

Corporate Medical Policy

Acute and Maintenance Tocolysis

File Name: acute_and_maintenance_tocolysis
Origination: 10/1989
Last CAP Review: 9/2011
Next CAP Review: 9/2012
Last Review: 9/2011

Description of Procedure or Service

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 preterm mother (< 37 weeks' gestation). Successful delay of preterm delivery allows further fetal development and precludes the complications of preterm delivery, especially neonatal respiratory distress syndrome.

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Ritodrine was approved by the FDA for use as a tocolytic agent, but was voluntarily withdrawn from the U.S. market in 1998.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

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******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 investigational. BCBSNC does not provide coverage for investigational services or procedures.

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.

Any member who is pregnant is eligible to have access to the Member Health PartnershipsSM – Pregnancy program. This program provides up-to-date information on pregnancy, labor and delivery options and costs, newborn care, and choosing a pediatrician, car seat and day-care with access to one-on-one health coaching from a pregnancy case manager.

When Acute and Maintenance Tocolysis is covered

Acute tocolytic therapy with betamimetics, calcium channel blockers, magnesium sulfate, and prostaglandin inhibitors 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 investigational.

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.

The American College of Obstetricians and Gynecologists (ACOG), Management of preterm labor practice bulletin guideline (issued in 2003 and reaffirmed in 2008) states:

“The following recommendations are based on good and consistent scientific evidence (Level A):

- There are no clear "first-line" tocolytic drugs to manage preterm labor. Clinical circumstances and physician preferences should dictate treatment.
- Antibiotics do not appear to prolong gestation and should be reserved for group B streptococcal prophylaxis in patients in whom delivery is imminent.
- Neither maintenance treatment with tocolytic drugs nor repeated acute tocolysis improve perinatal outcome; neither should be undertaken as a

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- general practice.
- Tocolytic drugs may prolong pregnancy for 2 to 7 days, which may allow for administration of steroids to improve fetal lung maturity and the consideration of maternal transport to a tertiary care facility.”

There is sufficient evidence that the commonly used tocolytic agents are effective at inducing tocolysis in patients with preterm labor or threatened preterm labor. Thus, these agents are considered medically necessary for the acute prevention of preterm delivery. There are data suggesting 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. There are fewer studies on medications to maintain tocolysis. The available evidence does not suggest that maintenance tocolysis improves health outcomes, and therefore maintenance tocolysis is considered investigational.

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

Consultant review 7/89

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

1997 USPDI

From policy entitled: Preventing Premature Labor and Delivery

Specialty Matched Consultant Advisory Panel - 11/1999

Medical Policy Advisory Group - 12/2/1999

ECRI Executive Briefing No. 91 - July 2000

Specialty Matched Consultant Advisory Panel - 9/2001

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, 10/8/02; 2.04.11

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

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Specialty Matched Consultant Advisory Panel - 8/2003

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

BCBSA Medical Policy Reference Manual, [Electronic Version]. 5.01.07, 12/17/03.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.03, 2/25/04.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.11, 2/25/04.

BCBSA Medical Policy Reference Manual [Electronic Version]. 4.01.09, 2/25/04.

Meis PJ, Klebanoff M, Thom E et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. *N Eng J Med* 2003; 348(24):2379-85.

da Fonseca EB, Bittar RE, Carvalho MH et al. Prophylactic administration of progesterone by vaginal suppository to reduce the incidence of spontaneous preterm birth in women at increased risk: a randomized placebo-controlled double-blind study. *Am J Obstet Gynecol* 2003;188(2):419-24.

American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 291. Use of Progesterone to Reduce Preterm Birth. *Obstet Gynecol* 2003;102:1115-6

Specialty Matched Consultant Advisory Panel - 12/2004.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.03, 12/14/05.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.11, 3/7/06.

BCBSA Medical Policy Reference Manual [Electronic Version]. 4.01.09, 12/14/05.

BCBSA Medical Policy Reference Manual [Electronic Version]. 4.04.16, 12/14/05.

Specialty Matched Consultant Advisory Panel - 12/13/2006

For policy entitled: Tocolysis with Intravenous or Subcutaneous Terbutaline

Letter from Stuart L. Nightengale, M.D., Associate Commissioner for Health Affairs, Food and Drug Administration, regarding subcutaneous administration, via infusion pump, of terbutaline sulfate for the treatment and prevention of preterm labor (tocolytic therapy), Rockville, MD: FDA; November 13, 1997. Retrieved on October 3, 2008 from <http://www.fda.gov/medwatch/SAFETY/1997/terbut.htm>.

California Technology Assessment Forum (CTAF). Maintenance tocolytic therapy with oral terbutaline or subcutaneous terbutaline infusion by pump for prevention of preterm delivery. Technology Assessment. San Francisco, CA: CTAF; June 12, 2002. Retrieved on October 3, 2008 from <http://ctaf.org/ass/viewfull.ctaf?id=6048341338>.

Institute for Clinical Systems Improvement (ICSI). Tocolytic therapy for preterm labor. ICSI Technology Assessment No. 49. Bloomington, MN: ICSI; March 2000. Retrieved on October 3, 2008 from http://www.icsi.org/technology_assessment_reports_-_active/ta_tocolytic_therapy_for_preterm_labor.html.

American College of Obstetricians and Gynecologists (ACOG) Committee on Practice Bulletins. ACOG Practice Bulletin. Clinical management guidelines for obstetrician-gynecologist. Number 43, May 2003. Management of preterm labor. *Obstet Gynecol*. 2003; 101(5 Pt 1):1039-1047.

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BCBSA Medical Policy Reference Manual, [Electronic Version]. 5.01.07, 4/1/05.

BCBSA Medical Policy Reference Manual, [Electronic Version]. 5.01.07, 12/05

BCBSA Medical Policy Reference Manual, [Electronic Version]. 5.01.07, 3/7/06

BCBSA Medical Policy Reference Manual, [Electronic Version]. 5.01.07, 9/18/07

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

For policy renamed: Acute and Maintenance Tocolysis

BCBSA Medical Policy Reference Manual, [Electronic Version]. 5.01.07, 12/10/2009

BCBSA Medical Policy Reference Manual, [Electronic Version]. 5.01.07, 4/14/2011

Policy Implementation/Update Information

From Policy entitled: Portable Infusion Pump for Administration of Terbutaline

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| 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

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| 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 women with triplet or higher-order gestations (carrying more than 2 fetuses)....". Benefits Application and Billing/Coding sections revised. |

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- 1/6/2005 Specialty Matched Consultant Advisory Panel review - 12/9/04. Added Section re: Progesterone Therapy in High Risk Pregnancies. Reference sources added.
- 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

- 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)
- 1/18/2011 Specialty Matched Consultant Advisory Panel review 12/16/2010. Policy Statement unchanged. Policy accepted as written. (adn)
- 10/11/11 Description section revised. Policy Statement revised to read: "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 investigational." Policy Guidelines updated. Specialty Matched Consultant Advisory Panel review 9/28/11. (adn)

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