Tocolysis refers to the suppression of preterm labor to delay delivery. A variety of medications are proposed as tocolytic agents; none of the currently available options are approved by the U.S. Food and Drug Administration (FDA) for this indication. The same medications have also been used as maintenance therapy following successful tocolysis.

General indications for tocolysis, or the suppression of preterm labor, include continued regular uterine contractions associated with cervical changes in a pregnant individual at less than 37 weeks of gestation. Successful delay of preterm delivery allows further fetal development and precludes the complications of preterm delivery, especially neonatal respiratory distress syndrome (RDS). Even short-term delay of delivery is thought to be beneficial in that it allows treatment of the patient with corticosteroids, which has proved beneficial in ameliorating the effects of neonatal RDS. In some cases, a short delay in delivery may also allow transport of the pregnant individual to a medical center better equipped to handle premature delivery and neonatal intensive care.

The only FDA-approved tocolytic drug is ritodrine, a beta-sympathomimetic. Ritodrine is no longer available in the United States and thus only off-label medications are available. Terbutaline sulfate, also a beta-sympathomimetic, is an alternative to ritodrine, for acute and maintenance tocolysis. Terbutaline is available as an oral or intravenous medication and, more recently, terbutaline has been administered by continuous subcutaneous infusion via a portable pump for maintenance tocolysis. Other tocolytic drugs include calcium channel blockers (e.g., nifedipine), magnesium sulfate, oxytocin receptor antagonists (e.g., atosiban), prostaglandin inhibitors (e.g., indomethacin), and nitrates (e.g., nitroglycerin).

Regulatory Status:

Ritodrine was approved by the FDA for use as a tocolytic agent, but was voluntarily withdrawn from the U.S. market in 1998.

Terbutaline sulfate is FDA-approved for the prevention and treatment of bronchospasm in patients with asthma and reversible bronchospasm associated with bronchitis and emphysema. Like other tocolytic agents, its use in tocolysis is off-label. In response to a citizen petition in June, 2008, the FDA reviewed safety data on terbutaline sulfate. They issued a safety announcement on February 17, 2011. Based on animal studies, the FDA reclassified terbutaline sulfate from pregnancy risk category B to pregnancy risk category C. In addition, the FDA required a boxed warning stating that injectable terbutaline should not be used for prevention or prolonged (beyond 2-3 days) treatment of preterm labor and oral terbutaline should not be used for acute or maintenance tocolysis. The labeling change is based on a review of post-marketing
Acute and Maintenance Tocolysis

safety reports submitted to the FDA’s Adverse Event Reporting System (AERS) of maternal death and serious maternal cardiovascular events associated with use of terbutaline.

Related Policy
Progesterone Therapy in High Risk Pregnancies

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

Acute tocolytic therapy with calcium channel blockers, magnesium sulfate, prostaglandin inhibitors and parenteral terbutaline may be considered medically necessary for the induction of tocolysis in patients with preterm (< 37 weeks’ gestational age) labor.

Maintenance tocolytic therapy (beyond 48-72 hours) with any medication is considered not medically necessary.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

The Healthy Outcomes Maternity program is available to most members who are pregnant. This program gives mothers-to-be helpful tools and information so they can make healthy choices throughout their pregnancy.

When Acute and Maintenance Tocolysis is covered

Acute tocolytic therapy with calcium channel blockers, magnesium sulfate, prostaglandin inhibitors, and parenteral terbutaline may be considered medically necessary for the induction of tocolysis in patients with preterm (< 37 weeks’ gestational age) labor.

When Acute and Maintenance Tocolysis is not covered

Maintenance tocolytic therapy with any medication, including but not limited to subcutaneous or intravenous terbutaline, is considered not medically necessary, as the treatment is ineffective in prolonging gestation after acute tocolysis.

Policy Guidelines

Patient selection criteria for induction of tocolysis (aka acute tocolysis) include regular uterine contractions associated with cervical changes. Induction of tocolysis typically requires hospitalization to monitor for incipient delivery.

American College of Obstetricians and Gynecologists (ACOG), Management of preterm labor practice bulletin (2012):
The practice bulletin contains the following recommendations based on “good and consistent” scientific evidence:
Acute and Maintenance Tocolysis

- “A single course of corticosteroids is recommended for pregnant individuals between 24 weeks of gestation and 34 weeks of gestation who are at risk of preterm delivery within 7 days.

- 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. Hospitals that elect to use magnesium sulfate for fetal neuroprotection should develop uniform and specific guidelines for their departments regarding inclusion criteria, treatment regimens, concurrent tocolysis, and monitoring in accordance with one of the larger trials.

- The evidence supports the use of first-line tocolytic treatment with beta-adrenergic agonist therapy, calcium channel blockers, or non-steroidal anti-inflammatory drugs (NSAIDs) for short-term prolongation of pregnancy (up to 48 hours) to allow for the administration of antenatal steroids.

- 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 individuals with pre-term labor and intact membranes.”

The evidence on acute tocolytic therapy for preterm labor includes multiple randomized controlled trials (RCTs) and meta-analyses. Relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related morbidity. Overall, the body of evidence found that the commonly used tocolytic agents presented herein are effective at inducing tocolysis in patients with preterm labor or threatened preterm labor. Data suggest that oral terbutaline is associated with more adverse events than parenteral terbutaline for acute tocolysis. Each medication has a different risk-benefit profile, and there is no clear first-line tocolytic agent. The evidence is sufficient to determine quantitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence on maintenance tocolytic therapy after successful acute tocolysis includes RCTs and meta-analyses. Relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related morbidity. Studies have generally not found that maintenance tocolysis lowers the rate of preterm birth or perinatal mortality, or increases the birthweight. The evidence is insufficient to determine the effects of the technology on health outcomes.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: J3105, J3475, S9349

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

From policy entitled: Portable Infusion Pump for the Administration of Terbutaline
Acute and Maintenance Tocolysis

Consultant review 7/89

Independent Review by Corporate Medical Director 10/89; 1/94.

1997 USPDI

From policy entitled: Preventing Premature Labor and Delivery


Medical Policy Advisory Group - 12/2/1999

ECRI Executive Briefing No. 91 - July 2000


BCBSA Medical Policy Reference Manual, 07/12/02; 4.01.09

BCBSA Medical Policy Reference Manual, 07/12/02; 5.01.07


BCBSA Medical Policy Reference Manual, 12/18/02; 2.04.03


BCBSA Medical Policy Reference Manual, 12/17/03; 4.01.16


Acute and Maintenance Tocolysis


For policy entitled: Tocolysis with Intravenous or Subcutaneous Terbutaline


Specialty Matched Consultant Advisory Panel review - 12/18/2008

For policy renamed: Acute and Maintenance Tocolysis


Acute and Maintenance Tocolysis


Policy Implementation/Update Information

From Policy entitled: Portable Infusion Pump for Administration of Terbutaline

10/89 Original policy issued
1/94 Reaffirmed
5/96 Policy archived
10/97 Policy taken out of archive and reaffirmed. Additions to policy include statement that Terbutaline is not approved by FDA. Deleted statement regarding Personal Benefits Management and Case Management.

From Policy entitled: Preventing Premature Labor and Delivery

5/99 Reformatted, changed descriptions of procedures or services, added Medical term definitions. Combined Fetal Fibronectin, Salivary Estriol test, Home Uterine Monitoring, and Portable Pump for the administration of Terbutaline into one policy and renamed policy Preventing Premature Labor and Delivery.
12/99 Approved by Medical Policy Advisory Group
10/00 System coding changes.
2/01 Added new source to Scientific Background and Reference Sources
9/01 Specialty Matched Consultant Advisory Panel review. No change in criteria.
10/01 Coding format changes.
12/03 Specialty Matched Consultant Advisory Panel review 8/2003. Under "When Fetal Fibronectin is covered", third bullet changed to "who have singleton (one fetus) or twin gestations"; fourth bullet-changed "cervical" membranes to "amniotic" membranes. Under "When Fetal Fibronectin is not covered", last bullet changed to "in individuals with triplet or higher-order gestations (carrying more than 2 fetuses)...". Benefits Application and Billing/Coding sections revised.
1/17/07 Specialty Matched Consultant Advisory Panel review - 12/13/06. Under Section II - Progesterone Therapy in High Risk Pregnancies, second paragraph, added "by a health care professional" to the following sentence: "Administration of 17 alpha-hydroxyprogesterone caproate or vaginal suppositories in the home setting by a health professional is considered not medically necessary." Reference sources added. Added CPT code 90772 to the "Billing /Coding" section. Deleted CPT code 90782 from "Billing /Coding" section. No other changes. (pmo)

For policy entitled: Tocolysis with Intravenous or Subcutaneous Terbutaline
Acute and Maintenance Tocolysis

1/12/09  Section V., Portable infusion pump for administration of Terbutaline removed from policy entitled Preventing Premature Labor and Delivery. Separate policy issued entitled "Tocolysis with Intravenous or Subcutaneous Terbutaline". Administering Terbutaline over an extended time to prevent or suppress preterm labor remains investigational (maintenance tocolytic therapy with intravenous or subcutaneous terbutaline). Intravenous or subcutaneous terbutaline therapy may be considered medically necessary for the induction of tocolysis (acute tocolysis) in patients with preterm labor. Description and Policy Guidelines section revised with additional information regarding preterm labor and tocolytic agents. Key words and Reference sources added. (pmo)

For policy renamed Acute and Maintenance Tocolysis

4/13/2010  Policy renamed from “Tocolysis with Intravenous or Subcutaneous Terbutaline” to “Acute and Maintenance Tocolysis”. Description section extensively revised. “When covered” and “When not covered” sections revised. Policy Guidelines updated with new research information. CPT added. Reference source added.(mco)

6/22/10  Policy Number(s) removed. (amw)


11/13/12  Related policy added. Specialty Matched Consultant Advisory Panel review 9/19/12. No change to policy statement. (sk)

11/26/13  Reference added. Specialty Matched Consultant Advisory Panel review 9/18/13. Policy statement changed to read “Maintenance tocolytic therapy (beyond 48-72 hours) with any medication is considered not medically necessary”. Statement added to Policy Guidelines that maintenance tocolytic therapy is “not medically necessary, as the treatment is ineffective in prolonging gestation after acute tocolysis”. (sk)

10/14/14  Specialty Matched Consultant Advisory Panel review 9/30/14. No change to Policy statement. (sk)

12/30/14  Reference added. (sk)

10/30/15  Specialty Matched Consultant Advisory Panel review 9/30/15. (sk)

11/24/15  Reference added. Policy Guidelines updated. (sk)

11/22/16  Specialty Matched Consultant Advisory Panel review 9/28/2016. No change to policy statement or guidelines. (an)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment
Acute and Maintenance Tocolysis

and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.