INTRAUTERINE FETAL SURGERY

Guideline Number: MMG065.I **Effective Date**: May 1, 2019

Instructions for Use

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Related Policies

None

COVERAGE RATIONALE

See Benefit Considerations

Intrauterine fetal surgery (IUFS) is proven and medically necessary for treating the following conditions:

- Congenital cystic adenomatoid malformation (CCAM) and extralobar pulmonary sequestration (EPS): Fetal lobectomy or thoracoamniotic shunt placement for CCAM and thoracoamniotic shunt placement for EPS
- Sacrococcygeal teratoma (SCT): SCT resection
- Urinary tract obstruction (UTO): Urinary decompression via vesicoamniotic shunt placement
- Twin-twin transfusion syndrome (TTTS): Fetoscopic laser surgery
- Twin reversed arterial perfusion (TRAP): Ablation or occlusion of anastomotic vessels (e.g., laser coagulation or radiofrequency ablation)
- Myelomeningocele (MMC) repair

Due to insufficient evidence of efficacy, IUFS is unproven and not medically necessary for treating all other conditions, including but not limited to:

- Congenital diaphragmatic hernia (CDH)
- Congenital heart disease (CHD)

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 guideline 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 and Guidelines may apply.

CPT Code	Description
59072	Fetal umbilical cord occlusion, including ultrasound guidance
59074	Fetal fluid drainage (e.g., vesicocentesis, thoracocentesis, paracentesis), including ultrasound guidance
59076	Fetal shunt placement, including ultrasound guidance
59897	Unlisted fetal invasive procedure, including ultrasound guidance, when performed

HCPCS Code	Description
S2400	Repair, congenital diaphragmatic hernia in the fetus using temporary tracheal occlusion, procedure performed in utero

HCPCS Code	Description
S2401	Repair, urinary tract obstruction in the fetus, procedure performed in utero
S2402	Repair, congenital cystic adenomatoid malformation in the fetus, procedure performed in utero
S2403	Repair, extralobar pulmonary sequestration in the fetus, procedure performed in utero
S2404	Repair, myelomeningocele in the fetus, procedure performed in utero
S2405	Repair of sacrococcygeal teratoma in the fetus, procedure performed in utero
S2409	Repair, congenital malformation of fetus, procedure performed in utero, not otherwise classified
S2411	Fetoscopic laser therapy for treatment of twin-to-twin transfusion syndrome

DESCRIPTION OF SERVICES

This policy addresses the use of intrauterine fetal surgery (IUFS), an open surgical treatment of fetuses with specific life-threatening conditions that involve a fetal malformation. During IUFS, a hysterotomy is performed, and the fetus is partially removed to correct a fetal malformation.

IUFS uses minimally invasive techniques (i.e., small incisions) and instruments to correct the fetal malformation. The primary medical conditions indicated for IUFS include the following:

- Congenital cystic adenomatoid malformation
- Extralobar pulmonary sequestration
- Sacrococcygeal teratoma
- Urinary tract obstruction
- Twin-twin transfusion syndrome
- Twin reversed arterial perfusion syndrome
- Myelomeningocele repair
- Congenital diaphragmatic hernia
- Congenital heart disease

Thoracic Lesions

Congenital cystic adenomatoid malformation (CCAM) and bronchopulmonary sequestration are congenital anomalies of the lung. Appropriate candidates for in utero treatment include a small subset of fetuses with congenital pulmonary airway malformations. In this subset, the fetal mediastinum is compressed, leading to impaired venous return with resulting fetal hydrops, secondary to cardiac failure (Walsh et al., 2011).

Sacrococcygeal Teratoma (SCT)

Fetuses with large, vascular SCTs have a high incidence of prenatal mortality from high-output cardiac failure or spontaneous hemorrhage of the growing tumor. Fetal surgical procedures for SCT have focused on the small subgroup of fetuses with SCT and hydrops because untreated cases are expected to die in utero or at birth. In severe cases, SCT with hydrops is associated with a maternal risk of developing mirror syndrome, a severe form of preeclampsia (Walsh et al., 2011).

Urinary Tract Obstruction (UTO)

Fetal UTO interferes with normal development of the kidneys and lungs, particularly when involving the lower urinary tract. Goals of fetal surgery have emphasized decompression procedures, such as percutaneous shunting, rather than repair of the specific lesion. The goal of decompression of the distended portion of the urinary tract is to protect function of the remaining kidney and to promote lung development (Walsh et al., 2011).

Twin-twin Transfusion Syndrome (TTTS)

In TTTS, twins share a single chorionic membrane and a single placenta but have separate amniotic sacs. Women with severe TTTS who have not undergone treatment before 26 weeks will usually experience loss of both fetuses. However, if both twins survive, they often experience severe neurologic compromise and organ failure. Treatment options include amnioreduction to relieve pressure and uterine size, termination of the sicker twin, or fetoscopic laser ablation of the communicating vessels. In nonselective ablation, all vessels crossing the dividing membrane are ablated, whereas selective ablation is limited to certain vessels connecting the two fetuses (Walsh et al., 2011).

Twin Reversed Arterial Perfusion (TRAP)

TRAP sequence is a condition in which an acardiac/acephalic twin receives all of its blood supply from a normal twin, the so-called "pump" twin. Blood enters the acardiac twin through a retrograde flow via the umbilical artery and exits

via the umbilical vein. The extra work places an increased demand on the heart of the pump twin, resulting in cardiac failure. Twin death occurs more frequently when the size of the acardiac twin is greater than half that of the pump twin. The goal of fetal surgery is to interrupt blood supply to the non-viable twin.

Myelomeningocele (MMC)

MMC (also known as spinal bifida) is a neural tube defect in which the spinal cord forms but remains open. Although MMC is rarely fatal, individuals affected with it have a range of disabilities, including paraplegia, hydrocephalus, skeletal deformities, bowel and bladder incontinence and cognitive impairment. Standard therapy is postnatal surgical closure of the MMC followed by shunting for hydrocephalus if needed (Walsh et al., 2011).

Congenital Diaphragmatic Hernia (CDH)

CDH results from abnormal development of the diaphragm, which allows abdominal organs like the bowel, stomach, and liver to protrude into the chest cavity. Fetuses diagnosed in utero as a result of maternal symptoms have a high mortality risk. Less invasive fetal procedures are being developed that focus on methods to accomplish tracheal occlusion (Walsh et al., 2011).

Congenital Heart Disease

In utero procedures are performed for cardiac conditions such as pulmonary atresia with intact ventricular septum, critical aortic stenosis with impending hypoplastic left heart syndrome, and hypoplastic left heart syndrome with intact atrial septum. All of these conditions, if untreated either in utero or soon after birth, are fatal (Walsh et al., 2011).

BENEFIT CONSIDERATIONS

When deciding coverage for intrauterine fetal surgery, refer to the member specific benefit plan document language for further information on benefit coverage for treatment of life-threatening conditions. In some benefit documents, coverage exists for unproven services for persons with life-threatening conditions, under certain circumstances.

CLINICAL EVIDENCE

Congenital Cystic Adenomatoid Malformation (CCAM) and Extralobar Pulmonary Sequestration (EPS)

A 2017 ECRI Health Technology report reviewed full text of 2 studies (available by subscription only) and abstracts of 7 studies published between January 1, 2012 and August 4, 2017. The evidence indicated that thoracoamniotic shunting results in better survival rates in fetuses without hydrops than those with hydrops. Survival benefit in fetuses with fetal hydrothorax associated with trisomy 21 is unclear because studies report inconsistent findings.

Litwińska et al. conducted a retrospective study of 12 fetuses with a large thoracic cyst treated with thoracoamniotic shunting between 2004 and 2014 in a tertiary fetal therapy center. In all cases the thoracic cyst was associated with major mediastinal shift, the CCAM volume ratio (CVR) was >1.6, and in 8 cases there was associated hydrops. Shunt insertion was successfully carried out in all cases at a median gestational age of 24 weeks (range 18-34). In 10 cases there was live birth at a median age of 38 weeks (range 35-41), but in two hydropic fetuses there was intrauterine death. A literature search identified a total of 98 fetuses with CCAM treated with thoracoamniotic shunting between 1987 and 2016. In the combined data from the previous and the current study, the survival rate was 77% for hydropic and 90% for nonhydropic fetuses. The authors concluded that the role of thoracoamniotic shunting in macrocystic lung lesions associated with hydrops is well accepted, and that intrauterine intervention is also likely to be beneficial in the subgroup of nonhydropic fetuses with a CVR >1.6 (2017).

A prospective study evaluating 58 fetuses with CCAM found that 29% were at risk for hydrops and required fetal intervention. The overall survival rate was 71% after fetal surgery; however, the survival rate for hysterotomy and open fetal lobectomy was 29% compared with 100% for fetoscopic shunting or cyst aspiration. The perinatal mortality rate was 29% in those fetuses who were considered unlikely to survive (Crombleholme et al., 2002).

Professional Societies

Society for Maternal-Fetal Medicine (SMFM)

A SMFM guideline includes fetal needle drainage or thoracoamniotic shunting as a possible treatment for nonimmune hydrops fetalis caused by fetal hydrothorax, chylothorax, large pleural effusion associated with bronchopulmonary sequestration, and fetal congenital pulmonary airway malformation (2015).

Sacrococcygeal Teratoma (SCT)

Sananes et al. conducted a retrospective multicenter cohort study in 13 fetuses with high-risk large SCTs between 2004-2010. Additionally, the researchers performed a systematic literature review of all cases that underwent tumor ablation in order to compare the survival rates after 'vascular' and 'interstitial' ablation. Study objectives were to evaluate the efficacy of minimally invasive ablation of high-risk large SCTs and to compare the efficacy of the vascular

versus interstitial tumor approach. Five of the 13 underwent tumor ablation. The estimated difference in hydrops resolution rate and survival rate between the fetal intervention and the no fetal intervention groups was 44.6% and 31%, respectively. The 5 cases were then analyzed with 28 cases from the literature. Researchers estimated the difference in survival rate and in hydrops resolution rate between the vascular and interstitial ablation groups was 19.8% and 36.7%, respectively. The authors concluded that minimally invasive surgery seemed to improve perinatal outcome in cases of high-risk large fetal SCT. Their findings also suggested that vascular ablation may improve outcome and may be more effective than interstitial tumor ablation. Further investigation in a larger multicenter prospective study is needed (2016).

Fetal surgery is not considered appropriate in the presence of the maternal mirror syndrome or in cases of advanced high-output cardiac failure (Hedrick et al., 2004).

Urinary Tract Obstruction (UTO)

In utero fetal surgery for UTO improves perinatal survival in selected fetuses and children, who are at high risk for mortality due to renal failure and pulmonary complications. Perinatal survival rates ranged from approximately 57% to 80%. The prognosis appears to be worse for fetuses with elevated urinary electrolytes or prolonged anhydramnios at the time of surgery. Despite initial surgical success and improved survival, more than 25% of children have residual renal disease that require subsequent transplantation, urinary tract surgery, or other medical interventions. Most children also demonstrate growth retardation, and many void spontaneously. Pulmonary dysfunction is apparent, despite fetal surgery, and has been reported to result in death in 18% to 25% of children followed for a period up to 114 months. A meta-analysis evaluated the efficacy and safety of prenatal bladder drainage. Results showed significantly improved perinatal survival among 195 fetuses in controlled trials that received the intervention compared with those who did not (Clark et al., 2003; Freedman et al., 1999; McLorie et al., 2001; Welsh et al., 2003).

Twin-Twin Transfusion Syndrome (TTTS)

Ozawa et al. (2017) conducted a prospective interventional study to investigate the feasibility and safety of fetoscopic laser photocoagulation (FLP) for amniotic fluid discordance (AFD) bordering on TTTS with an absent or reverse end-diastolic velocity in the umbilical artery, as well as evaluating the perinatal and long-term outcomes. Surgical intervention took place on the fetuses of 11 women during weeks 20-25 of gestation. Neurodevelopmental outcome was evaluated at 6 months and at 3 years of age. There were 9 cases of selective intrauterine growth restriction in which the growth discordant rate exceeded 25%. The survival rates of the donor and recipient twins were 27.3% and 100%, respectively. None of the surviving donor twins and two of the 11 recipient twins had hemiplegia at 6 months of age. One additional recipient twin had developmental delay at 3 years of age. Researchers concluded that FLP does not seem to be a promising treatment option for AFD bordering on TTTS. While feasible without complications, donor twin death occurred frequently and there were some cases of neurodevelopmental abnormalities in the surviving recipient twin.

A total of 120 infants with TTTS were enrolled in a randomized clinical trial (RCT) of laser photocoagulation versus amnioreduction. Investigators assessed long-term neurological and developmental outcomes. The primary outcome was a composite of death and major neurological impairment. The authors found that, at 6 years of age, 82% of the children in the laser group and 70% of the children in the amnioreduction group had a normal neurological evaluation; the differences between the groups were not significant. Laser therapy was associated with a 40% reduction in the risk of fetal death or long-term neurologic impairment when compared with amnioreduction (Salomon et al., 2010).

A systematic review and meta-analysis was conducted by Rossi and D'Addario (2008) to review the controversy on laser therapy (LT) versus serial amnioreduction (SA) performed for TTTS. Inclusion criteria were diamniotic monochorionic pregnancy, TTTS diagnosed with standard parameters, and peri- and neonatal outcomes well defined. Ten articles published between 1997-2007 provided 611 cases of TTTS (LT: 70%; SA: 30%) with 4 studies comparing the 2 treatments (395 cases: LT, 58%; SA, 42%). The meta-analysis showed that LT was associated with better outcomes than SA.

Roberts et al. (2008) assessed which treatments for TTTS improved fetal, childhood and maternal outcomes. The authors compared outcomes from 3 randomized and quasi-randomized studies of amnioreduction, laser coagulation, and septostomy (253 women). Laser coagulation resulted in reduced overall mortality and neonatal mortality when compared with amnioreduction. There was no difference in perinatal outcome between amnioreduction and septostomy. The results suggest that endoscopic laser coagulation of anastomotic vessels should be considered for treatment of all stages of TTTS to improve perinatal and neonatal outcome. In a later publication, Roberts et al. (2014) concluded that endoscopic laser coagulation of anastomotic vessels should be considered in the treatment of all stages of TTTS to improve neurodevelopmental outcomes. Further research to assess the effect of treatment on milder and more severe forms of TTTS and long-term survival outcomes are still required.

Senat et al. (2004) conducted a RCT, evaluating pregnant women with severe TTTS before 26 weeks of gestation who were randomly assigned to laser therapy (n = 72) or amnioreduction (n = 70). The study concluded early because an

interim analysis demonstrated a significant survival benefit in the laser group. Compared to the amnioreduction group, the laser group had a higher likelihood of survival (of at least 1 twin) to 28 days of age (76% in laser group and 56% in amnioreduction group). The laser group also had a lower incidence of cystic periventricular leukomalacia, and were more likely to have no neurological complications at 6 months of age (52% in laser group and 31% in amnioreduction group).

Graef et al. evaluated 167 children (median age 3 years, 2 months) to investigate long-termneurodevelopment after intrauterine laser coagulation for TTTS. A total of 145 children (86.8%) demonstrated normal development, 12 children (7.2%) showed minor neurological abnormalities, and 10 children (6%) demonstrated major neurological abnormalities. The investigators concluded that intrauterine laser coagulation was the relatively best treatment option for severe TTTS (2006).

A National Institute for Health and Care Excellence (NICE) interventional procedures guideline states that current evidence on the safety and efficacy of intrauterine laser ablation of placental vessels for the treatment of TTTS appears adequate to support the use of this procedure provided that the normal arrangements are in place for clinical governance (2006).

Professional Societies

Society for Maternal-Fetal Medicine (SMFM)

A SMFM clinical guideline states that over 75% of stage I TTTS cases remain stable or regress without invasive intervention, with perinatal survival of about 86%. Therefore, many patients with stage I TTTS can often be managed expectantly. For stages II-IV, fetoscopic laser photocoagulation of placental anastomoses is considered by most experts to be the best available approach in continuing pregnancies at <26 weeks. However, expectant management and amnioreduction remain 2 options for TTTS > stage I at <26 weeks when the patient does not have the ability to travel to a center that performs fetoscopic laser photocoagulation. Published meta-analysis data have demonstrated no significant survival benefit and long-term neurologic outcomes in the Eurofetus trial were not different between the laser and non-laser groups. Laser-treated TTTS has been shown to be associated with a perinatal mortality rate of 30-50%, and a 5-20% chance of long-term neurologic handicap. For stage ≥III TTTS and for those undergoing invasive interventions, steroids for fetal maturation should be considered at 24 0/7 to 33 6/7 weeks (2013).

Twin Reversed Arterial Perfusion (TRAP)

Lee et al. (2013) reported the North American Fetal Therapy Network (NAFTNet) Registry data on the outcomes of using radiofrequency ablation (RFA) to treat TRAP. This was a retrospective review of all patients who underwent percutaneous RFA of an acardiac twin after referral to a NAFTNet institution. The primary outcome was neonatal survival to 30 days of age. Of the 98 patients identified, there were no maternal deaths. Mean gestational age at delivery was 33.4 weeks overall and 36.0 weeks for survivors. Median gestational age at delivery was 37 weeks. Survival of the pump twin to 30 days was 80% in the overall cohort. The authors concluded that this data suggests that RFA of the acardiac twin is an effective treatment for TRAP sequence.

Pagani et al. (2013) conducted a retrospective cohort study and meta-analysis of intrafetal laser treatment for TRAP sequence. A total of 23 cases of TRAP were identified during the study period. Of these, 6 were managed conservatively and 17 were treated with laser therapy. All cases managed conservatively were complicated by intrauterine death (IUD) at a median gestational age of 14 weeks. Among the treated cases, 14 (82%) delivered a healthy twin at a median gestational age of 37 weeks. The overall neonatal survival was 80%. Adverse pregnancy outcome was significantly lower when the treatment was performed before 16 weeks' gestation.

Cabassa et al. (2013) evaluated the treatment of monochorionic twin pregnancies complicated by TRAP using RFA. Between July 2007 and October 2010, 11 monochorionic twin pregnancies complicated by TRAP were identified. A total of 7 patients underwent intrafetal ablation of the acardiac twin with RFA. Median gestational age at the intervention was 17 weeks. A total of 5 fetuses (71%) were delivered at a median gestational age of 33 weeks; all were alive and had a normal examination at 6 months of age. The overall neonatal survival was 85%. The authors noted that further research is needed to define the best timing of the procedure.

Lee et al. (2007) evaluated the treatment of 29 patients with TRAP sequence using RFA to stop perfusion to the acardiac twin and protect the pump twin. The investigators concluded that RFA of the acardiac twin effectively protects the pump twin from high-output cardiac failure and death. Greater than 90% survival can be achieved in monochorionic-diamniotic pregnancies complicated by TRAP sequence with a mean gestation age at time of delivery close to term.

Myelomeningocele (MMC)

Relating to MMC, a 2018 Hayes report (consisting of 1 good-quality RCT and supporting evidence from 1 prospective cohort study and several retrospective studies) suggests that prenatal MMC repair significantly decreases the need for shunts and may decrease hindbrain herniation compared with postnatal MMC repair.

Araujo Júnior et al. (2016) conducted a systematic review and meta-analysis of RCTs and observational studies on treatment of human spina bifida by endoscopic or open fetal surgery techniques. Only studies with ≥ 10 cases that were published in or after 2000 were included in the meta-analysis in order to reduce the risk of bias. The search identified 1080 records, of which 19 records met all criteria for eligibility. Primary outcomes (complete dehiscence, focal dehiscence and/or markedly thin hysterotomy scar; preterm delivery < 34 weeks; mean gestational age at delivery) and secondary outcomes (oligohydramnios, prelabor rupture of membranes, placental abruption, chorioamnionitis and perinatal death) were assessed for both techniques. When comparing endoscopic versus open fetal surgery, the rate of complete dehiscence, focal dehiscence and/or markedly thin hysterotomy scar was, respectively, 1%. The researchers concluded that open fetal surgery for spina bifida seems to show lower rates of procedure-related complications than endoscopic surgery, but the rate of hysterotomy scar complications is high after open surgery. Because of the low quality of evidence, the conclusions should be interpreted with caution.

The Management of Myelomeningocele Study (MOMS) compared outcomes of prenatal versus postnatal repair of MMC. Patients (n = 183) were randomized to undergo either prenatal surgery before 26 weeks of gestation or standard postnatal repair. Primary outcomes were fetal or neonatal death, the need for a cerebrospinal shunt by the age of 12 months and mental development and motor function at 30 months. The children of 158 patients were available for evaluation at 12 months. The children of 134 patients were available for evaluation at 30 months. = The trial was stopped after recruiting 183 of the planned 200 patients due to demonstrated efficacy of prenatal versus postnatal repair. Despite having more severe lesions and an increased risk of preterm delivery, the study found that the prenatal surgery group had significantly better outcomes than the postnatal surgery group. Prenatal surgery for MMC decreased the risk of death or need for shunting by the age of 12 months. Prenatal surgery also improved scores on a composite measure of mental and motor function at 30 months. However, prenatal surgery was associated with an increased risk of preterm delivery and uterine dehiscence at delivery. The authors noted that the potential benefits of prenatal surgery must be balanced against the risks of prematurity and maternal morbidity (Adzick, 2011).

Danzer et al. (2009) evaluated lower extremity neuromotor function (LENF) and short-term ambulatory potential following fetal MMC (fMMC) closure in a retrospective chart review of 54 children. Neonatal LENF was compared to predicted function based on spinal lesion level assigned by prenatal ultrasound. A total of 31 out of 54 of fMMC children (57.4%) had better than predicted, 13/54 (24.1%) same as predicted and 10/54 (18.5%) worse than predicted LENF at birth. At a median follow-up age of 66 months, 37/54 (69%) walk independently, 13/54 (24%) are assisted walkers, and 4/54 (7%) are wheelchair dependent. Despite the observed improved ambulatory status, structured evaluation of coordinative skills revealed that the majority of independent walkers and all children that require assistive devices to walk experience significant deficits in lower extremity coordination. The investigators concluded that fMMC surgery results in better than predicted LENF at birth and short-term ambulatory status. However, fMMC children continue to demonstrate deficits in movement coordination that are characteristic for children with spina bifida.

Danzer et al. (2008) evaluated the incidence and clinical implications of the development of cutaneously derived intradural inclusion cysts following fMMC closure in retrospective databases and responses to a parental questionnaire. The investigators found that cutaneously derived intradural inclusion cysts can develop following fMMC surgery. Deterioration of bladder function, risk of recurrence, and loss of lower-extremity function appear to be the most important long-term complications of inclusion cysts in children with fMMCs.

Koh et al. (2006) compared urodynamic findings in patients who underwent prenatal closure of MMC (n = 5) with those of patients who underwent postnatal closure (n = 88). All 5 prenatally treated patients had lower lumbosacral lesions on neurological examination. In comparison, 34 of the 88 patients in the postnatal cohort (39%) lacked sphincter activity at newborn examination, with similar findings noted at 1-year evaluation. In terms of bladder function, all 5 patients in the prenatal cohort showed detrusor overactivity, compared to 33 of the 88 patients (38%) in the postnatal cohort at the newborn examination, with similar findings at 1-year evaluation. The investigators concluded that fetal closure of MMC is associated with a higher incidence of complete denervation of the external urethral sphincter and detrusor overactivity compared to postnatal closure.

Professional Societies

American College of Obstetricians and Gynecologists (ACOG)

ACOG's Maternal-Fetal Management Task Force published a position statement (Cohen et al., 2014) regarding fMMC repair with the goal of developing "optimal practice criteria for medical and surgical leadership." Members of the task force reported the following:

- fMMC repairs should be performed in established fetal therapy centers using a multidisciplinary team approach.
- The fetal surgery team must have experience working together and individual members have a level of expertise in their field.
- The level of fetal surgical technical expertise demanded requires an adequate annual volume of open fetal and EXIT procedures to maintain competency.

- The level of technical expertise in fMMC repair requires an initial experience of at least 5 cases and an ongoing adequate annual volume of cases evaluated for fetal surgery to maintain competency.
- Centers developing new programs must receive guidance and training from established programs and experienced individuals.
- The MOMS protocol should be followed for preoperative, intraoperative, and immediate postoperative care. This applies to inclusion and exclusion criteria for in utero MMC repair.
- Modification of the long-term postoperative and delivery care is acceptable in certain circumstances.
- Modifications to the perioperative protocol are only permissible after the results of fMMC repair performed by an expanded number of centers have been shown to be consistent with the results obtained in the MOMS trial. Such modifications would, ideally, be developed by means of a series of cooperative trials.
- Ongoing neonatal and pediatric care should be performed in multidisciplinary spina bifida clinics. This can be done at outside centers but must be standardized.
- Counseling should be full disclosure and nondirective in nature. It should also include reproductive implications for future pregnancies.
- A reflective period of at least 24 hours is recommended.
- Short-term and long-term outcomes data from all centers should be kept in a national registry with periodic review.
- Centers performing open MMC repair must maintain a collaborative approach to outcomes reporting and future research, including participating in the long-term outcomes data collection and evaluation. Close links between fetal centers throughout the country and community providers are essential.

An ACOG practice bulletin states that despite the maternal and obstetric risks, in utero repair is an option for women who meet appropriate criteria. Counseling should be nondirective and include all options, with full disclosure of all potential benefits and risks for the fetus and woman, including the implications for future pregnancies (2017).

An ACOG committee opinion states open maternal–fetal surgery for MMC repair is a major procedure for the woman and her affected fetus. Although there is demonstrated potential for fetal and pediatric benefit, there are significant maternal implications and complications that may occur acutely, postoperatively, for the duration of the pregnancy, and in subsequent pregnancies. It is a highly technical procedure with potential for significant morbidity and possibly mortality, even with the best and most experienced surgeons. Maternal–fetal surgery for MMC repair should only be offered to carefully selected patients at facilities with an appropriate level of personnel and resources (2017).

Congenital Diaphragmatic Hernia (CDH)

A 2018 Hayes report concludes that fetal endoscopic tracheal occlusion (FETO) for fetuses with mild CDH, cannot be evaluated due to a lack of evidence in the peer reviewed literature. The evidence also suggests that FETO may not benefit fetuses with moderate CDH, although this was only evaluated in a single RCT and thus the evidence is insufficient. In fetuses with severe CDH, there may be clinical benefits over postnatal treatment alone in terms of improved survival and a reduction in severe pulmonary hypertension in infants; however, reviewed evidence is limited to 3 fair-quality RCTs.

A systematic review and meta-analysis by Grivell et al. (2015) compared the effects of prenatal versus postnatal interventions for CDH on perinatal mortality and morbidity, longer-term infant outcomes and maternal morbidity. The review also looked to compare the effects of different prenatal interventions with each other. Three studies were included involving 97 women. Two trials examined in utero FETO with standard (postnatal) care in fetuses with severe diaphragmatic hernia. One trial examined the effect of antenatal corticosteroids versus placebo. The authors concluded that there is currently insufficient evidence to recommend inutero intervention for fetuses with CDH as a part of routine clinical practice. Only 1 of the studies adequately reported on perinatal mortality, but there were no data suitable for inclusion in the analysis. More studies are needed to further examine the effect of both in utero FETO and the use of antenatal corticosteroids on important neonatal outcomes and long-term infant survival and health.

Ruano et al. (2012) conducted a RCT to determine whether FETO improved survival in cases of CDH. Patients whose fetuses had severe isolated CDH (lung-to-head ratio < 1.0, liver herniation into the thoracic cavity and no other detectable anomalies) were randomly assigned to FETO (n = 20) or to standard postnatal management (n = 21). Tracheal balloon placement was achieved with ultrasound guidance and fetoscopy between 26 and 30 weeks of gestation. Postnatal therapy was the same for both treated fetuses and controls. The primary outcome was survival to 6 months of age. Delivery occurred at 35.6 ± 2.4 weeks in the FETO group and at 37.4 ± 1.9 weeks in the control group. In the intention-to-treat analysis, 10/20 (50.0%) infants in the FETO group survived, while 1/21 (4.8%) controls survived. In the received-treatment analysis, 10/19 (52.6%) infants in the FETO group and 1/19 (5.3%) controls survived. The authors concluded that FETO improved infant survival in isolated severe CDH; however, the risk of prematurity and preterm premature rupture of membranes was high.

Ruano et al. (2011) treated 16 fetuses with severe CDH with FETO and compared their outcome to 18 similar cases treated with standard neonatal therapy. The primary outcome was neonatal survival (up to 28 days after birth).

Survival in the FETO group was 53% compared to 6% in the standard therapy group. This study is limited by small sample size and lack of randomization.

A case series reported the results of 24 fetuses with severe CDH who underwent percutaneous FETO with a balloon. Premature prelabor rupture of the membrane occurred in 16.7% and 33.3% at 28 and 32 weeks, respectively. Seven-day, 28-day, and survival at discharge were 75%, 58.3%, and 50%, respectively. The investigators concluded that FETO may improve survival in highly selected CDH cases (Deprest et al., 2006).

Hirose et al. (2004) conducted a retrospective review of 52 patients who underwent an ex utero intrapartum treatment (EXIT) procedure. Fifty-one of 52 patients were born alive. At the time of the study, 27 of 52 patients (52%) were alive. All deaths have been in patients with CDH. The investigators concluded that the EXIT procedures can be performed with minimal maternal morbidity and with good outcomes.

Kunisaki et al. (2007) evaluated whether the EXIST procedure with extracorporeal membrane oxygenation (EXIT to ECMO) is a reasonable approach for managing patients antenatally diagnosed with severe CDH. Fourteen patients underwent EXIT with a trial of ventilation. Fetuses with poor preductal oxygen saturations despite mechanical ventilation received ECMO before their delivery. Three neonates passed the ventilation trial and survived, but 2 of them required ECMO within 48 hours. The remaining 11 fetuses received ECMO before their delivery. Overall survival after EXIT-to-ECMO was 64%. At 1-year follow-up, all survivors had weaned off supplemental oxygen, but 57% required diuretics and/or bronchodilators. The investigators concluded that the EXIT-to-ECMO procedure is associated with favorable survival rates and acceptable pulmonary morbidity in fetuses expected to have a poor prognosis under conventional management.

Congenital Heart Disease (CHD)

Araujo Júnior et al. completed a systematic review and meta-analysis to assess perinatal outcomes and intrauterine complications following fetal intervention for CHD. Outcome measures included fetal death, live birth, preterm delivery < 37 weeks' gestation and neonatal death. Intrauterine complications that were assessed included bradycardia requiring treatment and hemopericardium requiring drainage. Out of 2279 records identified in the database search, 29 studies (11 retrospective cohort and 18 case reports) were considered eligible for analysis. Fetal death after treatment of CHD by aortic valvuloplasty was reported in 3 studies, with a rate of 31%; after pulmonary valvuloplasty in 1 study, with a rate of 25%; after septoplasty in 1 study, with a rate of 14%; and after pericardiocentesis and/or pericardioamniotic shunt placement in 24 studies, with a rate of 29%. Bradycardia requiring treatment was reported after aortic valvuloplasty in 2 studies, with a rate of 52%; after pulmonary valvuloplasty in 1 study, with a rate of 44%; and after septoplasty in 1 study, with a rate of 27%. The authors concluded that current evidence on the effectiveness of prenatal intervention for CHD derives mostly from case reports and a few larger series; no study was randomized. Although the results of the meta-analysis are encouraging in terms of perinatal survival, they should be interpreted with caution when comparing with procedures performed after delivery (2016).

Pedra et al. (2014) reported results of a small case series of fetal cardiac procedures for various cardiac conditions (21 fetuses; 22 procedures). The procedures included atrial septostomy, fetal aortic valvuloplasty (FAV), pulmonary valvuloplasty, or a combination of aortic septostomy and FAV. The fetal clinical conditions consisted of critical aortic stenosis (AS) (n = 13), hypoplastic left heart syndrome (HLHS) and intact interatrial septum or small patent foramen ovale (n = 4), pulmonary atresia with intact ventricular septum (n = 1), and critical pulmonary stenosis (n = 3). A total of 91% of procedures (20 of 22) were considered successful. Two procedures, FAV and pulmonary valvuloplasty, failed. One fetus died and no maternal complications were reported. Long-term morbidity was frequent, and 12 fetal deaths eventually occurred.

A retrospective review was conducted of 100 patients who underwent FAV for severe mid-gestation AS with evolving HLHS from March 2000 to January 2013. The median gestational age at intervention was 23.8 weeks. Patients were categorized based on postnatal management as biventricular (BV) or HLHS. Eighty-eight fetuses were live-born, and 38 had a BV circulation (31 from birth, 7 converted after initial univentricular palliation). Left-sided structures, namely aortic and mitral valve sizes and left ventricular (LV) volume, were significantly larger in the BV group at the time of birth. After a median follow-up of 5.4 years, freedom from cardiac death among all BV patients was 96±4% at 5 years and 84±12% at 10 years, which was better than HLHS patients. There was no cardiac mortality in patients with a BV circulation from birth. All but 1 of the BV patients required postnatal intervention; 42% underwent aortic and/or mitral valve replacement. On most recent echocardiogram, the median LV end-diastolic volume z-score was +1.7 (range: -1.3, +8.2), and 80% had normal ejection fraction. The authors concluded that short- and intermediate-term survival among patients who underwent FAV and achieved a BV circulation postnatally is encouraging. However, morbidity still exists, and on-going assessment is warranted (Freud et al., 2014).

A total of 70 fetuses underwent attempted FAV for critical AS with evolving HLHS. The procedure was technically successful (increased flow across the valve) in 52 fetuses (74%). Forty-five of these resulted in a viable live birth. Relative to 21 untreated comparison fetuses, subsequent prenatal growth of the aortic and mitral valves, but not the

left ventricle, was improved after intervention. Nine pregnancies (13%) did not reach a viable term or preterm birth. Seventeen patients had BV circulation postnatally, 15 from birth. Larger left heart structures and higher left ventricular pressure at the time of intervention were associated with BV outcome. Technically successful FAV alters left heart valvar growth in fetuses with AS and evolving HLHS and, in a subset of cases, appeared to contribute to a BV outcome after birth. The authors note that FAV carries a risk of fetal demise. Further studies from well-designed clinical trials are needed to confirm these results (McElhinney et al., 2009).

Vida et al. (2007) retrospectively identified 32 neonates with a diagnosis of HLHS and intact or highly restrictive atrial septum who underwent left atrial decompression in utero or postnatally before surgery. Fourteen patients (44%) underwent fetal intervention, either atrial septoplasty (n = 9) or FAV (n = 5). The investigators concluded that prenatal decompression of the left atrium may be associated with greater hospital survival. Proposed effects of fetal intervention on lung pathology and longer-term survival require further study.

A 2018 NICE interventional procedures guideline states that current evidence on the safety and efficacy of percutaneous balloon valvuloplasty for fetal critical aortic stenosis is limited in quantity and the results are inconsistent. Therefore, this procedure should only be used in the context of research.

There are many ongoing clinical trials evaluating various types of IUFS for multiple conditions. Additional information is available at www.clinicaltrials.gov. (Accessed January 28, 2019)

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

The fetal interventions described in this policy are surgical procedures and not subject to FDA approval.

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GUIDELINE HISTORY/REVISION INFORMATION

Date	Action/Description

05/01/2019	• Reorganized policy template; simplified and relocated *Instructions for Use* and *Benefit Considerations* section
	• Updated coverage rationale; replaced language indicating "intrauterine fetal surgery (IUFS) is unproven and not medically necessary for treating the conditions [listed in the policy]" with "intrauterine fetal surgery (IUFS) is unproven and not medically necessary for treating *all other* conditions*, including but not limited to* [the conditions listed in the policy]"
	• Updated list of applicable CPT codes:
	  ○ Removed 59070
	  ○ Revised description for 59897
	• Updated supporting information to reflect the most current clinical evidence and references
	• Archived previous policy version MMG05.H

INSTRUCTIONS FOR USE

This Medical Management Guideline provides assistance in interpreting UnitedHealthcare 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 benefit plan. In the event of a conflict, the member specific benefit plan document governs. Before using this guideline, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Management Guideline is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare West Medical Management Guidelines 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.

Member benefit coverage and limitations may vary based on the member's benefit plan Health Plan coverage provided by or through UnitedHealthcare of California, UnitedHealthcare Benefits Plan of California, UnitedHealthcare of Oklahoma, Inc., UnitedHealthcare of Oregon, Inc., UnitedHealthcare Benefits of Texas, Inc., or UnitedHealthcare of Washington, Inc.