilated Corticosteroid use, +/- tocolysis, +/- magnesium sulfate are being considered Singleton and twin pregnancy 	<ul style="list-style-type: none"> Other complications have been identified that warrant delivery within the next seven days (and admission/use of corticosteroids) e.g. abruption PPROM Higher order multiple pregnancy (\geq triplets)
<p>* Relative contraindications to use of fFN include; current vaginal bleeding, sexual intercourse within last 24 hours, speculum or digital vaginal examination within the last 24 hours, transvaginal ultrasound examination within the last 24 hours. These factors will increase the likelihood of a positive fFN result (but may represent a false positive). However, a negative result will be a true negative result and women can be managed according to that result. The use of a fFN test can still be considered if the result may influence management provided e.g. the clinician would be confident to discharge the woman and withhold corticosteroids and tocolysis</p>	

if the result is negative. It is recommended that these cases are discussed with the specialist obstetrician on-call.

**** fFN can be taken at time of first examination at 23⁺⁰ - 23⁺⁶ weeks and only sent after consideration of case and full discussion with specialist obstetrician on-call, neonatologist and parents (refer to [Section 13](#) - Threatened and active PTL at < 24⁺⁰ weeks).**

The use of a gel lubricant at the time of testing may produce a false negative result. This should be avoided.

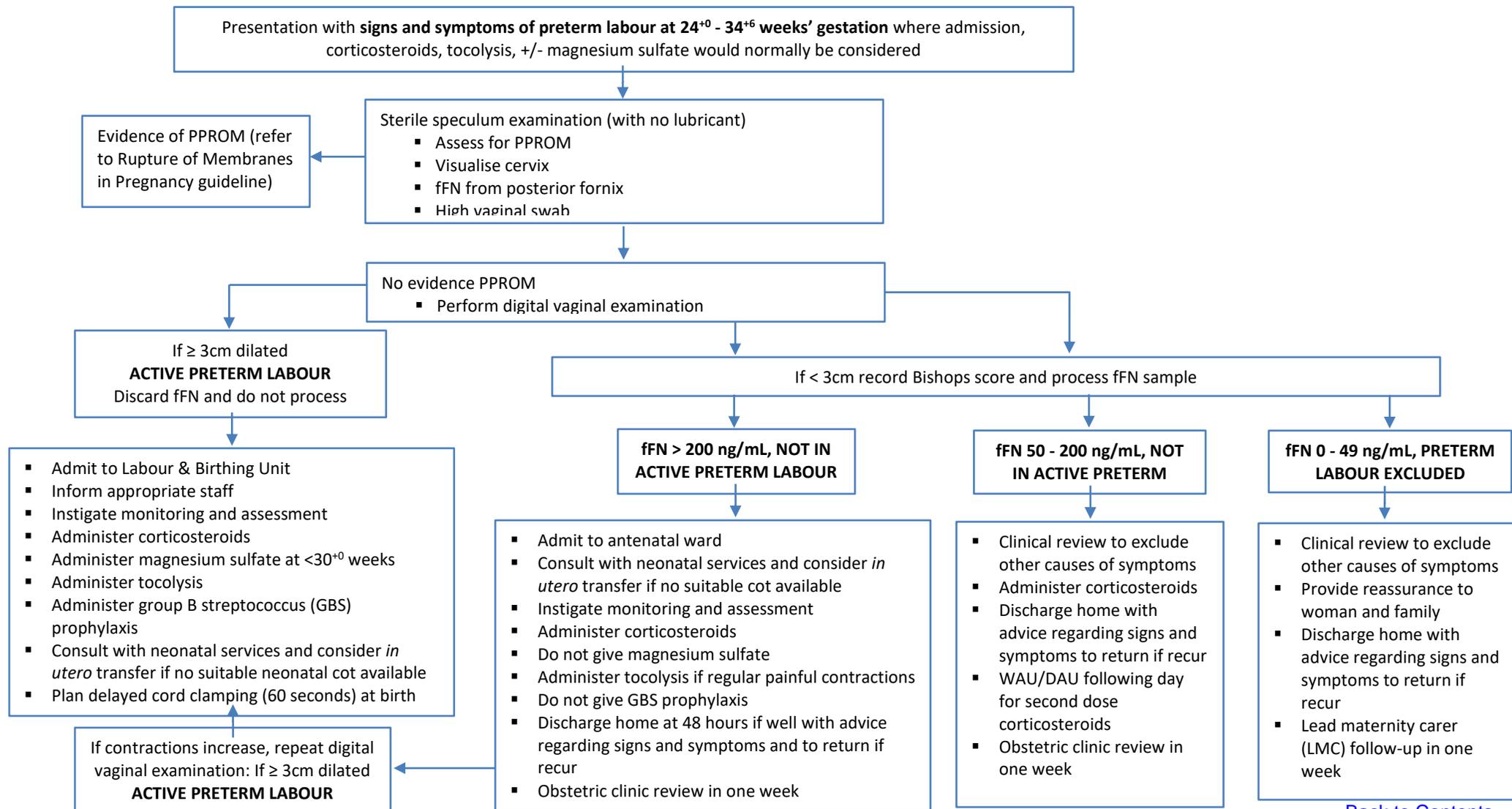
Specimen collection:

This should be done at the time of first speculum examination. The speculum examination should use water as a lubricant (no gel). Collection of the fFN specimen should be prior to any other cervical examination or swab. Place fFN swab into posterior fornix of vagina and rotate for 10 seconds. Place the swab into the fFN plastic specimen collection tube.

Proceed with remainder of vaginal assessment and follow the [PTL Care Plan Algorithm](#) for on-going care. If assessment is not suggestive of significant risk of PTL, the fFN sample can be stored before processing for up to six hours at room temperature and three days in the refrigerator if required.

Note: there is no cost involved in taking the swab, cost to Auckland DHB is only incurred when sample is processed.

5. PTL Care Plan Algorithm



6. Management of confirmed active Preterm Labour 24⁺⁰- 34⁺⁶ weeks

6.1 Admission to Labour and Birthing Unit

6.2 Staff to be informed

- Labour and Birthing Unit clinical charge midwife
- Specialist obstetrician on-call
- Neonatal staff
 - Level 3 team if < 32⁺⁰ weeks
 - Level 2 team if ≥ 32⁺⁰ weeks

6.3 Monitoring and assessment

- Insert intravenous (IV) line
- Obtain full blood count, c-reactive protein (CRP) and group and hold sample
- Confirm fetal presentation by ultrasound scan
- Maternal monitoring (see *Intrapartum Care - Normal Labour and Birth guideline* in [Associated documents](#)).
- Fetal monitoring (see *Fetal Surveillance policy* in [Associated documents](#)). Continuous cardiotocography (CTG) should be performed while in active labour.
- At peri-viable gestations 23⁺⁰- 25⁺⁰ weeks - individual plan to be made in consultation with parents and specialist obstetrician on-call (+/-Maternal Fetal Medicine specialist) and neonatal team regarding degree of monitoring and level of intervention (e.g. whether intrapartum caesarean section (C/S) should be performed for fetal distress). At < 24⁺⁰ refer to Threatened and active PTL at < 24⁺⁰ weeks for further guidance ([section 13](#)).

6.4 Antenatal Corticosteroids

- Refer to *Antenatal Corticosteroids to Improve Neonatal Outcomes* guideline in [Associated documents](#).
 - Should be considered for all women ≤ 34⁺⁶ weeks gestation
 - In women who have received previous corticosteroids in this pregnancy, refer to guideline for repeat doses.

6.5 Magnesium sulfate

- Should be considered for all women < 30⁺⁰ weeks gestation
- Refer to *Magnesium sulfate for Pre-eclampsia and for Neuroprotection in Pre-term Births < 30⁺⁰ Weeks* guideline in [Associated documents](#).
- Magnesium sulfate therapy should not be offered at 30⁺⁰ - 33⁺⁶ weeks gestation until the results of the MAGENTA trial are available and considered (recruitment completed February 2018).

6.6 Tocolysis

- Should be considered for all women ≤ 34⁺⁶ weeks gestation to allow time for corticosteroid, +/- magnesium sulfate administration (and rarely *in utero* transfer).
- Nifedipine ([section 11](#)) should be the first-line tocolytic agent. It is administered orally with less side effects than other available tocolytic agents (betamimetics).

- Refer to and follow the [Nifedipine use flowchart](#).

6.7 Neonatal Group B Streptococcal disease prevention

- Preterm birth is a risk factor for neonatal group B streptococcal disease.
- Group B streptococcus prophylaxis should be offered for all women in active PTL Refer to *Group B Streptococcus (GBS) - prevention of early - Onset Neonatal Infection* guideline in [Associated documents](#).
- Treatment should continue until birth or until the patient is transferred from Labour and Birthing Unit if symptoms of PTL settle and the patient remains undelivered.

6.8 In utero transfer

- The case should be discussed with the neonatal team to ensure that the required level of care is currently available at ACH NICU.
- Consider antenatal transfer if it is necessary and if it is deemed safe.

6.9 Cord clamping

- Delayed cord clamping (60 seconds) at the time of preterm birth has a beneficial effect on neonatal outcome reducing mortality for all births < 37 weeks (relative risk (RR) 0.68, 95% confidence incidence (CI) 0.52 - 0.90) and ≤ 28 weeks (RR 0.70, 95% CI 0.51-0.95) with no reported adverse effects for mother or neonate and so should be used for all births regardless of mode of delivery, plurality or indication for preterm birth, except where there is indication or contraindication to placental transfusion, in view of parent or doctor.
- Contraindications may include, but are not limited to:
 - Fetal haemolytic disease
 - Fetal hydrops
 - Monochromic twin pregnancies in which there is confirmed twin-twin transfusion syndrome
 - Major malformations considered incompatible with survival.
 - Senior clinicians should review these cases and make case-by-case decision.
- At the time of birth, the neonate should be held below the level of introitus or placenta with no palpation or milking of the cord. A clock or stopwatch should be used to time 60 seconds before clamping the cord in the usual way and handing the baby to the neonatal team.
- Oxytocic drugs should be used in the usual manner and can be given before or after cord clamping. Delayed cord clamping is not associated with an increased risk of postpartum haemorrhage.

6.10 Future pregnancy risks after preterm birth

- Medical review should occur prior to hospital discharge and advice regarding the risk of recurrence should be given.
- If delivery < 34⁺⁰ weeks gestation, recommendation should be given for early specialist review during the next pregnancy.
- Consider referral to the Preterm Birth Clinic for pre-pregnancy consult or in future pregnancy.

7. Management of fFN > 200 ng/mL, not in active Preterm Labour

7.1 Admission to antenatal ward for observation

7.2 Staff to be informed

- Neonatal staff
 - Level 3 team if < 32⁺⁰ weeks
 - Level 2 team if ≥ 32⁺⁰ weeks

7.3 Monitoring and assessment

- Insert intravenous line
- Obtain full blood count, CRP and group and hold sample
- Confirm fetal presentation and assessment of estimated fetal weight by ultrasound scan (USS).
- Maternal monitoring: four hourly pulse, BP and temperature (more frequent in first three hours of nifedipine use, refer to the [Nifedipine use flowchart](#)).
- Fetal monitoring: daily CTG unless uterine activity (refer to the [Nifedipine use flowchart](#)).

7.4 Antenatal Corticosteroids

- Refer to *Antenatal Corticosteroids To Improve Neonatal Outcomes* guideline in [Associated documents](#)
 - Should be considered for all women ≤ 34⁺⁶ weeks gestation
 - In women who have received previous corticosteroids in this pregnancy, refer to guideline for repeat doses.

7.5 Magnesium sulfate

- Should not be routinely used. Consider in women < 30⁺⁰ weeks gestation only if they progress to active PTL.
- Refer to *Magnesium sulfate for Pre-eclampsia and for Neuroprotection in Pre-term Births < 30⁺⁰ Weeks* guideline in [Associated documents](#).

7.6 Tocolysis

- Should be considered for all women ≤ 34⁺⁶ weeks gestation with on-going painful uterine contractions to allow time for corticosteroid administration.
- [Nifedipine](#) (section 11) should be the first-line tocolytic agent. It is administered orally with less side effects than other available tocolytic agents (betamimetics).
- Refer to and follow the [Nifedipine use algorithm](#).

7.7 Neonatal Group B Streptococcal disease prevention

- Should not be routinely used. Consider in women < 37⁺⁰ weeks gestation if they progress to active PTL.
- Refer to *Group B Streptococcus (GBS) - prevention of early - Onset Neonatal Infection* guideline in [Associated documents](#).

7.8 In utero transfer

- The case should be discussed with the neonatal team to ensure that the required level of care is currently available at ACH NICU.

- Consider antenatal transfer if it is necessary and if it is deemed safe.

7.9 Cord clamping

- Document a plan for delayed cord clamping (60 seconds) in event of woman going onto preterm birth <37 weeks.

7.10 On-going care

- The majority of women admitted with symptoms of PTL and fFN > 200 ng/mL will not deliver within the next seven days. If they are well and symptom free they should be discharged home at 48 hours.
- A referral should be made for a specialist clinic review in one week.
- All women should be advised of signs and symptoms of preterm labour with a plan for return if symptoms recur.

8. Management of fFN 50 - 200 ng/mL, not in active preterm labour

Patients with symptoms of PTL and a fFN 50 - 200 ng/mL are unlikely to deliver within the next few days but may be at risk of preterm birth (at a later time) and hence admission to hospital at current time is unlikely to make a significant impact on improving outcomes.

8.1 Clinical review in WAU

- Exclude other causes of symptoms e.g. UTI, placental abruption

8.2 Antenatal Corticosteroids

- Refer to *Antenatal Corticosteroids To Improve Neonatal Outcomes* guideline in [Associated documents](#)
 - Should be considered for all women $\leq 34^{+6}$ weeks gestation
 - In women who have received previous corticosteroids in this pregnancy, refer to guideline for repeat doses

8.3 Discharge home with plan for review in WAU/DAU on the following day

- Advice should be given regarding signs and symptoms of preterm labour and plan for earlier return if symptoms recur.

8.4 Next day review in WAU/DAU

- Review any current symptoms
- Administer the second dose of corticosteroid
- Follow-up in obstetric clinic in one week.

9. Management of fFN 0 - 49 ng/mL, preterm labour excluded

Patients with symptoms of PTL and fFN 0 - 49 ng/ml are very unlikely to deliver within the next seven days (< 2%)

- Reassurance should be given to these patients
- Clinical review to exclude other causes of symptoms e.g. UTI, placental abruption

- Discharge home with advice regarding signs and symptoms of preterm labour and plan for return if symptoms recur
- Follow-up with LMC in one week.

10. Nifedipine tocolysis

Tocolysis therapy has only been shown to have limited effects on outcome in relatively small studies and is not a standard of care in some countries, regions and hospitals. However, it has been demonstrated to delay delivery > 48 hours and so its use should be considered in women receiving a first course of antenatal corticosteroids at $\leq 34^{+6}$ weeks, magnesium sulfate at $< 30^{+0}$ weeks or if antenatal transfer is required to access appropriate NICU facilities.

There are a number of tocolytic agents. Of those available in New Zealand and where there is evidence to support use, nifedipine is first-line therapy. Manufacturers may not recommend nifedipine use in pregnancy, however, there are a number of studies of its use as a tocolytic agent and it is accepted as a standard treatment for hypertension in pregnancy. It is administered orally with less side effects than other available tocolytic agents (betamimetics). Two preparations of nifedipine are used within the tocolysis flowchart - short acting nifedipine and modified release nifedipine.

Medicine: Nifedipine 5 mg capsules (short acting) (section 29), Nyefax Retard® 20 mg tablets (modified release nifedipine)

Mechanism of action: Calcium channel blocker

Contraindications:

Absolute:

- Suspected/confirmed intrauterine infection
- Suspected/confirmed placental abruption
- Significant hypotension
- Maternal shock
- Previous allergic response to nifedipine

Relative:

- Use of β -blocker (risk of hypotension)
- Lethal congenital anomalies of the fetus
- Severe fetal growth restriction with suspected fetal compromise
- Abnormal CTG

Possible adverse effects:

- Most common: transient palpitation, headaches and facial flushing
- Less common: constipation, dizziness, nausea, tachycardia, fatigue, peripheral oedema, increased liver enzymes. Liver enzyme changes are not a concern with such a limited use, but care should be taken in those with known liver disease.

Dose and administration:

- Refer to [Nifedipine use algorithm](#)
- Initial dosing: Short acting nifedipine 10 mg (two x 5 mg capsules) every 15 minutes if still contracting (up to four doses)
- Maintenance: Modified release nifedipine 20 - 40 mg eight hourly (maximum of 160 mg in 24 hours) (Nyefax Retard)
- Dose can be adjusted according to clinical symptoms
- Modified release nifedipine should be discontinued 12 hours after the last corticosteroid dose. There is no data to support continued maintenance therapy.

Monitoring:

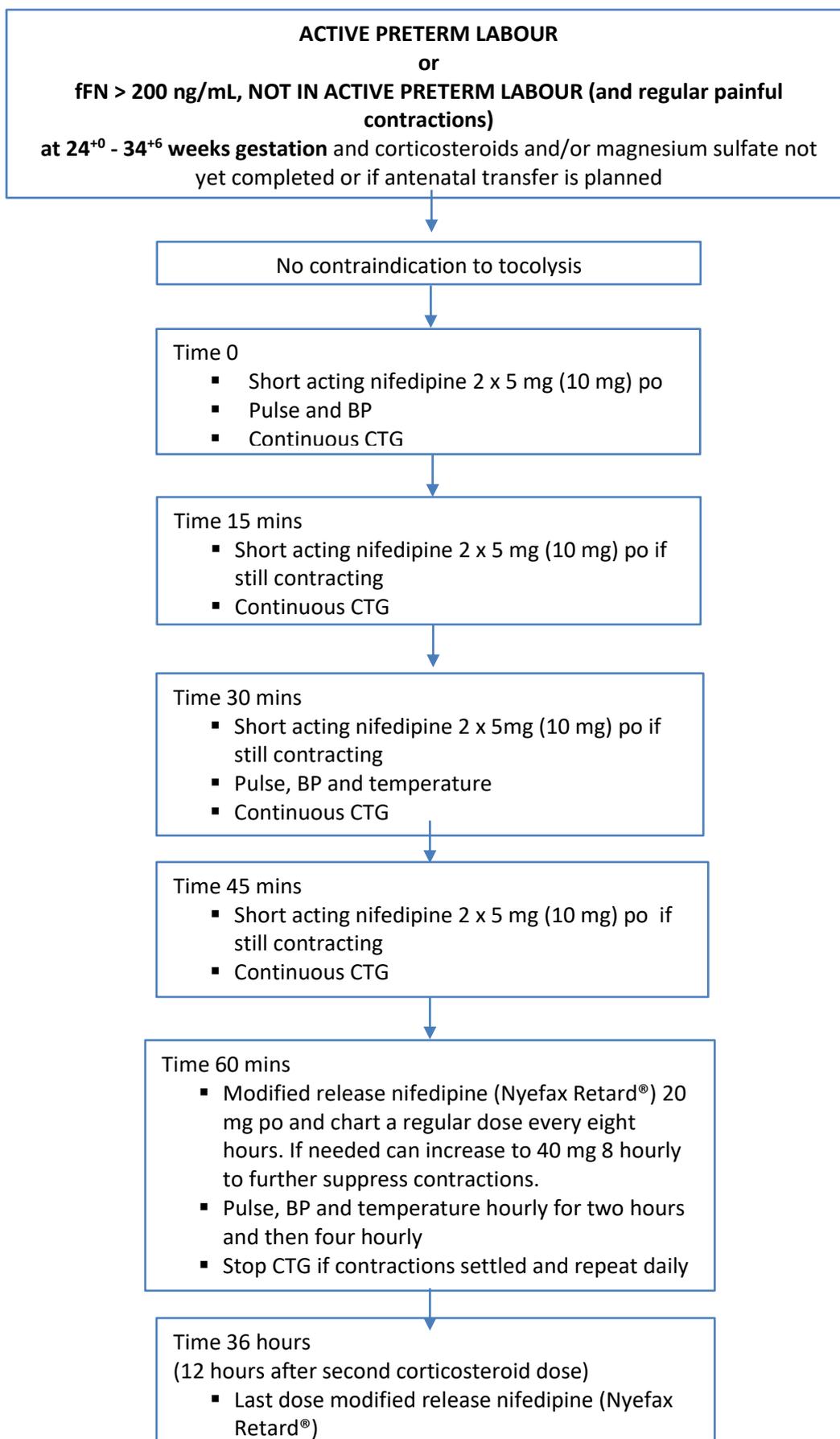
Maternal:

- First hour: pulse, Blood Pressure (BP) at 0, 30 and 60 minutes
- Next two hours: pulse, BP and temperature hourly
- Remaining time on treatment: pulse and BP four hourly.

Fetal:

- Baseline CTG must be normal before commencement of therapy
- CTG at commencement of treatment
- Continuous CTG for the first hour and until painful contractions cease
- Subsequent CTG daily or as clinically indicated e.g. increase in maternal temperature or pulse rate or return/increase in contractions.

11. Nifedipine tocolysis flowchart



12. Repeat presentation with symptoms of preterm labour

Women who present with symptoms of PTL but who do not go onto to deliver will be discharged from hospital with advice to return if symptoms recur (fFN 0 - 200 ng/mL, on day of review and fFN > 200 ng/mL 48 hours after admission). If they represent with recurrence of symptoms of PTL ≤ 34⁺⁶ weeks they should undergo the same clinical review as those presenting for the first time (refer to [Diagnosis of Preterm Labour](#) - section 4).

For women in active preterm labour, follow [management of confirmed active Preterm Labour](#) algorithm (section 7).

For women with fFN > 200 ng/mL but cervical dilatation < 3 cm, follow [Management of fFN > 200 ng/mL, but not in active Preterm Labour](#) algorithm (section 8).

For women with fFN 50 - 200 ng/mL, follow management of [Management of fFN > 200 ng/mL, but not in active Preterm Labour](#) algorithm (section 9)

For women with fFN 0 - 49 ng/mL, follow [Management of fFN 0-49 ng/mL, Preterm Labour excluded](#) algorithm (section 10).

13. Threatened and active PTL at < 24⁺⁰ weeks

Over the last 10 - 20 years there have been significant improvements in survival and survival free of major morbidity in infants born at peri-viable gestational ages (23⁺⁰ - 25⁺⁰ weeks). Active interventions including the use of antenatal corticosteroids and magnesium sulfate are likely to be significant influencing factors on survival and survival free from major morbidity. It is therefore appropriate to *consider* a more pro-active approach to care when women present with symptoms of PTL at 23⁺⁰ - 23⁺⁶ weeks.

'Active intervention' < 24⁺⁰ weeks should not form standard routine care but each case must be individualised and tailored ensuring a multidisciplinary and family-centred approach to the care that is offered. All cases must be discussed with the specialist obstetrician on-call +/- Maternal Fetal Medicine (MFM) subspecialist and a review of factors likely to influence outcome should be made. These factors include; presence of small for gestational age (SGA) and markers of fetal well-being (umbilical and other fetal Doppler waveforms, amniotic fluid volume); evidence of PPRM +/- chorioamnionitis; abnormal fetal heart rate recording; presence of suspected fetal anomaly/malformation; fetal sex (where known); multiple gestation; and whether antenatal corticosteroids and magnesium sulfate have been administered (or sufficient time may be gained to administer them).

After careful consideration of these factors and discussion in advance with the on-call neonatology team, 'active intervention' should be offered to parents as an option but support also given for a more conservative approach to care. Ideally counselling should be provided by the specialist obstetrician on-call and specialist neonatologist on-call. If 'active intervention' is planned, the [PTL Care Plan Algorithm](#) (section 6) including the use of a fFN swab, where appropriate, should be followed.

If 'active intervention' is planned, the neonatology team should attend delivery. Assessment may include on-going appraisal of any intra-partum factors that have developed, birth weight, baby's condition at birth and response to resuscitation in addition to factors known in advance. A plan for 'active intervention' at the time of presentation does not commit caregivers to full resuscitation after birth if this is not deemed to be in the baby's best interest, and antenatal counselling should cover this eventuality.

Discussion regarding use of caesarean section (C/S) at gestational age 23⁺⁰ - 23⁺⁶ weeks should be included in parental counselling. A plan for 'active intervention' at the time of presentation does not commit parents or caregivers to perform a C/S but this should be considered and discussed and there should be a plan documented. It is likely that a classical C/S (or high transverse incision) may be required and the implications for a future pregnancy considered (i.e. need for elective C/S). It is not clear that C/S in some cases (e.g. for breech presentation or for CTG evidence of fetal distress) will improve outcome for the fetus/neonate, however, in others (e.g. transverse lie) where a decision for 'active intervention' has been made, it is likely to be beneficial. If a decision has been made not to perform C/S for fetal indications, continuous CTG monitoring in labour is not recommended. However, intermittent fetal heart rate auscultation may aid the neonatal team's care at time of delivery and should be performed and documented.

Fetal fibronectin testing can be used at gestational ages > 22⁺⁰ weeks but should only be considered if it is likely to significantly influence management decisions.

14. Research

The optimal management and care of women presenting with symptoms of preterm labour is constantly evolving. Over the last 30 - 40 years clinical trial research has led to significant improvements in neonatal survival and survival free from major morbidity due to preterm birth. However, it is still a leading cause of perinatal death and has a huge cost both financially and emotionally to the families we care for and for our society as a whole. National Women's Health has a strong history of contribution to trials around preterm birth, for example, APTS (Australian Placental Transfusion Study), ASTEROID (Dexamethasone vs Betamethasone prior to Preterm Birth), MAGENTA (use of magnesium sulfate prior to delivery 30 - 34 weeks) and PPRMOT (management of PPRM at 34 - 37 weeks). National Women's Health are committed to on-going research to further improve the care provided and all women presenting with symptoms of PTL who are eligible for on-going clinical trials that may be of benefit must be offered and actively encouraged to participate.

15. Future audit

There are a number of auditable standards within this guideline. These should be reviewed regularly and practice should be audited. Examples include:

- Use of fFN in women presenting with symptoms of PTL
- Invitation to join relevant research studies
- Adherence to use of management strategies according to [PTL Care Plan algorithm](#)
 - Admission rates
 - Use of tocolysis

- Use of corticosteroids, use of magnesium sulfate
- Discharge with next day WAU/DAU review in women with fFN 50 - 200 ng/mL not in active PTL
- Discharge at 48 hours in women with fFN > 200 ng/mL not in active PTL.

16. Supporting evidence

- Abbott, D. S., Radford, S. K., Seed, P. T., Tribe, R. M., & Shennan, A. H. (2013). Evaluation of a quantitative fetal fibronectin test for spontaneous preterm birth in symptomatic women. *American Journal of Obstetrics & Gynecology*, 208(2), 122-e1.
- Antenatal Corticosteroid Clinical Practice Guidelines Panel. *Antenatal corticosteroids given to women prior to birth to improve fetal, infant, child and adult health*. Clinical Practice Guidelines. 2015. Liggins Institute, University of Auckland, Auckland. New Zealand. Retrieved from, http://www.ligginsinstitute.org/ANC_CPG/
- Auckland District Health Board. (2013). *National Women's Annual Clinical Report*. Retrieved from, [http://nationalwomenshealth.adhb.govt.nz/National Women's Annual Clinical Report/2013 external link](http://nationalwomenshealth.adhb.govt.nz/National%20Women's%20Annual%20Clinical%20Report/2013%20external%20link).
- Chien, L. Y., Whyte, R., Aziz, K., Thiessen, P., Matthew, D., Lee, S. K., *et al.* (2001). Canadian Neonatal Network. Improved outcome of preterm infants when delivered in tertiary care centers. *Obstetrics & Gynecology*, 98(2), 247-252.
- Conde-Agudelo, A., Romero, R., & Kusanovic, J. P. (2011). Nifedipine in the management of preterm labor: a systematic review and metaanalysis. *American journal of obstetrics and gynecology*, 204(2), 134-e1.
- Dawes, L., Prentice, L., & Groom, K. (2018). A Blinded Prospective Observational Study Comparing Qualitative Fetal Fibronectin, Quantitative Fetal Fibronectin and Partosure (PAMG-1) to Assess the Risk of Preterm Birth in Women with Threatened Preterm Labour. *Journal of Paediatrics and Child Health*, 54(S1), 17-17.
- Ecker, J. L., Kaimal, A., Mercer, B., Blackwell, S. C., O de Reigner, R. A., Farrell, R. M., Grobman, W. A., Resnik, J. L., & Sciscione, A. C. (2015). Periviable Birth, Consensus Statement Number 3 ACOG/SMFM. *Obstet Gynceol*, 126(5), e82-94.
- Fogarty, M., Osborn, D. A., Askie, L., Seidler, A. L., Hunter, K., Lui, K., *et al.* (2018). Delayed vs early umbilical cord clamping for preterm infants: a systematic review and meta-analysis. *American Journal of Obstetrics & Gynecology*, 218(1), 1-18.
- Gomez, R., Romero, R., Medina, L., Nien, J. K., Chaiworapongsa, T., Carstens, M., *et al.* (2005). Cervicovaginal fibronectin improves the prediction of preterm delivery based on sonographic cervical length in patients with preterm uterine contractions and intact membranes. *American journal of obstetrics and gynecology*, 192(2), 350-359.
- Honest, H., Bachmann, L. M., Gupta, J. K., Kleijnen, J., & Khan, K. S. (2002). Accuracy of cervicovaginal fetal fibronectin test in predicting risk of spontaneous preterm birth: systematic review. *Bmj*, 325(7359), 301.
- Iams, J. D., Casal, D., McGregor, J. A., Goodwin, T. M., Kreaden, U. S., Lowensohn, R., & Lockitch, G. (1995). Fetal fibronectin improves the accuracy of diagnosis of preterm labor. *American journal of obstetrics and gynecology*, 173(1), 141-145.
- King, J. F., Flenady, V., Papatsonis, D., Dekker G & Carbonne, B. (2010). Calcium channel blockers for inhibiting preterm labour. *Cochrane Database of Systematic Reviews*.

- Lockwood, C. J., Senyei, A. E., Dische, M. R., Casal, D., Shah, K. D., Thung, S. N., ... & Garite, T. J. (1991). Fetal fibronectin in cervical and vaginal secretions as a predictor of preterm delivery. *New England Journal of Medicine*, 325(10), 669-674.
- Ministry of Health. (2017). *Diagnosis and treatment of hypertension and preeclampsia in pregnancy in New Zealand guidelines*.
- Roberts, D. & Dalziel, S. (2013). Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database of Systematic Reviews*. Retrieved from, http://www.cochrane.org/CD004454/PREG_antenatal-corticosteroids-for-accelerating-fetal-lung-maturation-for-women-at-risk-of-preterm-birth
- Tarnow-Mordi, W., Morris, J., Kirby, A., Robledo, K., Askie, L., Brown, R., *et al.* (2017). Delayed versus Immediate Cord Clamping in Preterm Infants. *New England Journal of Medicine*, 377(25), 2445-2455.
- The Antenatal Magnesium sulfate for Neuroprotection Guideline Development Panel. *Antenatal magnesium sulfate prior to preterm birth for neuroprotection of the fetus, infant and child*. National Clinical Practice Guidelines. Adelaide: The University of Adelaide, 2010. Retrieved from, https://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/cp128_mag_sulphate_child.pdf.
- World Health Organisation. WHO Factsheet no.363. *Preterm Birth*. Nov 2012. Retrieved from, <http://www.who.int/mediacentre/factsheets/fs363/en/>

17. Associated documents

Auckland DHB policies and guidelines

- Antenatal Corticosteroids to Improve Neonatal Outcomes
- Diabetes in Pregnancy
- Fetal Surveillance Policy
- Group B Streptococcus (GBS) - Prevention of Early - Onset Neonatal Infection
- Intrapartum Care – Physiological Labour and Birth
- Magnesium sulfate for Pre-eclampsia and for Neuroprotection in Pre-term Births < 30 Weeks
- Rupture of Membranes in Pregnancy

18. Disclaimer

No guideline can cover all variations required for specific circumstances. It is the responsibility of the health care practitioners using this Auckland DHB guideline to adapt it for safe use within their own institution, recognise the need for specialist help, and call for it without delay, when an individual patient falls outside of the boundaries of this guideline.

19. Corrections and amendments

The next scheduled review of this document is as per the document classification table (page 1). However, if the reader notices any errors or believes that the document should be reviewed **before** the scheduled date, they should contact the owner or [Document Control](#) without delay.