Ministry of National Health
Services Regulations & Coordination
GOVERNMENT OF PAKISTAN

World Health Organization

Pakistan Guidelines for Antenatal Corticosteroids Use

National Guidelines for Antenatal Use of Corticosteroids (ACS) for the Management of Preterm Births in Pakistan

2024

Special Acknowledgement to:

Association for Mothers and Newborn (AMAN),

Society of Gynaecologist and Obstetricians of Pakistan (SOGP),

Pakistan Pediatric Association and Neonatology Group

Midwifery Association of Pakistan (MAP).

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Acronyms and abbreviations

ANC	Antenatal Care
APH	Antepartum Hemorrhage
ACOG	American College of Obstetricians & Gynaecologists
ACS	Antenatal Corticosteroids
AMAN	Association for Mothers & Newborns (Pakistan)
APH	Antepartum haemorrhage
BMI	Body mass index
BEmONC	Basic Emergency Obstetric and Newborn Care
CPAP	Continuous positive airway pressure
CS	Caesarean Section
CEmONC	Comprehensive Emergency Obstetric and Newborn Care
ETAT	Emergency Triage Assessment and Treatment
EmONC	Emergency Obstetric and Newborn Care
FIGO	International Federation of Gynecology and Obstetrics
GDG	Guideline Development Group
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
HSA	Health Services Academy
IM	Intramuscular
IV	Intravenous
KMC	Kangaroo mother care
LHWs	Lady Health Workers
LLETZ	Large loop excision of the Transformation zone
LCG	Labour Care Guide
MAP	Midwifery Association of Pakistan
MoNHSRC	Ministry of National Health Services, Regulations and Coordination, Pakistan
NCMNH	National Committee for maternal & neonatal health Pakistan
NICU	Neonatal intensive care unit
NICE	National Institute for Health and Care Excellence England (guidelines)
NMR	Neonatal mortality rate
PCO	Polycystic ovaries
PMMS	Pakistan Maternal Mortality Survey

PDHS	Pakistan Demographic and Health Survey
PPA	Pakistan Paediatrics Association
PTB	Preterm birth
PTL	Preterm labour
PPROM	preterm prelabour rupture of membranes
RDS	Respiratory distress syndrome
RCOG	Royal College of Obstetricians & Gynaecologists
SDGs	Sustainable Development Goals
SOGP	Society of Obstetricians & Gynaecologists of Pakistan
SRH	[WHO Department of] Sexual and Reproductive Health and Research
SSNC	Sick and small newborn care
UNDP	United Nations Development Programme
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
UTI	Urinary tract infection
WHO	World Health Organization

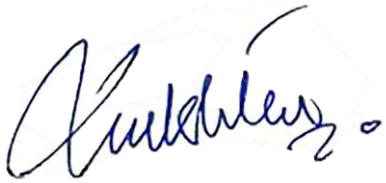
Message from Coordinator to PM on Health

The Neonatal Mortality Rate (NMR) for Pakistan is 42 per 1000 live births (Pakistan Demographic Health Survey (PDHS) 2017-18) which is a huge improvement on the NMR reported in PDHS 2012-13 that was 55 per 1000 live births. It is estimated that almost 300,000 newborns die annually in the country, accounting for around 7% of neonatal deaths happening globally.

Being a signatory to the Sustainable Development Goals (SDGs), Pakistan is committed to make all efforts to accelerate progress towards the set targets including the reduction in Neonatal Mortality Rate (NMR) to as low as 12 per 1000 live births by 2030. Unfortunately, the majority of neonatal deaths occur on the first day of life making it critical to improve care of the neonate during pregnancy and around the time of birth. For improving neonate survival, one of the most important interventions is to address the challenge of very high prevalence of prematurity. As a precaution, the administration of corticosteroids to the pregnant mother at risk of pre-term delivery is recommended to improve the lung maturation of the unborn infant and therefore, improve its survival.

In order to standardize the practices of healthcare providers for provision of antenatal corticosteroids, these National Guidelines are deemed significant contributions in fulfilling the deficiency of a standardized protocol. I am pleased that this document has been finalized and once rolled out across the country can be a tool that will save many precious lives.

I appreciate the efforts of my team at the Ministry of National Health Services, Regulations and Coordination, World Health Organization, technical experts from professional associations and the development partners who have collaborated to give shape to this document. The implementation of this document in all provinces and areas will only be possible with continued collaborative efforts.



Mr Malik Mukhtar Ahmad Bharath
Coordinator to PM on Health
Ministry of National Health Services, Regulations and Coordination

Message from Secretary

Unfortunately, 46 per cent of total deaths among children under five comprised of newborns dying on the day of their birth in 2021 – that too of mostly preventable causes. While mortality among children under five years has declines globally, the reported child deaths are concentrated in the first days of life. This makes the focus on newborn care more critical than ever before. Globally in 2021, an estimated 2.3 million children died in their first month of life, which is approximately 6,400 newborns every day, with about a third of all newborn deaths occurring within the first day after birth and close to three quarters occurring within the first week of life.

Targeting the time around child birth with proven high impact interventions and quality care for small and sick newborns may prevent close to 80 per cent of newborn deaths. One of these interventions is focused on managing prematurity which is a major cause of newborn morbidity and mortality both globally and in Pakistan. The World Health Organization has published global guidance on the administration of antenatal corticosteroid administration among mothers presenting with signs of a premature impending delivery. In Pakistan, the lack of a national guideline/protocol for the same leaves a caveat that promotes varied practices and sub-optimal quality of care.

I am pleased that this gap identified by many practitioners has been aptly filled by the National Guidelines for use of antenatal corticosteroids. This could not have been possible without the hard work of the lead consultant (Association for Mothers and Newborn), technical advisory group involving Society of Obstetricians & Gynecologists of Pakistan (SOGP), Midwifery Association of Pakistan (MAP) and Neonatology Group of Pakistan Pediatrics Association (NG-PPA) and other relevant stakeholders who have contributed. The technical assistance from the World Health Organization from all three levels remained pivotal throughout the development of these guidelines.

These guidelines constitute a much-needed resource for all those striving to save the lives of newborn across the country.

Mr. Nadeem Mahbub
Secretary of Health
Ministry of National Health Services, Regulations and Coordination (MoNHSRC)

Message from WHO Representative

In line with the fourteenth Global Programme of Work and the Sustainable Development Goals, improving quality of care for mothers and newborn is one of the prioritized actions. Approximately 80% of newborn deaths can be prevented through known effective interventions. Unfortunately, in Pakistan, the neonatal mortality rate has remained stagnant during first two decades of the 21st century. It has shown some improvement, but the annual rate of reduction (2.1%) falls too short of the required rate of 6% to achieve the SDG target. It is also a matter of great concern that the total number of newborn deaths in Pakistan account for almost 7% of all newborn deaths globally. Consi dering the significance of this public health challenge in the country, the Ministry of National Health Services, Regulations and Coordination engaged with development partners and technical experts to steer implementation of evidence-based life-saving interventions for improved newborn survival. Access to and the quality of care for newborns must be enhanced in order to meet the international commitments under SDG 2030 the joint EPMM/ENAP 2035 (ending preventable maternal mortality/ every newborn action plan).

Prematurity is a major cause of newborn mortality in Pakistan. One important intervention is the use of antenatal corticosteroids for saving lives of premature newborns. This intervention is in clinical use in the country since long. However, there was no standardized protocol to guide its use. The World Health Organization highly commends the stewardship of Ministry of National Health Services, Regulations and Coordination in spearheading the participatory process of developing national guidelines on administration of Antenatal Corticosteroids (ACS). Appreciation is also due to the technical partner, Association for Mothers & Newborns (AMAN) and the technical advisory group including experts from Society of Obstetricians & Gynecologists of Pakistan (SOGP), Midwifery Association of Pakistan (MAP), Neonatology Group of Pakistan Pediatrics Association (NG-PPA) and UN agencies (UNICEF & UNFPA) together with the WHO team from all three levels of the organization.

Having national guidelines on the subject will encourage healthcare providers to use the standardized treatment protocol with confidence and will improve quality of newborn care ultimately saving lives of the preterm newborns.

Dr. Dapeng Lou
WHO Representative and Head of Mission in Pakistan,
WHO Islamabad.

Foreword

Pakistan was among the first countries to integrate the SDGs into its national development agenda in February 2016. The country made significant progress by mainstreaming these goals in national policies and strategies. In 2018, a National SDGs framework was designed to prioritize and localise SDG targets. The report on SDG Localization 2018 mentions that at the current rate of reduction, Pakistan's NMR can be reduced to only 32/1000 live births which is considerably far from the SDG target of 12/1000 live births. In order to achieve the target for reduction in neonatal mortality, Ministry of National Health Services, Regulations and Coordination (MoNHSRC), with the support of the World Health Organization, has set into motion multiple initiatives to safeguard the lives and wellbeing of the unborn and the newborn. Prematurity remains the major cause of newborn deaths in Pakistan accounting for more than one third of the mortality figure. One evidence-based intervention for improving the survival of the preterm baby is the administration of Antenatal Corticosteroids. Global WHO Guidelines for administration of antenatal corticosteroids were updated recently in 2021 and therefore supersedes the Guidelines that had been rolled out in 2015. In Pakistan, lack of a national guidelines document is recognized by practitioners who kept following varied guidelines resulting in variation in practice and suboptimal outcomes.

The national guidelines on use of antenatal corticosteroids all over the country will bring in standardization of care and establishment of minimum criteria for maintaining quality of newborn care and minimizing the potentially harmful injudicious use of antenatal corticosteroids.

The Ministry of National Health Services, Regulations and Coordination is grateful to the team of experts from Association for Mother and Newborn (AMAN), Society of Obstetricians & Gynecologists of Pakistan (SOGP), Midwifery Association of Pakistan (MAP) and Neonatology Group of Pakistan Pediatrics Association (NG-PPA) who has been instrumental in the development of this document. I would also like to appreciate the World Health Organization from all three levels for supporting this initiative and to all the multiple provincial stakeholders who participated in the consultative meetings to give shape to this critical guidance. I am confident that this guideline will be implemented in its true letter and spirit for saving precious newborn lives in the country.

Dr Shabana Saleem
Director General (PPW)
Ministry of National Health Services, Regulations and Coordination

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The Ministry of National Health Services, Regulations and Coordination (MoNHSRC) acknowledges the support of World Health Organization, Association for Mothers and Newborns (AMAN), Society of Obstetricians & Gynecologists of Pakistan (SOGP), Midwifery Association of Pakistan (MAP) and Neonatology Group of Pakistan Pediatrics Association (NG-PPA), who have jointly developed the National Guidelines for Antenatal Use of Corticosteroids (ACS) for the Management of Preterm Births in Pakistan.

The eminent members of Technical Working Group that was established for steering the development of these guidelines are as follows:

WHO Consultants (AMAN)
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Introduction

Globally, preterm birth complications are the leading cause of death among children under 5 years of age, responsible for approximately 900,000 deaths in 2019.[1] Across countries, the rate of preterm birth ranges from 4–16% of babies born in 2020. An estimated 13.4 million babies were born preterm in 2020 (before 37 completed weeks of gestation) that is, >1 in 10 babies.[2] The majority of global premature births are in South Asia and Sub-Saharan Africa (around 80%). Three-quarters of these deaths could be prevented with current, cost-effective interventions. Unfortunately, majority of the survivors face a lifetime of disability, including learning disabilities and visual and hearing problems.

Inequalities in survival rates around the world are stark. In low-income settings, half of the babies born at or below 32 weeks (2 months early) die due to a lack of feasible, cost-effective care such as warmth, breastfeeding support and basic care for infections and breathing difficulties. In high-income countries, almost all these babies survive. Suboptimal use of technology in low-resource settings results in an increased burden of disability among preterm babies who survive the neonatal period.[3]

Pakistan has one of the highest perinatal morbidity and mortality in the region, and preterm delivery is a major contributor to neonatal mortality statistics. Newborns are directly influenced by the state of maternal health. In Pakistan, there has been a gradual decrease in the neonatal mortality rate (NMR) from 52 deaths per 1000 live births in 2006-07 to 42 deaths per 1000 live births as reported in the Pakistan Demographic and Health Survey (PDHS) of 2017-18. The current rate of progress suggests that Pakistan's projected NMR by the year 2030 would still be 32 deaths per 1000 live births, which is considerably higher than the Sustainable Development Goals (SDG) target of less than 12 deaths per 1000 live births.[4]

Evidence based management of preterm labour with Antenatal corticosteroids (ACS) administration is one antenatal intervention which is cost-effective and feasible to implement, and can have a major impact in reducing mortality from preterm birth in Pakistan.[5]

Rationale

ACS has been in use for over two decades in obstetric practice in Pakistan. However, there is a lack of standard practice guidance for their use, leading to variability in practice and potential suboptimal outcomes. The Society of Obstetricians & Gynaecologists of Pakistan (SOGP) published guidelines on prevention of Pre term birth, but they do not provide guidance on ACS use or tocolysis, once preterm birth is imminent.[6] The tertiary care hospitals in public and private setups have their institutional guidelines, which are not freely available and their utilization is limited to respective settings.

In general, most obstetricians have individual preferences in following the standard textbooks, Royal College of Obstetricians & Gynaecologists (RCOG) UK/ NICE guidelines (UK), World Health Organization (WHO) or American College of Obstetricians & Gynaecologists (ACOG) guidelines, with differences in indications, gestational age range, dosing regimens, repetitive dosage, who can administer, where to administer and lack of availability of desired regimens.[5, 7, 8] Stakeholders in Pakistan recognized the urgent need for evidence-based guidelines to improve newborn survival. These evidence-based recommendations to optimize/ standardize the use of ACS, have the potential to greatly impact the care and outcomes of preterm babies in Pakistan, reducing neonatal mortality and morbidity. They are specifically tailored to the local context to improve the quality of care provided to preterm infants and their mothers. This is especially relevant as SSNC & NICU service facilities are limited even in major cities of Pakistan.

In this document, in addition to ACS use guidelines, recommendations for Management of Preterm Labour (PTL) and Preterm birth (PTB) are also included (Tocolysis, Antibiotic use, and Magnesium Sulphate for Neuroprotection of the newborn). These would be in agreement with the current evidence based WHO guidelines, the WHO Management of Complications of Pregnancy and childbirth 2023 (MCPC 2023 Pakistan edition)[9] & (Pregnancy, Childbirth, Postpartum & Newborn Care 2023 (PCPNC) manuals[10] and EmONC management Protocols (2023) and the National Guidelines on Small & Sick Newborn Care at District Level in Pakistan (2023) recently published by the MoNHRSC.[11] In addition, other professional/ international guidelines on PTB have also been reviewed and suggestions suitable for Pakistan have been incorporated. [12, 13, 14] Other published research on the topic related to Pakistan were also reviewed. [15, 16, 17, 18 19, 20]

Target Audience:

includes national public health policy-makers, implementers and managers of maternal, newborn and child health programmes, health-care facility managers, supervisors/instructors for in-service training, health workers (including midwives, auxiliary nurse-midwives, nurses, paediatricians, neonatologists, general medical practitioners and community health workers), non-governmental organizations, professional societies involved in the planning and management of maternal, newborn and child health services, academic staff involved in research and in the pre-service education and training of health workers, and those involved in the education of parents.

Guidelines for the use of Antenatal Corticosteroids in the Management for Preterm Labour (PTL) in Pakistan

Definitions: Preterm birth (PTB) is defined as birth before 37 weeks of gestation. It is the single most important determinant of adverse infant outcomes, in terms of survival and quality of life. Further subdivisions of preterm birth (as defined by WHO) are:

- **Extremely preterm** (less than 28 weeks)
- **Very preterm** (28–31 weeks plus six days)
- **Moderate to late preterm** (32–36 weeks plus six days)

Risk Factors for Preterm Birth

Risk factors should be identified at first antenatal contact. They are:

i) Maternal Risk factors:
- Age <18 or above 40 years,
- nulliparity,
- high or low Basal Metabolic Index (BMI),
- Poly Cystic Ovary Syndrome (PCOS),
- Smoking/Substance abuse,
- Low socioeconomic status

ii) Obstetric risk factors:
- Previous or family history of Preterm birth is the strongest risk factor.
- Previous history of second trimester abortion, polyhydramnios, nulliparity,
- lack of antenatal care, Multiple pregnancy, Vaginal bleeding, IVF pregnancy

iii) Uterine conditions:
- Conditions causing excessive myometrial stretching/ overdistention (multiple pregnancy, polyhydroamnios, large fetus).
- Stretching of fetal membrane also results in formation of prostaglandins and cytokines which can trigger initiation of labour.
- Congenital Uterine malformations (e.g bicornuate uterus)
- Cervical insufficiency after cervical surgery & cervical cone biopsy,
- large loop excision of the transformation zone (LLETZ),
- Obstetric trauma & Multiple dilatation and evacuation of the cervix and uterus (D&E)

iv) Infections:
- UTI (urinary tract infection),
- bacterial vaginosis,
- Beta Haemolytic
- Streptococcus vaginal infection

Management of Preterm Birth

History: Presence of Obstetric risk factors; increased vaginal discharge, gush of fluid, abdominal/ pelvic pain, true labour pains with increasing frequency, intensity and duration of contractions; cervical changes/ dilatation.

Examination: Check vital signs; confirm gestational age, abdominal examination (presentation/ contractions/ fundal height in cm); Per-speculum vaginal examination (also take High vaginal swab (HVS) for Culture sensitivity (CS); Per-vaginal digital examination

Provisional Diagnosis:

a) Suspected preterm labour? or
b) Established preterm labour?

Investigations:

a) CBC (Complete blood count),
b) HVS (High Vaginal swab) for culture & sensitivity (CS),
c) Ultrasound for fetal wellbeing, presentation, gestational age, amount of amniotic fluid;
d) TVS (Transvaginal ultrasound) to Check Cervical length (<25mm), funneling of membranes
e) Fetal fibronectin: <50 ng/ml (negative), >50 ng/ml (positive) -currently not available in Pakistan.

Recommendation on Management Plan when Preterm Birth is Inevitable

Provide information and counselling to the mother and accompanying family members to involve them in decision-making about her diagnosis, management options and estimated time for in-patient care and possible in-utero transfer and expenses involved.

1. Antenatal Corticosteroids (ACS)

ACS improves fetal lung maturity and chances of neonatal survival from 24 weeks to 34 weeks of gestation, with fewer reported fetal and neonatal deaths, reduced rate of respiratory distress syndrome (RDS) and duration of mechanical ventilation or oxygen supplementation required for the neonate.

ACS therapy is recommended for women with a high likelihood of preterm birth from 24 weeks to 34 weeks of gestation when the following conditions are met:

- **Accurate gestational age (GA) assessment** using all available information including last menstrual period (LMP), physical examination in early pregnancy, ultrasound performed in the first trimester and symphysis fundal height (SFH) measurement in cm (from 20 to 40 weeks of gestation). The risk of harm of ACS administration may outweigh benefits in late preterm births (between 34 to 37 weeks). The result of ACTION III trial are expected in 2025 to confirm this as a recommendation.

- **High likelihood of preterm birth** within 7 days of starting the therapy. Prior to administration of ANC, the diagnosis of preterm labour should be confirmed by documenting cervical effacement / dilatation over 2 hours of observation. The high likelihood can be assessed in cases of PPROM, pre-eclampsia and APH.
- There is **no clinical evidence of maternal infection**. Reliable identification and treatment of maternal infection takes priority.
- **Adequate childbirth care is available** including the capacity to recognize and safely manage preterm labour and birth. There should be adequate emergency obstetric care and childbirth care, as well as adequate care for newborns
- The **preterm newborn can receive adequate care** including resuscitation, thermal care, Kangaroo mother care (KMC), feeding support, infection treatment, safe oxygen use is available at the health facility. Special care of the preterm newborn to prevent and treat complications of prematurity is critical for newborn survival.

✓ **ACS therapy is recommended for women with a high likelihood of giving birth in the next 7 days, even if it is anticipated that the full course of corticosteroids may not be completed:**

- ACS therapy should be started even when the completion of a full course before preterm birth is uncertain. ACS should not be administered to women without a high likelihood of preterm birth, due to the potential harms to the newborns associated with prolonged administration-to-birth intervals (e.g. 3 or more weeks) or administration to women who are likely to give birth at term.
- The mothers and families should be counseled for shared decision-making regarding the use of ACS in the context of uncertainties surrounding the prediction of spontaneous preterm birth.
- When considered safe, tocolytic therapy should be considered as an intervention to gain time to complete a single course of ACS following the WHO guidelines on use of tocolytic therapy for women with high likelihood of preterm birth prior to 34 week's gestation.

✓ **ACS therapy is recommended for women with high likelihood of preterm birth, irrespective of whether single or multiple birth is anticipated:**

- This recommendation precludes the routine or prophylactic use of ACS to any woman with a multiple pregnancy on the basis of increased risk of preterm birth.
- Women with multiple pregnancy are inherently more likely to deliver preterm, however, there is reported overall improvement in critical outcomes among singleton infants as well as reduced risks of adverse critical outcomes reported in multiple pregnancy.
- It is important to segregate reports on outcomes for single and multiple preterm births where ACS has been used to generate more evidence.

✓ **ACS therapy is recommended for women with preterm prelabour rupture of membranes and no clinical signs of infection:**

- Use of prophylactic antibiotics should be included as part of standard care for the woman once preterm prelabour rupture of the membranes (PPRM) is confirmed.
- A considerable proportion of women at risk of preterm birth would present with ruptured membranes. It is therefore, important to note that the benefits of using ACS for reducing adverse neonatal outcomes overweigh the anticipated harms of increased risk of infection to the mother or baby (without evidence) with PPRM.
- ACS should NOT be used in women with prolonged rupture of membranes and with confirmed or suspected bacterial infection.

✓ **ACS therapy is NOT recommended for women with chorioamnionitis who are likely to give birth preterm:**

- Priority should be to timely deliver the baby to avoid further intrauterine insult in such cases.
- ACS should be avoided in women with evidence of ongoing systemic infection e.g. septicemia or tuberculosis.

✓ **ACS therapy is NOT recommended for women undergoing planned caesarean section at 34 weeks 0 days to 36 weeks 6 days:**

- Considering the overall evidence on ACS which does not support its use in women undergoing provider-initiated (planned) preterm birth (C-section) and also suggested potential harms in late preterm infants (after 34 weeks of gestation).

✓ **ACS therapy is recommended for women with hypertensive disorders in pregnancy who have a high likelihood of preterm birth:**

- ACS therapy should be combined with an appropriate standard of care for the management of women with hypertensive disorders in pregnancy.

✓ **ACS therapy is recommended for women with a high likelihood of preterm birth of a growth-restricted fetus:**

- ACS therapy has potential benefits in terms of reduced neurodevelopmental disability among surviving intrauterine growth-restricted infants and there is evidence of reduced odds of adverse newborn mortality and morbidity outcomes.
- There are concerns about the effect of ACS on fetal growth but there is no evidence that ACS will perform differently in this subgroup compared to the overall preterm population.

✓ **ACS therapy is recommended for women with pre-gestational and gestational diabetes when there is a high likelihood of preterm birth, and this should be accompanied by interventions to optimize maternal blood glucose control:**

- ACS therapy has potential benefits on terms of reducing the higher risk of newborn respiratory morbidity posed by maternal diabetes and the potential impact on overall newborn survival.

- There are concerns about the maternal hypoglycemic effects of ACS, but it should be avoided with appropriate measures to ensure glycemic control in view of the potential benefits for the baby.
- Clinicians should ensure strict control of maternal blood glucose prior to and/or during pregnancy to reduce the risk of newborn respiratory distress syndrome and ensure neonatal glucose monitoring.
- Delay in fetal lung maturity is generally more frequent in pregnant women with diabetes compared with the general obstetric population. Therefore, in pregnant women with poorly controlled diabetes, the use of ACS could also be considered at >34 week of gestation.

✓ **Either intramuscular (IM) dexamethasone or IM betamethasone (total 24 mg in divided doses) is recommended as the ACS of choice:**

- A total dose of 24 mg administered in divided doses 12 hours or 24 hours apart is recommended. The preferred choice of ACS regimen is:
  - ✓ four doses of IM dexamethasone 6 mg 12 hours apart OR
  - ✓ 2 doses of IM betamethasone 12 mg 24 hours apart.
- When deciding on dosing frequency, consideration should be given to the likely timing of preterm birth to ensure that the woman completes the total course of ACS or receives a substantial amount of the total dose before birth.
- The treatment protocols should be informed by the preparations that are readily available locally.

✓ **A single repeat course of ACS is recommended for women who have received a single course of ACS at least 7 days prior and, on clinical assessment, have a high likelihood of giving birth preterm in the next 7 days:**

- There is evidence that a repeat course of ACS is associated with a reduction in the composite outcomes (comprising one or more of perinatal deaths, respiratory distress syndrome, intraventricular hemorrhage, bronchopulmonary dysplasia, necrotizing enterocolitis, periventricular leukomalacia and neonatal sepsis), as well as respiratory morbidity and less oxygen supplementation and surfactant use (which could save costs).
- There is evidence that newborn benefits of ACS may be conferred beyond 7 days and may peak around 14 days after the initiation of the first treatment dose, and therefore recommends that the repeat course of ACS should be administered between 7 and 14 days after first treatment dose.
- Clinical assessment occurring between 7 and 14 days after initiation of first course of ACS should consider the gestational age of the pregnancy (between 24 and 34 weeks) and ensuring the woman has a high likelihood of preterm birth in the next 7 days. ACS administration to women with a pregnancy >34 week's gestation should be avoided.

Referral guidance:

If adequate childbirth and preterm newborn care are not available, the woman should be referred to a hospital where adequate care is available before she gives birth (**in-utero**

transfer). If all criteria are met to safely provide corticosteroids, with the exception of the availability of care for preterm infants, consider administration of the first dose of antenatal corticosteroids before transfer.

2. Magnesium Sulfate: [8, 9, 10]

Is indicated if gestational age is less than **32 weeks** (when delivery is imminent in 24 hours) to prevent preterm birth-related neurologic complications. It is given as an intravenous (IV) infusion or intramuscular (IM) injections to prevent cerebral palsy in the infant.

Dose: Initial dose 4 g IV over 20 minutes

Maintenance dose: IV 4 g over 30 minutes, then 1 g per hour for 24 hours or until birth, whichever occurs earlier

OR

IV bolus of 4 g given as single dose and IV 6 g over 20–30 minutes, 2 g per hour

OR

IM 5 g initial dose, followed by 5 g IM every four hours for 24 hours or until the woman has given birth, whichever occurs earlier

Caution: Monitor urinary output and signs of magnesium overdose or toxicity (respiratory rate less than 16 breaths per minute and/or absent patellar reflexes). Withhold magnesium sulfate if there are signs of magnesium toxicity. Restart only after signs of overdose or toxicity disappear.

NOTE: The most commonly used regimen is 4g loading dose followed by 1g/hour. For this regimen there is no 2nd bolus of 4g given. An alternative regimen is 6g over 20-30 minutes followed by 2g/hour but this is used less frequently because of toxicity concerns. The IM regimen is not recommended currently but the practice is often 4g IV loading dose followed by 2 injections of 5g in each buttock.

3. Antibiotics [21]

If amniotic membranes are intact and there are no clinical signs of infection, do not give prophylactic antibiotics.

Antibiotics are indicated for women with preterm pre-labour rupture of membranes (PPROM) and/or when there are clinical signs of infection, to reduce the risk of chorioamnionitis in the mother and the risk of neonatal infections (e.g. pneumonia, cerebral abnormality).

- ✓ Oral **Erythromycin** 250 mg every six hours for 10 days (or until birth)
- ✓ OR **Ampicillin** 2 g IV every six hours.

If the woman has confirmed Group B streptococcal colonization, give **amoxicillin** 500 mg by mouth every eight hours for 7 days. Do not use amoxicillin plus clavulanic acid (co-amoxiclav) in case of PPROM; it increases the risk of necrotizing enterocolitis.

RCOG recommendation:

- ✓ **Erythromycin** 250 mg P/O QID for 10 days or until established labour (whichever is sooner)

ACOG recommendation:

- ✓ **Ampicillin** 2gm I/V QID + Erythromycin 250mg I/V QID for 2 days
- ✓ **Amoxicillin** 250mg P/O TID + Erythromycin 333 mg P/O TID for 5 days

4. Tocolytics [8, 9, 10, 21]

i) Nifedipine is the drug of choice for tocolysis, as the benefits outweigh the risks, cost, acceptability and feasibility is superior to other tocolytic agents. It provides a window for administration of ACS and/or in-utero fetal transfer to an appropriate neonatal health care setting. It is recommended for women with a high likelihood of preterm birth for the purpose of improving newborn outcomes, when the following conditions are met:

- Spontaneous preterm labour is suspected or diagnosed and
- Gestational age is accurately assessed to be between 24 weeks to 34 weeks.

It is contraindicated when there is vaginal bleeding, placental abruption or intrauterine infection. It permits a single course of ACS to be administered and enables transfer of the mother (in utero transfer) to a facility where the preterm infant can receive adequate birth care (including management of preterm birth, newborn resuscitation, kangaroo mother care, thermal care, feeding support, infection treatment and respiratory support including continuous positive airway pressure as needed)

Women and families should receive adequate information about the benefits and risks of tocolysis, including the lack of information on long-term outcomes. Recommended dosage is:

- ✓ a loading dose of 20 mg Nifedipine immediate-release capsule orally (do not puncture the capsule)
- ✓ if required, give an additional 10 mg every 15 minutes up to a maximum of 40 mg in the first hour; can also give repeated doses of 10mg every 6 hours and titrate based on contractions for a maximum of 180mg/day
- ✓ follow up with 20 mg (or 30mg) sustained-release tablet orally daily for up to 48 hours or until transfer is completed, whichever comes first.

RCOG recommendation:

- ✓ 30mg loading then 10-20mg orally every 6 to 8 hours
- ✓ Maximum 180 mg/day

Side effects: Hypotension, palpitations, flushing, dizziness, itching

Concurrent use with magnesium sulphate is not supported due to risk of pulmonary edema (although not contraindicated if considered necessary).

Monitor maternal and fetal condition (pulse, blood pressure, signs of respiratory distress, uterine contractions, loss of amniotic fluid or blood, fetal heart rate, fluid balance).

Caution:

- Do not give tocolytic drugs for more than 48 hours.
- Do not give a combination of tocolytic agents as there is no additional benefit.
- Tocolytics should not be used in the following conditions:
  - preterm prelabour rupture of membranes (PPROM). It should be noted that tocolytics could be considered for women with PPROM as most trials included women with PPROM, especially if an ACS course is given and there are ongoing contractions or there is a need for transfer.
  - chorioamnionitis
  - placental abruption
  - cardiac disease.

ii) Oxytocin receptor antagonists: Atosiban (not available in Pakistan, more costly), and **nitric oxide donors** can also prolong pregnancy. Based on the available trials COX inhibitors do have a tocolytic effect (delaying birth up to 48 hours) and may be considered in the management of preterm labour prior to 28 weeks. They are contraindicated, however, in the 3rd trimester due to an association with increased risk of premature closure of the ductus arteriosus and potential renal dysfunction leading to oligohydramnios.

iii) Magnesium sulfate has a tocolytic effect (delaying birth by 48 hours), but other tocolytic agents have greater benefits and fewer side-effects.

iv) Betamimetics are effective in delaying birth, but are associated with a risk of serious maternal adverse effects, which may be life-threatening. They are not recommended

v) Combination therapy does not have more benefits than monotherapy and is not recommended.

There is a lack of information on the long-term outcomes following tocolysis, which should be discussed with the woman and her family so an informed decision can be made.

In the 2015 WHO guideline, tocolytic treatments (acute and maintenance treatments) were not recommended for women at risk of preterm birth, due to the lack of substantive benefits of tocolytic treatment, compared with no tocolytic treatment, in terms of reducing adverse perinatal and neonatal outcomes and frequency and severity of side effects. A review of the evidence in 2022 however, has recommended in favour of Nifedipine for acute and maintenance tocolytic therapy for women with a high likelihood of preterm birth, when certain conditions are met. [21]

Clinical Management of Preterm Labour & Delivery

If labour continues and gestation is less than 37 weeks:

Monitor progress of labour using the **LCG** (Labour Care Guide). Routine caesarean birth is not recommended to improve newborn outcomes for preterm infants, regardless of cephalic or breech presentation.

Avoid vacuum-assisted birth, as the risks of intracranial bleeding in the preterm baby are high. **Prepare for management of preterm** or low birth weight baby and anticipate the need for resuscitation.

Mode of Delivery:

- Cephalic- vaginal delivery is safe.
- Breech- consider C-Section

Fetal monitoring:

- CTG or Intermittent auscultation
- Avoid fetal scalp electrodes & fetal scalp blood sampling before 34 weeks.

Antibiotics:

- Give Intrapartum antibiotic prophylaxis for suspected and confirmed Group B Streptococcus (GBS) infection.
- If no history of penicillin allergy: benzylpenicillin 3gm I/V after the onset of labour and 1.5 gm 4 hourly until delivery.
- If Penicillin allergy is not severe: Cefuroxime 1.5gm I/V followed by 750mg every 8 hours.
- Severe penicillin allergy: vancomycin 1gm I/V every 12 hours.
- Chorioamnionitis: benzylpenicillin + gentamicin + metronidazole

Cord clamping:

- Wait at least 1 min before clamping (if fetal and maternal conditions are stable).
- Keep baby at or above the level of the placenta. [8, 9, 10]

Key Recommendations for the Care for Preterm Infant after Birth (Minimal Care Package):

- Newborn resuscitation
- Thermal care
- Feeding support
- Infection treatment
- Kangaroo mother care (KMC) when infant weighs less than 2,500 g
- Continuous positive airway pressure (CPAP) for preterm infants with respiratory distress syndrome (RDS)
- Surfactant for preterm infants with RDS in facilities meeting minimum criteria*
- Oxygen (O2) treatment with 30% O2 or air (if blended O2 is not available) or preferably CPAP during ventilation of preterm infants born ≤32 weeks
- Progressively higher concentrations of O2 preferably blended oxygen for neonates undergoing O2 treatment as per defined criteria
- Respiratory support including continuous positive airway pressure [CPAP] as needed

* Refer to National Guidelines on small and sick newborn care at district level

Additional Recommendations [22]

- **Caffeine (Methylxanthines) for treatment of apnoea** for prematurity in all preterm infants <37 weeks gestation is strongly recommended (benefits include decreased death, bronchopulmonary dysplasia and neurodevelopmental disability and decreased mechanical ventilation in trials of caffeine in preterm infants, with no evidence of harms.
- **Caffeine for prevention of apnoea** for prematurity may be considered in preterm infants <34 weeks gestation, based on low certainty evidence. Inclusion criteria for the seven RCTs relevant to this comparison were gestational age at birth below 34 weeks and no evidence of apnoea. Evidence of small to moderate benefits was found for decreased bronchopulmonary dysplasia and decreased apnoeic episodes in trials of preterm infants <34 weeks gestation, and uncertain evidence of harms was found for increased mortality and mechanical ventilation (low certainty evidence)
- If caffeine is not available, **other methylxanthines (aminophylline or theophylline)** may be considered. While evidence for use of methylxanthines for prevention of apnoea was available only for preterm infants <34 weeks gestation, caffeine (or other methylxanthines) may also be considered for prevention of apnoea in preterm infants 34– <37 weeks depending on clinical judgement.
- The suggested dosing of caffeine is a 20 mg/kg loading dose and 5 mg/kg/day maintenance doses for 6 weeks. Given until corrected gestational age of >34 weeks gestation and the baby is event free for at least 5 days.
- Caffeine is also recommended for **extubation of preterm infants <34 weeks gestation,** based on evidence of moderate benefits of decreased death, bronchopulmonary dysplasia, failed extubation, and neurodevelopmental disability and no evidence of harms.
- Caffeine should be started 24 h before a planned extubation. If the extubation is unplanned, the infant should receive caffeine as soon as possible after the extubation and within 6 h. A 20 mg/kg loading dose and 5 mg/kg/day maintenance doses continued for 6 days is suggested.

Domain	Recommendation	Status	Strength
B.4 Methylxanthines for treatment of apnoea	Caffeine is recommended for the treatment of apnoea in preterm infants. (Strong recommendation, moderate-certainty evidence)	New	Strong
B.5 Methylxanthines for extubation	Caffeine is recommended for the extubation of preterm infants born before 34 weeks' gestation. (Strong recommendation, moderate-certainty evidence)	New	Strong
B.6 Methylxanthines for prevention of apnoea	Caffeine may be considered for the prevention of apnoea in preterm infants born before 34 weeks' gestation. (Conditional recommendation, low-certainty evidence)	New	Conditional

Family involvement and support

- Involvement of, and support of families in caring for preterm/LBW infants is recommended. It involves participation of mothers, fathers, and other family members in routine care of the newborn infant while in the newborn care unit. It may include providing direct bedside care, family involvement in medical decision making, hospital culture change, and hospital infrastructure changes (e.g., rooming in, couplet care or zero-separation of mother and infant, family rooms). Other interventions (sometimes called 'cointerventions') which were implemented in the studies included neurodevelopmental and neurobehavioural care, skin-to-skin care, KMC, infant massage, psychosocial support, and financial incentives.

- A strong recommendation based on low-to moderate-certainty evidence was made for family involvement in routine care of preterm or LBW babies in health facilities. This recommendation was made on the basis of evidence of moderate benefits, including decreased morbidity (infection, intraventricular haemorrhage, retinopathy of prematurity, bronchopulmonary dysplasia), increased weight and length at hospital discharge, increased length at 18 months, increased neurodevelopment, decreased length of hospital stay, and increased breastfeeding in trials of infants <37 weeks gestation or <2.5 kg birth weight, with no evidence of harms.

- Family involvement strategies also reduced parental anxiety and stress

- **Home visits by trained health workers** is strongly recommended, to support mothers, fathers and families to care for their preterm or LBW infant. Evidence of benefits of home visits included a moderate decrease in mortality (moderate certainty evidence) and a small decrease in number of hospitalisations (very low certainty evidence) in trials of infants <37 weeks gestation or <2.5 kg birth weight, with no evidence of harms. Home visits also increased non-critical outcomes of exclusive breastfeeding rates, immunisation visits, parental-infant attachment and decreased parental stress. The GDG suggested that extra home visits (i.e., additional to the routine scheduled postnatal contacts for all babies) should be made and that their content, frequency, duration and intensity should be established

Prevention of Preterm Birth

Accurate diagnosis of cervical insufficiency is difficult. Both prophylactic cervical cerclage and prophylactic vaginal progesterone are effective in preventing or delaying preterm birth in women with a short cervix and a history of spontaneous preterm birth (up to 34+0 weeks of pregnancy) or mid-trimester loss (from 16+0 weeks of pregnancy onward)

Cervical insufficiency (cervical incompetence), is an underlying cervical structural defect that contributes to early delivery of an otherwise healthy pregnancy.

Diagnosis is based on history in which cervical dilatation occurs without contractions in one or more pregnancies. In most cases, this leads to delivery in the second trimester of pregnancy. Cervical cerclage is indicated in the 2nd trimester in women with singleton pregnancies who:

- Have a history of second-trimester pregnancy loss associated with painless cervical dilation without labor or placental abruption.
- Have had cerclage in a previous pregnancy due to painless dilation.
- Currently have painless cervical dilation.
- Previously had a spontaneous preterm birth before 34 weeks and, in the current pregnancy, have a cervical length under 25 mm before 24 weeks' gestation.
- It is not recommended for women with short cervical length in the second trimester without a history of preterm birth.

Scope of the Guidelines:

These guidelines have been adapted to the Pakistani healthcare system, considering the local epidemiology, resources, drug availability and challenges.

ACS is not a substitute for lack of surfactant and mechanical ventilation

ACS is protective against Respiratory Distress Syndrome (RDS), however preterm neonates are vulnerable and require special care with or without steroids. These guidelines emphasize adequacy of care of the preterm newborn in settings where ACS is given. [22]

Success of ACS depends on care of the preterm newborn. Scaling up ACS use on its own in the absence of strengthened small and/or sick newborn care will not suffice. The preterm newborn needs to receive appropriate care to survive into a healthy childhood. It is clear from the WHO guidelines, that sick small newborn care (SSNC) is a priority.

Scaling up ACS: Need for National Policy

The national guideline on ACS use is an effective tool for promoting newborn survival. It is important to have a consistent approach to the use of ACS and to focus on strengthening of small & sick newborn care (SSNC) to support in implementation of the guidelines.

Reporting & Monitoring

It is recommended to record patient data meticulously in the standardized intra-partum care / delivery register & hold regular (e.g. monthly) Perinatal and Maternal morbidity and mortality audit meetings (surveillance and response system). This will ensure proper data collection and improved patient care through scientific discussion between concerned departments and professionals. There should also be a central government based/ supervised reporting of data from health facilities, to monitor progress and effect of ACS and other best practice interventions. National protocols need to be defined for monitoring the response and potential adverse effects of ACS in pregnant women and fetuses. There is also need to develop guidelines for postnatal monitoring of the management of preterm babies born to mothers who received ACS.

Annexures

Table 1: WHO recommendations on antenatal corticosteroid therapy for improving preterm birth outcomes

Recommendation	Category of recommendation
1.0. Antenatal corticosteroid therapy is recommended for women with a high likelihood of preterm birth from 24 weeks to 34 weeks of gestation when the following conditions are met: ▪ Gestational age assessment can be accurately undertaken ▪ There is a high likelihood of preterm birth within 7 days of starting therapy ▪ There is no clinical evidence of maternal infection ▪ Adequate childbirth care is available (including capacity to recognize and safely manage preterm labour and birth) ▪ The preterm newborn can receive adequate care (including resuscitation, kangaroo mother care, thermal care, feeding support, infection treatment and respiratory support including continuous positive airway pressure [CPAPI as needed)	Context-specific recommendation
1.1. Antenatal corticosteroid therapy should be administered to women with a high likelihood of giving birth preterm in the next 7 days, even if it is anticipated that the full course of corticosteroids may not be completed.	Context-specific recommendation
1.2. Antenatal corticosteroid therapy is recommended for women with a high likelihood of preterm birth, irrespective of whether single or multiple birth is anticipated.	Context-specific recommendation
1.3. Antenatal corticosteroid therapy is recommended for women with preterm prelabour rupture of membranes and no clinical signs of infection.	Context-specific Recommendation
1.4. Antenatal corticosteroid therapy is not recommended for women with chorioamnionitis who are likely to give birth preterm.	Not recommended
1.5. Antenatal corticosteroid therapy is *not* recommended for women undergoing planned caesarean section at 34 weeks 0 days to 36 weeks 6 days.	Not recommended
1.6. Antenatal corticosteroid therapy is recommended for women with hypertensive disorders in pregnancy who have a high likelihood of preterm birth.	Context-Specific recommendation
1.7. Antenatal corticosteroid therapy is recommended for women with a high likelihood of preterm birth of a growth-restricted fetus.	Context-specific recommendation
1.8. Antenatal corticosteroid therapy is recommended for women with pre-gestational and gestational diabetes when there is a high likelihood of preterm birth, and this should be accompanied by interventions to optimize maternal blood glucose control.	Context-specific recommendation
1.9. Either intramuscular (IM) dexamethasone or IM betamethasone (total 24 mg in divided doses) is recommended as the antenatal corticosteroid of choice.	Recommended
1.10. A single repeat course of antenatal corticosteroids is recommended for women who have received a single course of antenatal corticosteroids at least 7 days prior and, on clinical assessment, have a high likelihood of giving birth preterm in the next 7 days.	Recommended

Estimate gestational age (GA) to manage risk of preterm birth

Job Aid

Certain last menstrual period? (LMP)

No → **Access to ultrasound?**

Yes

Date by ultrasound + LMP

Compare ultrasound and LMP dating

Timing of ultrasound and difference with dating by LMP:

- Up to 8^{+6} wks: +/- 5 days
- 9^{+0} to 15^{+6} wks: +/- 7 days
- 16^{+0} to 21^{+6} wks: +/- 10 days
- 22^{+0} to 27^{+6} wks: +/- 14 days
- >28^{+0} wks: +/- 21 days

Date by LMP

Timing of ultrasound and difference with dating by LMP:

- Up to 8^{+6} wks: >5 days
- 9^{+0} to 15^{+6} wks: >7 days
- 16^{+0} to 21^{+6} wks: >10 days
- 22^{+0} to 27^{+6} wks: >14 days
- >28^{+0} wks: >21 days

Date by ultrasound

Access to ultrasound?

No → **Attempt to obtain additional information, then use best clinical estimate**

Yes

Date by ultrasound based on careful clinical judgment

An LMP can be considered certain or reliable if the following criteria are met:

- The woman is certain of the date her menses began and can provide the date of the first day of her last normal menstrual period;
- She had a regular 24-32-day menstrual cycle occurring for at least 6 months prior to pregnancy;
- She had not been on hormonal contraceptive pills for at least 3 months or injectable hormonal contraceptives for at least 6 months before her LMP;
- She conceived using assisted reproductive technology.

If the LMP is certain, the LMP and ultrasound-derived gestational age estimates should be compared.

If the LMP is uncertain or unknown, the ultrasound-derived gestational age should be used (regardless of trimester).

Viability (depending on local context) 24^{+0}-28^{+0} weeks		*32^{+0} weeks*	*34^{+0} weeks*	*37^{+0} weeks*
Prepare for possible fetal demise	*Offer $MgSO_4$ for fetal neuroprotection* *Offer an ACS (dexamethasone or betamethasone) to improve lung maturity* *For PPROM, offer prophylactic antibiotics (e.g. erythromycin) to prevent infection* *For PTL offer nifedipine to delay birth for 24-48 hours* *Prepare for PTB*		*For PPROM, consider prophylactic antibiotics (e.g. erythromycin) versus delivery* *Prepare for PTB*	*Prepare for term delivery*

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Using ultrasound and LMP to estimate gestational age (GA)

Compare certain LMP gestational age (GA) to ultrasound GA		
Timing (by LMP) of earliest ultrasound to estimate GA	**Method of measurement on ultrasound**	**Use the ultrasound-generated due date and GA ONLY if the difference between the certain LMP GA and ultrasound-derived GA is:**
Up to 8^{+6} weeks	CRL	>5 days
9^{+0} to 13^{+6} weeks	CRL	>7 days
14^{+0} to 15^{+6} weeks	BPD, HC, AC, FL	>7 days
16^{+0} to 21^{+6} weeks	BPD, HC, AC, FL	>10 days
22^{+0} to 27^{+6} weeks	BPD, HC, AC, FL	>14 days
>28^{+0} weeks	BPD, HC, AC, FL	>21 days
If the LMP is uncertain or unknown, use ultrasound-derived due date and GA, based on careful clinical judgment.		
Because of the risk of re-dating a small fetus that may be growth-restricted, management decisions based on third-trimester ultrasonography alone can be problematic and need to be guided by consideration of the entire clinical picture.		

Care if High Risk of Preterm Birth (PTB)

ACTION PLAN

Use this Action Plan only in facilities able to:

- Accurately assess gestational age with ultrasound
- Identify if there is a high likelihood of PTB in the next 7 days
- Recognize / rule-out clinical evidence of maternal infection
- Provide adequate preterm newborn care (resuscitation, kangaroo mother care, thermal care, feeding support, infection treatment, monitoring of hypoglycemia, and respiratory support including CPAP as needed)
- Provide adequate childbirth care (including capacity to recognize and safely manage preterm labor and birth)

Condition with high risk of PTB in next 7 days


Preterm labor (PTL)

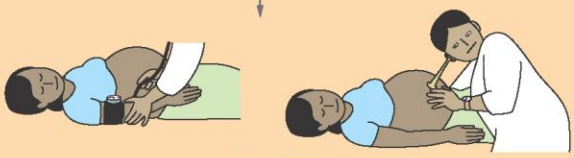

Preterm pre-labor rupture of membranes (PPROM)


Severe pre-eclampsia /eclampsia (SPE/E)


Antepartum hemorrhage (APH)


Indications for provider-initiated PTB

Within 15 min



Assess maternal and fetal condition

Not stable

Stabilize; consider delivery

Woman and fetus are stable

No fetal heart tones

Stabilize; Deliver

Confirm gestational age, fetal viability, and fetal presentation based on ultrasound

Within 30 min

≥37+0 weeks

Monitor woman and fetus; continue maternal care

<37+0 weeks

Counsel woman on PTB care options

<32+0 weeks

If delivery expected within 24 hours

Offer $MgSO_4$ for neuroprotection

34+0 - <37+0 weeks

<34+0 weeks

Offer  **IM dexamethasone or IM betamethasone**

If no maternal infection and PTB expected in 7 days

\+ For PTL

Offer nifedipine

If given dexamethasone or betamethasone

\+ For PPROM

Offer prophylactic antibiotics

\+ For SPE/E and APH

Treat as per protocols

For PPROM

Consider prophylactic antibiotics or delivery

Within 1 hr

Monitor frequently

Woman and fetus are stable?

Not Stable

Stabilize; consider delivery

Stable

Ensure follow-up doses

Offer single repeat course of ACS if PTB does not occur within 7 days of first course

Eligibility for repeat ACS course:

- GA <34 weeks
- High likelihood of PTB in the next 7 days
- No maternal infection

Prepare for PTB / Alert neonatal team

See HBS Essential Care for Small Babies

Monitor outcomes to improve care

Follow protocol for continuing care

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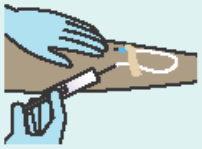
Care if High Risk of Preterm Birth (PTB) - Medication Information

	Eligibility	Benefits	Side effects/Risks	Regimen
Antenatal corticosteroids (ACS) *for fetal lung maturity* 	Risk of PTB from viability to <34+0 weeks of gestation in singleton and mulitple pregnancies ***IF:*** • Accurate U/S-derived GA assessment • High likelihood of PTB in the next 7 days (spontaneous or provider-initiated) • There is no clinical evidence of maternal infection • Adequate childbirth/preterm newborn care is available	Can reduce death in preterm babies by 22% by: • Maturing fetal lungs • Protecting fetal intestines and blood vessels in the brain	• May increase risk of: - Maternal sepsis when used in women with chorioamnionitis or other infections - Perinatal mortality in infants born at term • Benefits disappear after 7 days, a repeat course may restore benefits • More than two courses can be harmful to the fetus. • Might affect blood glucose levels in women with pre-existing or gestational diabetes	**Dexamethasone:** 6 mg IM every 12 hours x 4 doses **Betamethasone:** 12 mg IM every 24 hours x 2 doses **Monitor blood glucose in women with pre-existing or gestational diabetes and expect an increased insulin need.
Repeat course (single repeat course only) 	• PTB does not occur within 7 days of the first course of dexamethasone or betamethasone • GA is still < 34^{+0} weeks • There is a high risk of PTB in the next 7 days • No clinical evidence of maternal infection			May repeat **a course** of the selected regimen **ONCE only** if **all** eligibility criteria have been met
Nifedipine (standard / immediate release) *to slow or stop contractions and delay birth 24–48 hours*	• **Viability to GA < 34+0 weeks** • In preterm labor (based on skilled clinical assessment) **with or without ruptured membranes** • High likelihood of preterm birth in next 7 days • Is receiving ACS • No known cardiac problems • Prolonging pregnancy is not dangerous to the woman or baby	May delay birth by 24–48 hours to get the benefit of dexamethasone / betamethasone or to transport patient	**Common side effects:** hypotension, tachycardia, palpitations, flushing, headache, dizziness, and nausea **Risks:** Severe hypotension, shortness of breath **if clinical infection or abruption-related bleeding is present, tocolytics should not be used	**Loading dose:** 20 mg by mouth **Maintenance Dose:** 10–20 mg by mouth every 4–8 hours for up to 48 hours Do not exceed 180 mg in 24 hours Nifedipine can be used for 3-7 days, or until transfer is completed, whichever comes first. Monitor the woman for an excessive drop in blood pressure and hold or reduce medication as needed.
Prophylactic antibiotics *for PPROM to prevent infection*	• **Viability to GA < 37+0 weeks** • Ruptured membranes (confirmed) • No known allergy to prescribed antibiotic *Monitor closely and change to treatment protocol if signs of infection appear.*	• Helps prevent infection, which also reduces prematurity-related problems for baby	• Diarrhea, nausea, vomiting • Risk of allergic reaction	**Follow local protocols for the antibiotic.** *Erythromycin regimen: 250 mg by mouth four times/day for 10 days or until birth, whichever comes first. If erythromycin is unavailable, use a penicillin such as amoxicillin.* ***Do NOT use co-amoxiclav/Augmentin due to increased rates of necrotizing enterocolitis.***
Magnesium sulfate *for fetal neuroprotection* 	• **Viability to GA < 32+0 weeks** • Woman is in established spontaneous labor (5 cm or more) or having a provider-initiated planned birth in the next 24 hours • No known maternal cardiac problems or myasthenia gravis • Do not give maintenance doses to women with impaired renal functioning *Repeat dose is not recommended for neuroprotection.* ***If the woman has severe pre-eclampsia/eclampsia,*** *continue $MgSO_4$ for 24 hours after birth or last seizure, whichever is later.*	Decreases the risk of cerebral palsy and gross motor dysfunction	**Common side effects:** • Sweating • Flushing and feeling of warmth • Headache • Nausea / vomiting • Slight decrease in fetal heart rate **Risks:** • Respiratory or cardiac arrest related to magnesium toxicity (very rare)	**Use one of the following IV regimen:** 1) IV 4 g over 20 minutes, then IV 1 g/hour until delivery or for 24 hours, whichever comes first; 2) IV 4 g over 30 minutes or IV bolus of 4 g given as single dose; 3) IV 6 g over 20–30 minutes, then IV 2 g/hour until delivery or for 24 hours, whichever comes first **Hold if:** • Respirations < 16/minute • Patellar reflex absent • Urinary output < 120 mL over 4 hours **In case of toxicity, give:** • 1 g IV calcium gluconate over 3 minutes

**Never delay delivery for medication if delivery is necessary for the safety of the woman or fetus*

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