BlueCross BlueShield of Louisiana

An independent licensee of the Blue Cross and Blue Shield Association.

Amnioreduction and/or Fetoscopic Laser Therapy for Twin-Twin Transfusion Syndrome

Archived Medical Policy

Archived medical policies are no longer subject to periodic review, are maintained for reference, and may be returned to active status if the need is identified.

Policy # 00002
Original Effective Date: 03/25/2005
Archived Date: 04/19/2006

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May be Eligible for Coverage:
Note: Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met*

Based on review of available data, the Company may consider the following services as a treatment of twin-twin transfusion syndrome (TTTS) to be **eligible for coverage:**

- Amnioreduction
- Laser Coagulation Therapy
- Amnioreduction in combination with laser coagulation therapy

Patient Selection Criteria
Coverage eligibility will be considered when **any** of the following criteria met:

- Monochorionic-diamniotic twin pregnancy with discordance in size; or
- Polyhydramnios in the gestational sac of the recipient twin; or
- Oligohydramnios in the gestational sac of the donor twin; or
- Polyuria of the recipient; or
- Oliguria of the donor

When Services are Considered Investigational:
Note: Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products

Based on review of available data the Company considers the use of amnioreduction, laser coagulation therapy. or amnioreduction in combination with laser coagulation therapy when patient selection criteria are not met to be **investigational.***

Background/Overview

TTTS is a severe complication of monozygotic twinning. It is relatively common, occurring in 10%–15% of all monochorionic twins. It is often a lethal condition, accounting for 17% of perinatal deaths in twins overall. The pathophysiology of TTTS is not fully understood, but the primary defect is thought to be abnormal

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placentation, characterized by a paucity of superficial anastomosis together with the presence of a solitary unidirectional deep arteriovenous anastomosis flowing from the donor twin to the recipient twin. The imbalance created by this or other vascular anastomotic configurations, sometimes combined with other placental abnormalities, leads to a circulatory disequilibrium. Prenatal management strategies are aimed at amelioration of polyhydramnios and/or at correction of the underlying vascular anomalies in the shared placenta. If progressive, TTTS leads to polyhydramnios and eventually to cardiac dysfunction in the net "recipient" twin, and oligohydramnios or anhydramnios due to hypovolemic oliguria in the net "donor" twin, who is also often growth restricted and anemic.

Selection of treatment options for TTTS presenting before fetal viability is controversial. Most therapies have evolved only during the past 5 to 10 years and include expectant management, medical therapy (i.e., digoxin), delivery of the compromised twin, selective feticide, or septostomy. Outcomes from these options have been disappointing. Two treatments—serial amnioreduction and fetoscopic laser ablation of anastomotic vessels—are currently undergoing active investigation. Amnioreduction is a variant of amniocentesis in which amniotic fluid is removed to restore normal fluid volume. Fetoscopic laser therapy is designed to correct the underlying abnormality by separating the 2 fetal circulations. Refinements of laser therapy have focused on the selective ablation of those few arteriovenous anastomosis causing disease. Specific anastomosis can be targeted using angiography, Doppler ultrasonography, or direct fetoscopic visualization.

Amnioreduction (serial amniotic fluid volume reduction) was the earliest therapy available for TTTS and is still the most widely used treatment. This procedure employs ultrasonographic guidance to restore a normal level of fluid in the polyhydramniotic sac by placing an 18- or 20-gauge needle to drain the excess fluid. The amount of fluid drained at a single procedure can range from 1 to 7 L (multiple procedures may be necessary). Complications, which occur in about 8% of cases, include chorioamnionitis, preterm labor and delivery, preterm premature rupture of the membranes, and abruptio placentae. An extensive registry of TTTS patients undergoing amnioreduction has shown that earlier presentation of the disease and a higher number of procedures are associated with a poorer outcome.

Fetoscopic laser occlusion of chorioangiopagous placental vessels (FLOC) seeks to treat the source of the problem by interrupting vascular anastomosis within the placenta. FLOC is more invasive than amnioreduction, and confers a greater risk for maternal morbidity. Analysis of a large series of TTTS pregnancies suggests that fetal survival rates following amnioreduction versus FLOC are similar Although FLOC might have been expected to be more effective than amnioreduction, their similar outcomes may simply attest to the severity of the disease. They may also reflect differences in (or lack of) diagnostic criteria in various studies, technical difficulties encountered in the use of FLOC, failure to completely ablate all anastomosing vessels in many cases, or other unknown factors.

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FDA or other Governmental Regulatory Approval

Food and Drug Administration (FDA):
The FDA does not regulate surgical procedures

Rationale/Source

A 2000 (Technology Assessment Center (TEC) Assessment offered the following observations and conclusions:

- The primary evidence supporting amnioreduction with or without laser therapy consists of 15 uncontrolled case series that report consistent evidence of a survival advantage. There was an overall fetal survival of 54.8% among the 197 cases reported. This survival rate is similar to the 60% survival rate reported by the International Interim Amnioreduction Registry.
- The alternative to prenatal intervention is conservative management, which is associated with a fetal mortality rate of 90%–100%.

As of April 2004, there were 3 randomized controlled trials currently in progress, but no results have been reported from any of these trials. For example, 1 prospective randomized clinical trial sponsored by the National Institutes of Health (NIH) is comparing aggressive serial amnioreduction with selective fetoscopic laser photocoagulation. Studies conducted since the prior TEC Assessment report only on case series with outcomes similar to those reported in the TEC Assessment. However, complicating the assessment of these procedures is the improved outcomes of those managed conservatively. In a meta-analysis by Skupski et al., there were no differences in outcomes between those treated by either amnioreduction or laser therapy and those treated conservatively. However, small numbers and lack of control for confounding variables do not allow for firm conclusions. For all surviving twins, morbidity remains high, dominated by neurologic cardiovascular and renal complications. For example, the incidence of cerebral palsy and global developmental delay in the surviving twins varies from 4% to 23%.

None of the treatments for TTTS has been subjected to a randomized, controlled trial. The only three trials of any treatment for TTTS have compared historical controls with subjects undergoing amnioreduction. (In studies using historical controls, selection bias appears to favor a better outcome [of up to 30%-40%] for patients in the more recent time period--i.e., the treated patients.) In the three controlled trials of amnioreduction for TTTS, although P values ranged from 0.04 to 0.0000001, the treatment effect was 30% to 40% (risk ratio for fetal/neonatal death, 0.60-0.66) Thus, the effectiveness of serial amnioreduction has not been adequately demonstrated.

Successive studies of the efficacy of each TTTS therapy have shown increasing survival rates suggesting that this apparent efficacy may really be due to advances in neonatal care. Analysis of the deaths in the

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three controlled trials shows that 65% were neonatal and only 35% were fetal, allowing for this possibility. However, one study that did address this issue suggested a possible benefit of amnioreduction over and above the increased survival due to advances in neonatal care for TTTS twins delivered at 27 weeks' gestation or earlier. In addition, increased survival in later series using FLOC has been attributed to a lack of technical expertise in earlier cases (i.e., a learning curve), thereby providing some evidence for a true benefit from FLOC.

References

1. Blue Cross Blue Shield Association, Medical Policy Reference Manual, "*Treatment of Twin-Twin Transfusion Syndrome with Amnioreduction and/or Fetoscopic Laser Therapy*", *Policy #4.01.12*, *3:2004*.
2. University of Maryland Medical Center , Center for Advanced Fetal Care . "Twin-Twin Transfusion Syndrome" www.umn.edu/womenscenter
3. Skupski W, Daniel. Twin-Twin Transfusion Syndrome" www. Obgyn.net/The female patient.

Policy History

Original Effective Date: 03/25/2005

03/21/2002	Medical Policy Committee review
03/25/2002	Managed Care Advisory Council approval
03/08/2004	Medical Director review
03/16/2004	Medical Policy Committee review Format revision. No substance change to policy.
03/29/2004	Managed Care Advisory Council approval
03/01/2005	Medical Director review
03/15/2005	Medical Policy Committee review Format revision. No substance change to policy.
04/04/2005	Managed Care Advisory Council approval
04/05/2006	Medical Director review Format revisions, Fed/Governmental Regulations, Rationale/Source
04/19/2006	Medical Policy Committee review. Archived.

Next Scheduled Review Date: Archived Medical Policy

*Investigational – A medical treatment, procedure, drug, device, or biological product is investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination We make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, according to the consensus of opinion among experts as shown by reliable evidence, including:

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1. consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other non-affiliated technology evaluation center(s);
2. credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. in accordance with nationally accepted standards of medical practice;
B. clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.