Medical Policy
Acute and Maintenance Tocolysis

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Policy Number: 518
BCBSA Reference Number: 5.01.07
NCD/LCD: N/A

Related Policies
• Progesterone Therapy as a Technique to Reduce Preterm Birth in High-Risk Pregnancies, #552

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO BlueSM and Medicare PPO BlueSM Members

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

Maintenance (beyond 48-72 hours) tocolytic therapy administered via home infusion with any medication is INVESTIGATIONAL.

Authorization Information
Inpatient
• For services described in this policy, precertification/preauthorization IS REQUIRED for all products if the procedure is performed inpatient.

Outpatient
• For services described in this policy, see below for products where prior authorization might be required if the procedure is performed outpatient.

<table>
<thead>
<tr>
<th>Product</th>
<th>Prior Authorization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial Managed Care (HMO and POS)</td>
<td>not required</td>
</tr>
<tr>
<td>Commercial PPO and Indemnity</td>
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<tr>
<td>Medicare HMO BlueSM</td>
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<tr>
<td>Medicare PPO BlueSM</td>
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</table>
CPT Codes / HCPCS Codes / ICD Codes
Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes
There is no specific CPT code for this service.

<table>
<thead>
<tr>
<th>HCPCS codes:</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J3105</td>
<td>Injection, terbutaline sulfate, up to 1 mg</td>
</tr>
<tr>
<td>J3475</td>
<td>Injection, magnesium sulfate, per 500 mg</td>
</tr>
<tr>
<td>S9349</td>
<td>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</td>
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</tbody>
</table>

ICD-10-CM Diagnosis Coding

<table>
<thead>
<tr>
<th>ICD-10-CM diagnosis codes:</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>O60.00</td>
<td>Preterm labor without delivery, unspecified trimester</td>
</tr>
<tr>
<td>O60.02</td>
<td>Preterm labor without delivery, second trimester</td>
</tr>
<tr>
<td>O60.03</td>
<td>Preterm labor without delivery, third trimester</td>
</tr>
</tbody>
</table>

ICD-10-PCS Diagnosis Coding

<table>
<thead>
<tr>
<th>ICD-10-PCS diagnosis codes:</th>
<th>Code Description</th>
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</thead>
<tbody>
<tr>
<td>3E033GC</td>
<td>Introduction of Other Therapeutic Substance into Peripheral Vein, Percutaneous Approach</td>
</tr>
<tr>
<td>3E043GC</td>
<td>Introduction of Other Therapeutic Substance into Central Vein, Percutaneous Approach</td>
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</table>

Description
TOCOLYSIS
General indications for tocolysis, or the suppression of preterm labor, include continued regular uterine contractions associated with cervical changes in a pregnant woman at less than 37 weeks of gestation. Successful delay of preterm delivery allows further fetal development and precludes potential complications of preterm delivery, especially neonatal respiratory distress syndrome. 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 respiratory distress syndrome. In some cases, a short delay in delivery may also allow transport of the pregnant woman to a medical center better equipped to handle premature delivery and neonatal intensive care.

Treatment
Several agents have been used for tocolysis. The only tocolytic drug approved by the U.S. Food and Drug Administration (FDA) has been ritodrine, a beta-sympathomimetic. Ritodrine is no longer available in the United States, and thus only off-label medications are available. Terbutaline sulfate, FDA-approved for several nontocolytic indications, is also a beta-sympathomimetic. Terbutaline is available as an oral or intravenous medication and has been administered by continuous subcutaneous infusion via a portable...
pump for maintenance tocolysis. Other tocolytic drugs include calcium channel blockers (eg, nifedipine), magnesium sulfate, oxytocin receptor antagonists (eg, atosiban), prostaglandin inhibitors (eg, indomethacin), and nitrates (eg, nitroglycerin).

Tocolytic agents have potential to increase the risk of adverse events. The 2012 guidelines (reaffirmed 2014) issued by the American College of Obstetricians and Gynecologists summarized the potential adverse events of common classes of tocolytic agents: calcium channel blockers, nonsteroidal anti-inflammatory drugs, β-adrenergic receptor agonists, and magnesium sulfate.

**Calcium Channel Blockers**
- Maternal side effects: dizziness, flushing, and hypotension; suppression of heart rate, contractility, and left ventricular systolic pressure when used with magnesium sulfate; and elevation of hepatic transaminases
- Fetal or newborn adverse events: no known adverse events

**Nonsteroidal Anti-inflammatory Drugs**
- Maternal side effects: nausea, esophageal reflux, gastritis, and emesis; platelet dysfunction is rarely of clinical significance in patients without underlying bleeding disorder
- Fetal or newborn adverse events: in utero constriction of ductus arteriosus, a oligohydramnios, a necrotizing enterocolitis in preterm newborns, and patent ductus arteriosus in newbornb

a Greatest risk associated with use for more than 48 hours.
b Data are conflicting on this association.

**Beta-Adrenergic Receptor Agonists**
- Maternal side effects: tachycardia, hypotension, tremor, palpitations, shortness of breath, chest discomfort, pulmonary edema, hypokalemia, and hyperglycemia
- Fetal or newborn adverse events: fetal tachycardia

**Magnesium Sulfate**
- Maternal side effects: flushing, diaphoresis, nausea, loss of deep tendon reflexes, respiratory depression, and cardiac arrest; suppression of heart rate, contractility and left ventricular systolic pressure when used with calcium channel blockers; and produces neuromuscular blockade when used with calcium channel blockers
- Fetal or newborn adverse events: neonatal depression (note: the use of magnesium sulfate in doses and duration for fetal neuroprotection alone does not appear to be associated with an increased risk of neonatal depression when correlated with cord blood magnesium levels)

**Risks Associated With Terbutaline**
An FDA-conducted search of its Adverse Event Reporting System identified reports of 16 maternal deaths associated with terbutaline between 1976 and 2009. FDA documents indicate that, in 3 cases, it was specified that terbutaline was administered by a subcutaneous pump; and in 9 cases oral terbutaline was used instead of or in addition to injectable or subcutaneous terbutaline (presumably, in the remaining cases, the mode of administration was not reported). Moreover, between 1998 and July 2009, 12 cases of serious maternal cardiovascular events associated with terbutaline were submitted to the Adverse Event Reporting System; in 3 cases, subcutaneous terbutaline was specified and, in 5 cases, oral terbutaline was used alone or in addition to subcutaneous terbutaline.

An editorial by Rodier et al (2011) examined the human and animal evidence on risks of autism spectrum disorders associated with terbutaline. The commentators concluded that the literature did not support the hypothesis that β2-adrenergic agonists (including terbutaline) are associated with autism spectrum disorders in offspring.

**Summary**
For individuals who have preterm labor or threatened preterm labor who receive acute tocolytic therapy, the evidence includes multiple RCTs and systematic reviews. Relevant outcomes are overall survival, morbid events, functional outcomes, and treatment-related morbidity. Overall, the body of evidence has shown that the commonly used tocolytic agents presented herein are effective at inducing tocolysis in
patients with preterm labor or threatened preterm labor. Data have suggested 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 that the technology results in a meaningful improvement in the net health outcome.

For individuals who have successful acute tocolysis for preterm labor who receive maintenance tocolytic therapy, the evidence includes randomized controlled trials and systematic reviews. 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 birth weight. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Policy History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tr>
<td>9/2017</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>1/2016</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>12/2014</td>
<td>New references added from BCBSA National medical policy.</td>
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<tr>
<td>7/2014</td>
<td>Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.</td>
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<tr>
<td>12/2013</td>
<td>New references from BCBSA National medical policy.</td>
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</table>

**Information Pertaining to All Blue Cross Blue Shield Medical Policies**

Click on any of the following terms to access the relevant information:

- Medical Policy Terms of Use
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines

**References**