

PRETERM LABOR MANAGEMENT

Policy Number: MATERNITY 023.18 T2

Effective Date: December 1, 2018

[Instructions for Use](#) ⓘ

Table of Contents	Page
CONDITIONS OF COVERAGE	1
COVERAGE RATIONALE	1
APPLICABLE CODES	1
DESCRIPTION OF SERVICES	2
CLINICAL EVIDENCE	2
U.S. FOOD AND DRUG ADMINISTRATION	6
REFERENCES	6
POLICY HISTORY/REVISION INFORMATION	8
INSTRUCTIONS FOR USE	8

Related Policy

- [17-Alpha-Hydroxyprogesterone Caproate \(Makena™ and 17P\)](#)

CONDITIONS OF COVERAGE

Applicable Lines of Business/Products	This policy applies to Oxford Commercial plan membership.
Benefit Type	General benefits package
Referral Required (Does not apply to non-gatekeeper products)	No
Authorization Required (Precertification always required for inpatient admission)	Yes ¹
Precertification with Medical Director Review Required	Yes ¹
Applicable Site(s) of Service (If site of service is not listed, Medical Director review is required)	Home
Special Considerations	¹ Precertification with review by a Medical Director or their designee is required except for HCPCS Code J3105.

COVERAGE RATIONALE

Magnesium sulfate is proven and medically necessary for treating preterm labor for a short-term (up to 48 hours) when the following criteria are met:

- To allow for the prolongation of pregnancy for the administration of antenatal corticosteroids in pregnant women who are at risk of preterm delivery within 7 days, or
- Fetal neuroprotection before anticipated early preterm (less than 32 weeks of gestation) delivery

The following services are unproven and not medically necessary for preventing or delaying spontaneous preterm birth due to insufficient evidence of efficacy:

- The use of tocolytic therapy beyond 48 hours
- Subcutaneous terbutaline pump maintenance therapy
- Home uterine activity monitoring (HUAM)

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies may apply.

HCPCS Code	Description
J3105	Injection, terbutaline sulfate, up to 1 mg
J3475	Injection, magnesium sulphate, per 500 mg
S9001	Home uterine monitor with or without associated nursing services
S9349	Home infusion therapy, tocolytic infusion therapy; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem

DESCRIPTION OF SERVICES

Preterm labor is defined as regular uterine contractions, associated with cervical change, before 37 weeks of gestation. Deliveries that are early by five weeks or more are the leading cause of infant morbidity and mortality in the United States. Preterm labor risk factors include, but are not limited to previous premature birth, current multiple gestation, smoking, previous confirmed preterm labor during current pregnancy, and/or shortened cervix.

Tocolytics are drugs given to inhibit uterine contractions. Acute tocolysis is used to decrease or stop uterine contractions and slow or halt cervical change in women during preterm labor. Maintenance tocolysis refers to medication administered after acute tocolysis, in women with arrested preterm labor, to prevent a recurrence of preterm labor.

The therapeutic agents currently thought to be clearly associated with improved neonatal outcomes include antenatal corticosteroids, for maturation of fetal lungs and other developing organ systems, and the targeted use of magnesium sulfate for fetal neuroprotection.

CLINICAL EVIDENCE

Tocolytic Therapy

A systematic review and meta-analysis was conducted by Miyazaki et al. (2016) to identify available evidence on the effectiveness of tocolysis in inhibiting preterm delivery for women with threatened extremely preterm birth, multiple gestations, and growth-restricted babies and their infants' outcomes. Randomized controlled trials (RCTs) and non-randomized studies (non-RCTs) that compared tocolysis treatment to placebo or no treatment were considered. The analysis included seven studies, in which three were RCTs (n=1249) and four were non-RCTs (n=609). There were no eligible studies identified for women with multiple pregnancy and growth-restricted fetuses. Meta-analyses indicated no significant difference was found for the relative effectiveness of tocolytics versus placebo for prolonging pregnancy in women with extremely preterm birth or reducing the rate of perinatal deaths. The authors concluded that evidence from this review was not sufficient to provide specific recommendations for women with extremely preterm birth, and no conclusion could be drawn on the benefits or harms of tocolytic therapy in women carrying multiple pregnancies or growth-restricted fetuses at imminent risk of preterm birth. They further stated that the review provided a trend of generic evidences that tocolysis is highly uncertain to be effective.

Lorthe et al. (2017) reported on a French national prospective, population-based cohort study of preterm births that occurred in 546 maternity units. Inclusion criteria in this analysis were women with preterm premature rupture of membranes at 24-32 weeks' gestation and singleton gestations. The objective of the study was to investigate whether tocolytic therapy in cases of preterm premature rupture of membranes is associated with improved neonatal or obstetric outcomes. The study population consisted of 803 women; 596 (73.4%) received tocolysis. Women with and without tocolysis did not differ in neonatal survival without severe morbidity, latency prolonged by ≥48 hours, or histological chorioamnionitis. There was no association between the initial tocolytic drug used (oxytocin receptor antagonists or calcium-channel blockers vs no tocolysis) and the 3 outcomes. Sensitivity analyses of women with preterm premature rupture of membranes at 26-31 weeks' gestation, women who delivered at least 12 hours after rupture of membranes, women with direct admission after the rupture of membranes and the presence or absence of contractions gave similar results. The authors reported that tocolysis in cases of preterm premature rupture of membranes is not associated with improved obstetric or neonatal outcomes; its clinical benefit remains unproven.

A meta-analysis by Han et al. (2010) did not show any differences between magnesium sulfate maintenance therapy and either placebo or beta-adrenergic receptor agonists in preventing preterm birth after an initial treated episode of threatened preterm labor.

In a Cochrane systematic review, Chawanpaiboon et al. (2014) evaluated the effectiveness of terbutaline pump maintenance therapy after threatened preterm labor in reducing adverse neonatal outcomes. This report replaces an earlier Cochrane review by Nanda et al. (2002). Four randomized controlled trials (n=234) comparing terbutaline pump therapy with alternative therapy, placebo or no therapy after arrest of threatened preterm labor were included

in the review. The authors found no strong evidence that terbutaline maintenance therapy offered any advantages over saline placebo or oral terbutaline maintenance therapy in reducing adverse neonatal outcomes by prolonging pregnancy among women with arrested preterm labor.

In a Cochrane systematic review, Dodd et al. (2012) assessed the effects of oral betamimetic maintenance therapy after threatened preterm labor for preventing preterm birth. Randomized controlled trials comparing oral betamimetic with alternative tocolytic therapy, placebo or no therapy for maintenance following treatment of threatened preterm labor. Thirteen randomized controlled trials (RCTs) were included. The authors concluded that the available evidence does not support the use of oral betamimetics for maintenance therapy after threatened preterm labor.

Nijmana et al. (2016) performed a trial to study the effect of prolonged tocolysis with nifedipine versus placebo in women with preterm prelabor rupture of membranes (PPROM) on perinatal outcome and prolongation of pregnancy. The Apostel IV was a nationwide multicenter randomized, double-blind, placebo controlled trial at eight perinatal centers with neonatal intensive care unit facilities. Fifty women were included with PPRM without contractions between 24 and 33+6 weeks of gestation. Participants were randomly allocated to daily 80 mg nifedipine or placebo, until the start of labor, with a maximum of 18 days. Twenty-five women were randomized to nifedipine and 25 women to placebo. The primary outcome measure was a composite of poor neonatal outcome, including perinatal death, bronchopulmonary dysplasia, periventricular leukomalacia > grade 1, intraventricular hemorrhage > grade 2, necrotizing enterocolitis > stage 1 and culture proven sepsis. Antenatal corticosteroids were administered according to national guidelines, advising antenatal corticosteroids to women in preterm labor <34 weeks of gestation. Prophylactic antibiotic therapy and magnesium sulphate were administered according to local protocol, as was maternal and fetal monitoring. Adverse perinatal outcome occurred in 9 (33.3%) children in the nifedipine group versus 9 children (32.1%) in the placebo group. Two perinatal deaths occurred, both in the nifedipine group. Bronchopulmonary dysplasia occurred significantly less frequent in the nifedipine group (no children in the nifedipine group compared with five (17.9%) in the placebo group. Prolongation of pregnancy did not differ between the nifedipine and placebo group (median 11 versus 8 days). The authors concluded that this randomized trial did not show a beneficial effect of prolonged tocolysis on neonatal outcomes or prolongation of pregnancy in women with PPRM without contractions. Results are based on a small sample size.

In the APOSTEL III trial, van Vliet et al. (2016) aimed to compare the effectiveness and safety of the calcium-channel blocker nifedipine and the oxytocin inhibitor atosiban in women with threatened preterm birth. They conducted a multicenter, randomized controlled trial in ten tertiary and nine teaching hospitals. Women with threatened preterm birth (gestational age 25–34 weeks) were randomly assigned (1:1) to either oral nifedipine or intravenous atosiban for 48 hours. Two hundred and fifty-four women were randomly assigned to the nifedipine group and 256 to the atosiban group. The primary outcome was a composite of adverse perinatal outcomes, which included perinatal mortality, bronchopulmonary dysplasia, sepsis, intraventricular hemorrhage, periventricular leukomalacia, and necrotising enterocolitis. Analysis was done in all women and babies with follow-up data. The primary outcome occurred in 42 babies (14%) in the nifedipine group and in 45 (15%) in the atosiban group. Sixteen (5%) babies died in the nifedipine group and seven (2%) died in the atosiban group; all deaths were deemed unlikely to be related to the study drug. Maternal adverse events did not differ between groups. In the nifedipine group, 155 (52%) babies were admitted to the NICU, compared with 182 (62%) in the atosiban group. The authors concluded that in women with threatened preterm birth, 48 hours of tocolysis with nifedipine or atosiban results in similar perinatal outcomes. Future clinical research should focus on large placebo-controlled trials, powered for perinatal outcomes. Padovani et al. (2015) compared the impact of terbutaline versus nifedipine on inhibition of uterine contractions, preterm birth, neonatal sepsis, intracranial hemorrhage or necrotizing enterocolitis, death or admission to a neonatal intensive care unit and maternal adverse reactions. The randomized trial (n=66) was performed in three centers in Brazil between August 2010 and March 2012. Thirty two obstetrical patients received nifedipine 20mg orally and after 30 minutes a second dose was given if contractions did not stop. Once tocolysis was achieved, nifedipine 20 mg orally was administered every 8 hours for a period of 48 hours. Thirty four patients received terbutaline (ampoule 0.5 mg/mL): intravenous infusion of 2.5 lg/min. followed by an increase of 2.5 lg/min. every 15 minutes, to a maximum of 20 lg/min. When the minimum dose that stopped contractions was established, the infusion was maintained for 24 hours. After 24 hours of drug administration, the dose was decreased by 2.5 lg/min. every 15 minutes and discontinued. They found no difference between groups in tocolysis or preterm birth. Less serious maternal adverse effects less common with terbutaline included flushing (2.94% versus 43.7%) and headache (5.9% versus 31.2%). The administration of terbutaline increased tremor (76.4% versus 0%), nausea (58.8% versus 9.4%) and dizziness (29.4% versus 6.25%). Each drug has specific side effects, although overall, nifedipine was associated with fewer adverse effects. The authors concluded that the results of this study support previous evidence suggesting that nifedipine is as effective as terbutaline in its impact on tocolysis and neonatal outcome with fewer maternal and fetal adverse effects. The significance of this study is limited by its small sample size.

Theplib and Phupong (2016) conducted a retrospective study (n=385) to determine terbutaline success rate in postponing preterm labor for 48 hours and to identify factors associated with its efficacy, side effects, maternal and neonatal outcomes. They analyzed data from pregnant women suffering from preterm labor who had received

terbutaline for inhibition of labor from January 2007 to December 2013. Of the 385 cases, 83.4% delivered ≥ 48 hours and 16.6% delivered before 48 hours. The factors that affect the success rate of terbutaline administration in singleton pregnancy were cervical dilatation and cervical effacement. The most common side effect of terbutaline was tachycardia (95.1%), and there were no serious cardiovascular events or maternal death. Mean neonatal birth weight was 5 pounds. Neonatal complications included respiratory distress syndrome 16.2%, intraventricular hemorrhage 1.4%, necrotizing enterocolitis 0.7%, sepsis 5.3%, and neonatal death 0.9%. The authors concluded that the success rate of terbutaline in treatment of preterm labor was high, side effects were tolerable and terbutaline can be used safely for short-term treatment of preterm labor.

Klauser et al. (2016) conducted a single center, randomized trial with 92 patients in preterm labor with advanced cervical dilation (4-6cm) to compare the efficacy of tocolytic treatment with indomethacin, magnesium sulfate and nifedipine for acute tocolysis. Secondary analysis of women with advanced cervical dilation (cervix 4-6cm) at 24-32 weeks' gestation who received intravenous magnesium sulfate, oral nifedipine or indomethacin suppositories comprised this study population. The patients were randomized to one tocolytic type, over 38 months. Days gained in utero (11.7) and percent remaining undelivered at 48h (60.8%), 72h (53.1%) and >7 days (38.3%) were similar regardless of tocolytic utilized. The gestational age at delivery (30.7 ± 3.2) was similar between groups and neonatal statistics were not different. The authors concluded that all three tocolytics offered significant days gained in utero after therapy and a high percentage remaining undelivered after 48 or 72h and after 7 days.

Home Uterine Activity Monitoring (HUAM)

Home uterine activity monitoring (HUAM) uses a device to measure uterine activity away from the clinic or hospital. It is used to detect early-stage uterine contractions suggestive of preterm labor.

According to a multicenter study by the National Institute of Child Health and Human Development (NICHD), portable monitors that detect contractions of the uterus do not appear to be useful for identifying women likely to have a preterm delivery. "Although they are widely prescribed for women at risk of giving birth prematurely, the monitors are not useful for predicting or preventing preterm birth." (Iams et al., 2002)

In a Cochrane systematic review, Urquhart et al. (2012) evaluated whether home uterine activity monitoring is effective in improving outcomes for women and their infants considered to be at high risk of preterm birth. Fifteen randomized control trials ($n=6008$) were included in the review. The authors found that home uterine monitoring may result in fewer admissions to a neonatal intensive care unit but more unscheduled antenatal visits and tocolytic treatment. The report concluded that home uterine activity monitoring had no impact on maternal and perinatal outcomes such as perinatal mortality or incidence of preterm birth. Updated 2017 with no change to conclusions.

Reichmann (2009) systematically reviewed 3 Level I randomized, controlled trials; 1 level II matched cohort trial; and 5 level III case series evaluating home uterine activity monitoring in multiple gestations and found that contractions in multiple gestations are not predictive of preterm birth. In an earlier review, the same author analyzed published clinical trials examining HUAM for the management of current preterm labor. He concluded that HUAM has no clinical value, has virtually no scientific support and constitutes a gross deviation from evidence-based medicine. (Reichmann, 2008)

Neuroprotective Effects of Magnesium Sulfate

An individual participant data (IPD) meta-analysis was performed by Crowther et al. (2017) to assess the effects of antenatal magnesium sulfate, compared with no magnesium treatment, given to women at risk of preterm birth. Five randomized trials with 5,493 women and 6,131 babies were identified as including women at risk of preterm birth who were allocated magnesium sulfate or control treatment and in which neurologic outcomes for the baby were reported and included. In the sensitivity analysis from the 4 trials in which the intent of treatment was fetal neuroprotection, there was a significant reduction in the risk of death or cerebral palsy (CP) with magnesium sulfate treatment compared with no treatment. For the primary outcome of severe maternal outcome potentially related to magnesium sulfate treatment, no events were recorded. For cerebral palsy in survivors, magnesium sulfate treatment had a strong protective effect in both the overall analysis and the neuroprotective intent analysis. The authors concluded that antenatal magnesium sulfate given prior to preterm birth for fetal neuroprotection prevents CP and reduces the combined risk of fetal/infant death or CP. Benefit is seen regardless of the reason for preterm birth, with similar effects across a range of preterm gestational ages and different treatment regimens.

A systematic review and meta-analysis was performed by Zeng et al. (2016) to evaluate safety and effectiveness of magnesium sulfate ($MgSO_4$) on neuroprotection for preterm infants who had exposure in utero. They identified studies comparing magnesium sulfate ($MgSO_4$) with placebo or other treatments in patients at high risk of preterm labor. The primary outcomes included fetal death, cerebral palsy (CP), intraventricular hemorrhage, and periventricular leukomalacia. Secondary outcomes included various neonatal and maternal outcomes. A total of 10 studies including 6 randomized controlled trials and 5 cohort studies, and involving 18,655 preterm infants were analyzed. For the rate of CP, $MgSO_4$ showed the ability to reduce the risk of CP, and achieved statistically significant difference. The

comparison of mortality rate between the MgSO₄ group and the placebo group only presented small difference clinically, but reached no statistical significance. The analysis of adverse effects on babies showed no margin. For mothers, MgSO₄ exhibited side-effects, such as respiratory depression, nausea, but there existed great heterogeneity. MgSO₄ administered to women at high risk of preterm labor could reduce the risk of moderate to severe CP, without obvious adverse effects on babies. Although there were many unfavorable effects on mothers, they may be lessened through reduction of the dose of MgSO₄ and could be tolerable for mothers. The authors concluded that MgSO₄ is both beneficial and safe to be used as a neuroprotective agent for premature infants.

Professional Societies

American College of Obstetricians and Gynecologists (ACOG)

A practice bulletin on the management of preterm labor makes the following recommendations based on good and consistent scientific evidence (ACOG 2017):

- No evidence exists to support the use of home uterine activity monitoring to prevent preterm delivery in women with contractions but no cervical change.
- Accumulated available evidence suggests that magnesium sulfate reduces the severity and risk of cerebral palsy in surviving infants if administered when birth is anticipated before 32 weeks of gestation.
- Evidence supports the use of first-line tocolytic treatment for short-term prolongation of pregnancy (up to 48 hours) to allow for the administration of antenatal steroids.
- The use of first-line tocolytic treatment with beta-adrenergic agonist therapy, calcium channel blockers, or NSAIDs for short-term prolongation of pregnancy (up to 48 hours) to allow for the administration of antenatal steroids.
- Tocolysis is not recommended beyond 34 weeks of gestation and generally not recommended before 24 weeks of gestation but may be considered based on individual circumstances at 23 weeks.
- A single course of corticosteroids is recommended for pregnant women between 24 0/7 weeks and 33 6/7 weeks of gestation, who are at risk of preterm delivery within 7 days, including for those with ruptured membranes and multiple gestations.
- A single course of corticosteroids is recommended for pregnant women between 24 0/7 weeks and 33 6/7 weeks of gestation, and may be considered for pregnant women starting at 23 0/7 weeks of gestation, who are at risk of preterm delivery within 7 days, irrespective of membrane rupture status.
- Administration of corticosteroids for pregnant women during the periviable period who are at risk of preterm delivery within 7 days is linked to a family's decision regarding resuscitation and should be considered in that context.
- A single repeat course of antenatal corticosteroids can be considered in women who are less than 34 weeks of gestation, who are at risk of preterm delivery within the next 7 days, and whose prior course of antenatal corticosteroids was administered more than 14 days previously. Rescue course corticosteroids could be provided as early as 7 days from the prior dose, if indicated by the clinical scenario.
- Maintenance therapy with tocolytics is ineffective for preventing preterm birth and improving neonatal outcomes and is not recommended for this purpose.
- Antibiotics should not be used to prolong gestation or improve neonatal outcomes in women with preterm labor and intact membranes.

Committee on Obstetric Practice and the Society for Maternal-Fetal Medicine (SMFM)

Numerous large clinical studies have evaluated the evidence regarding magnesium sulfate, neuroprotection and preterm births. SMFM recognize that none of the individual studies found a benefit with regard to their primary outcome. However, the available evidence suggests that magnesium sulfate given before anticipated early preterm birth reduces the risk of cerebral palsy in surviving infants. Physicians electing to use magnesium sulfate for fetal neuroprotection should develop specific guidelines regarding inclusion criteria, treatment regimens, concurrent tocolysis and monitoring in accordance with one of the larger trials. (ACOG, 2010; reaffirmed 2016)

Following the FDA's safety announcement regarding the use of magnesium sulfate to stop preterm labor, ACOG and SMFM released a committee opinion on the use of magnesium sulfate in obstetrics. (ACOG, 2016b) The two professional societies continue to support the short-term (usually less than 48 hours) use of magnesium sulfate in obstetric care for appropriate conditions and for appropriate durations of treatment. These conditions include the following:

- Prevention and treatment of seizures in women with preeclampsia or eclampsia
- Fetal neuroprotection before anticipated early preterm (less than 32 weeks of gestation) delivery
- Short-term prolongation of pregnancy (up to 48 hours) to allow for the administration of antenatal corticosteroids in pregnant women between 24 and 34 weeks of gestation who are at risk of preterm delivery within seven days

In a SMFM 2016 Committee Statement on implementation of the use of antenatal corticosteroids in the late preterm birth period in women at risk for preterm delivery the Society made the following recommendation (SMFM, 2016):

- In women with a singleton pregnancy between 34 weeks 0 days and 36 weeks 6 days of gestation who are at high risk for preterm birth within the next 7 days (but before 37 weeks of gestation), we recommend treatment with betamethasone (2 doses of 12 mg intramuscularly 24 hours apart).

French College of Gynecologists and Obstetricians (CNGOF)

CNGOF makes the following recommendations based on good and consistent scientific evidence (Sentilhes, 2017):

- Maintenance treatment after the conclusion of 48 hours of initial tocolysis is not recommended.
- Administration of a single course of prenatal corticosteroid treatment before 34 weeks is associated with a significant reduction during the neonatal period of hyaline membrane disease, intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), and death.
- Magnesium sulfate administration is recommended for women at high risk of imminent preterm birth before 32 weeks to reduce cerebral palsy and motor development disorders in children born preterm.

American Academy of Family Physicians (AAFP)

The AAFP made the following clinical recommendations for the prevention and management of preterm labor (Rundell, 2017):

- Once preterm labor is confirmed, a single course of corticosteroids (betamethasone or dexamethasone) is the only intervention for improving neonatal outcomes. It is recommended between 24 and 34 weeks' gestation and may be considered as early as 23 weeks' gestation.
- Antenatal magnesium sulfate provides neuroprotection, decreasing the risk of cerebral palsy in infants born at less than 32 weeks' gestation.
- Tocolytics, such as prostaglandin inhibitors and calcium channel blockers, should be used to prolong the time to delivery so that antenatal corticosteroids and potentially magnesium sulfate can be administered.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

The Food and Drug Administration (FDA) is now requiring a black box warning on the terbutaline label stating that the use of injectable terbutaline should be limited to a maximum of 72 hours to treat preterm labor and that oral terbutaline shouldn't be used at all to treat preterm labor or prevent its recurrence. (AJN 2011)

The FDA describes HUAM as a prescription only electronic system (comprising of a tocotransducer, an at-home recorder, a modem and a monitor to receive, process, and display the data) for at-home antepartum measurement of uterine contractions and data transmission by telephone to a clinical setting where it will be displayed. The FDA also states that HUAM is indicated for use, in conjunction with current high-risk care, for the daily at home measurement of uterine activity in pregnancies > 24 weeks of gestation for women with a history of previous preterm birth, to aid in the early detection of preterm labor. Available at:

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM073596.pdf>. (Accessed March 25, 2018)

On May 30, 2013, the FDA issued a safety announcement advising health care professionals against using magnesium sulfate injection for more than 5-7 days to stop preterm labor in pregnant women. Administration of magnesium sulfate injection to pregnant women longer than 5-7 days may lead to low calcium levels and bone problems in the developing baby or fetus, including osteopenia and fractures. The shortest duration of treatment that can result in harm to the baby is not known. Magnesium sulfate injection should only be used during pregnancy if clearly needed. If the drug is used during pregnancy, the health care professional should inform the patient of potential harm to the fetus. Additional information available at: <http://www.fda.gov/downloads/Drugs/DrugSafety/UCM353335.pdf>. (Accessed March 25, 2018)

REFERENCES

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare national policy that was researched, developed and approved by UnitedHealthcare Medical Technology Assessment Committee. [2018T0352T]

American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 455. Magnesium sulfate before anticipated preterm birth for neuroprotection. *Obstet Gynecol.* 2010 Mar; 115(3):669-71. Reaffirmed 2016.

American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 652. Magnesium Sulfate Use in Obstetrics. *Obstet Gynecol* 2016a; 127:e52-3.

American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 171. Management of Preterm Labor. *Obstet Gynecol.* 2016c October;128:e155-64.

American College of Obstetricians and Gynecologists. Antenatal Corticosteroid Therapy for Fetal Maturation. Committee Opinion No. 677. *Obstet Gynecol* 2016;128:e187-94. Replaced with Committee Opinion 713.

American College of Obstetricians and Gynecologists. Antenatal Corticosteroid Therapy for Fetal Maturation. Committee Opinion No. 713. *Obstet Gynecol.* August 2017.

- American College of Obstetricians and Gynecologists. FAQ087. Preterm (premature) labor and birth. July 2014. Updated 2016.
- American Journal of Nursing. Warning Against Using Terbutaline to Prevent Preterm Labor. AJN. 2011 June; Vol. 111, No. 6.
- Chawanpaiboon S, Laopaiboon M, Lumbiganon P, et al. Terbutaline pump maintenance therapy after threatened preterm labour for reducing adverse neonatal outcomes. Cochrane Database Syst Rev. 2014 Mar 23; 3:CD010800.
- Crowther CA, Middleton PF, Voysey M, et al. Assessing the neuroprotective benefits for babies of antenatal magnesium sulphate: An individual participant data meta-analysis. PLoS Med. 2017 Oct 4;14(10):e1002398.
- Dodd JM, Crowther CA, Middleton P. Oral betamimetics for maintenance therapy after threatened preterm labour. Cochrane Database Syst Rev. 2012 Dec 12; 12:CD003927.
- Han S, Crowther CA, Moore V. Magnesium maintenance therapy for preventing preterm birth after threatened preterm labour. Cochrane Database Syst Rev. 2010 Jul 7;(7):CD000940.
- Hayes, Inc. Hayes Medical Technology Directory. Continuous subcutaneous terbutaline infusion for treatment of preterm labor. Lansdale, PA: Hayes, Inc.; May 2011. Updated May 2015. Archived June 17, 2016.
- Horton, A, Lai, Y, Rouse, D. et al. The effect of magnesium sulfate administration for neuroprotection on latency in women with preterm premature rupture of membranes. Am J Perinatol. 2015 March; 32(4): 387–392.
- Iams JD, et al. Frequency of uterine contractions and the risk of spontaneous preterm delivery. N Engl J Med. 2002 Jan 24; 346(4):250-5.
- Klauser CK, Briery CM, Tucker AR, et al. Tocolysis in women with advanced preterm labor: a secondary analysis of a randomized clinical trial. J Matern Fetal Neonatal Med. 2016 Mar; 29(5):696-700.
- Lorthe E, Goffinet F, Marret S, et al. Tocolysis after preterm premature rupture of membranes and neonatal outcome: a propensity-score analysis. Am J Obstet Gynecol. 2017 Aug;217(2):212.e1-212.e12.
- Miyazaki C, Moreno R, Ota E, et al. Tocolysis for inhibiting preterm birth in extremely preterm birth, multiple gestations and in growth-restricted fetuses: a systematic review and meta-analysis. Reproductive Health (2016) 13:4.
- Nanda K, Cook LA, Gallo MF, Grimes DA. Terbutaline pump maintenance therapy after threatened preterm labor for preventing preterm birth. Cochrane Database of Systematic Reviews 2002 ;(4):CD003933.
- Nijmana T, van Vlieta E, Naaktgeboren C, et al. Nifedipine versus placebo in the treatment of preterm prelabor rupture of membranes: a randomized controlled trial assessment of perinatal outcome by use of tocolysis in early labor—APOSTEL IV trial. European Journal of Obstetrics & Gynecology and Reproductive Biology 205 (2016) 79–84.
- Padovani, T, Guyatt, G and Cruz Lopes, L. Nifedipine versus Terbutaline, Tocolytic Effectiveness and Maternal and Neonatal Adverse Effects: A Randomized, Controlled Pilot Trial. Basic & Clinical Pharmacology & Toxicology, 2015, 116, 244–250.
- Reeves SA, Gibbs RS, Clark SL. Magnesium for fetal neuroprotection. Am J Obstet Gynecol. 2011 Mar; 204(3):202.e1-4.
- Reichmann JP. Home uterine activity monitoring: an evidence review of its utility in multiple gestations. J Reprod Med. 2009 Sep; 54(9):559-62.
- Reichmann JP. Home uterine activity monitoring: the role of medical evidence. Obstet Gynecol. 2008 Aug; 112(2 Pt 1):325-7.
- Rundell K and Panchal B. Preterm Labor: Prevention and Management. American Family Physician March 15, 2017; Volume 95, Number 6.
- Sentilhes L, Sénat M, Ancel P, et al. Prevention of spontaneous preterm birth: Guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF). European Journal of Obstetrics & Gynecology and Reproductive Biology 210 (2017) 217–224.
- Society for Maternal-Fetal Medicine (SMFM) Publications Committee. Implementation of the use of antenatal corticosteroids in the late preterm birth period in women at risk for preterm delivery. August 2016.
- Theplib A, Phupong V. Success rate of terbutaline in inhibiting preterm labor for 48 h. J Matern Fetal Neonatal Med. 2016 Mar;29(5):841-4.
- Urquhart C, Currell R, Harlow F, Callow L. Home uterine monitoring for detecting preterm labour. Cochrane Database Syst Rev. 2012 May 16; 5:CD006172.Updated 2017.
- van Vliet E, Nijman T, Schuit E, et al. Nifedipine versus atosiban for threatened preterm birth (APOSTEL III): a multicentre, randomised controlled trial. Lancet 2016 May 21; 387: 2117–24.
- Zeng X, Xue Y, Tian Q, et al. Effects and Safety of Magnesium Sulfate on Neuroprotection A Meta-analysis Based on PRISMA Guidelines. Medicine Volume 95, Number 1, January 2016.

POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
12/01/2018	<ul style="list-style-type: none"><li data-bbox="492 184 1203 214">• Simplified coverage rationale (no change to guidelines)<li data-bbox="492 214 1203 237">• Archived previous policy version MATERNITY 023.17 T2

INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting UnitedHealthcare Oxford standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare Oxford reserves the right to modify its Policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice.

The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Oxford Clinical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.