



# CIGNA HEALTHCARE COVERAGE POSITION

**Subject Transcatheter Closure of Septal Defects**

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## Hyperlink to Related Coverage Positions

### INSTRUCTIONS FOR USE

Coverage Positions are intended to supplement certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Positions are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Position. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Positions. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Positions and; 4) the specific facts of the particular situation. Coverage Positions relate exclusively to the administration of health benefit plans. Coverage Positions are not recommendations for treatment and should never be used as treatment guidelines. ©2007 CIGNA Health Corporation

## Coverage Position

**CIGNA HealthCare covers transcatheter closure as medically necessary for ANY of the following conditions:**

- **secundum atrial septal defect (ASD)**
- **patent ductus arteriosus (PDA)**
- **fenestrations following a Fontan procedure**
- **complex ventricular septal defect (VSD) when BOTH of the following criteria are met:**
  - The VSD is of significant size to warrant closure.
  - The patient is considered to be at high risk for standard transatrial or transarterial surgical closure.

**CIGNA HealthCare does not cover perventricular (transmyocardial) closure of ventricular septal defects (VSDs) because it is considered investigational, experimental or unproven.**

**CIGNA HealthCare does not cover transcatheter closure of patent foramen ovale (PFO) because there are not any PFO closure devices that have received U.S. Food and Drug Administration (FDA) approval for marketing. PFO closure devices are available only through an FDA Investigational Device Exemption (IDE). Transcatheter closure of PFO is therefore considered experimental investigational, or unproven.**

**CIGNA HealthCare does not cover transcatheter closure of ostium primum or sinus venosus atrial septal defects (ASDs) because it is considered experimental, investigational, or unproven.**

## General Background

Defects in the septal wall of the heart may cause abnormal ventricular volume and pressure load, atrial emptying, mixing of unoxygenated and oxygenated blood and inadequate systemic cardiac output. These abnormalities may result in cardiac enlargement, pulmonary hypertension, pulmonary vascular obstructive disease, tricuspid regurgitation, cardiac rhythm disturbances and stroke. Atrial and ventricular septal wall defects may be congenital or may be caused by increased intrathoracic pressure or myocardial infarction. Treatment of septal wall defects can range from medication to open heart surgical closure. Transcatheter closure of septal defects using implantable occlusive devices has been explored as an alternative to surgical interventions for repair. Transcatheter occlusion is accomplished via standard interventional cardiac catheterization techniques performed under conscious or unconscious sedation. The defect size is established by either angiogram or transthoracic or transesophageal echocardiography, and device size is selected accordingly.

### Atrial Septal Defect (ASD)

ASDs represent a communication between the left and right atria and account for 7–10% of all congenital heart defects. ASDs may be located at different sites in the septum and range in size from small to large. The three major types of ASDs, ostium secundum, ostium primum and sinus venosus, are named for their position in the atrial septum. Atrial septal defects result in left-to-right shunting of blood. Although approximately 20% of ASDs will close spontaneously in the first year or two of life, natural closure after age two is uncommon. Most patients with small defects experience few appreciable symptoms. Fatigue and shortness of breath are the most commonly reported complaints. The size of the defect in the atrial septum and the compliance of the right ventricle determine the pathophysiology of the defect. Moderate or large ASDs are associated with significant left-to-right shunting and increase in pulmonary blood flow. One percent of patients become symptomatic in the first year with an associated 0.1% mortality. There is a 25% lifetime risk of mortality in unrepaired ASDs. Risk factors associated with increased mortality from untreated ASDs include the development of pulmonary vascular obstructive disease (i.e., pulmonary arteries thicken from prolonged left-to-right shunting), right atrial or ventricular enlargement, tricuspid regurgitation, pulmonary hypertension, cardiac rhythm disturbances and stroke.

**Ostium Secundum ASDs:** Ostium secundum ASDs constitute 75–80% of all atrial septal defects and are located in the central portion of the septum (i.e., fossa ovalis). These defects are one of the most common cardiac malformations found in adults over the age of 40. Tissue may be completely deficient, or strands of tissue may cross the opening (fenestrated ASD). This ASD may close and be associated with mitral valve prolapse. Secundum ASDs are formed by excessive resorption of the septum primum or deficiency of the septum secundum.

Surgical repair has been considered the standard treatment for closure of secundum ASD. Surgical repair is generally performed by primary closure, pericardial patch or Gore-Tex patch (W.L. Gore & Associates, Inc., Flagstaff, AZ). Although perioperative mortality rates in most centers have approached zero, residual shunting incidence has been reported to be from 2–7.9% in long-term data (Du, 2002). Transcatheter closure of septal defects has been explored as an alternative because of reported advantages when compared to surgical closure, including fewer complications, avoidance of cardiopulmonary bypass and cardioplegia, shorter hospitalization, reduced need for blood products and less patient discomfort.

**U.S. Food and Drug Administration (FDA):** The Amplatzer® Septal Occluder (AGA Medical Corporation, Golden Valley, MN) received FDA approval through the PMA process on December 5, 2001, for the occlusion of atrial septal defects in secundum position and for patients who have undergone a fenestrated Fontan procedure and require closure of the fenestration. According to the FDA approval order, the Amplatzer system is indicated for patients who have echocardiographic evidence of ostium secundum atrial septal defect and clinical evidence of right ventricular volume overload (i.e., 1.5:1 degree of left-to-right shunt or right ventricle enlargement).

The Amplatzer system is a self-expanding double-disc centering device made of Nitinol wire mesh. The two discs are linked together by a short connecting waist corresponding to the size of the ASD. The discs and waist are filled with polyester fabric sewn with polyester thread.

**Literature Review:** Du et al. (2002) conducted a nonrandomized controlled trial in 29 pediatric cardiology centers comparing the safety, efficacy and clinical utility of ASD closure of secundum ASD using the Amplatzer device to surgical repair. A total of 442 patients were in the device closure group, and 154 were in the surgical group. For the device group, the presence of a distance of > 5 mm from the margins of the ASD to the coronary sinus, atrioventricular valves and right pulmonary vein was required. Exclusion criteria included primum ASDs, sinus venosus ASDs, and the presence of associated congenital cardiac anomalies requiring surgical repair. The authors reported success rates at discharge and at 12-month follow-up of 94.8% and 98.5%, respectively, for the device group and 96.1% and 100%, respectively, for the surgical group. The complication rate was 7.2% for the device group and 24% for the surgical group.

The presence of a sufficient rim of atrial tissue (at least 5 mm) surrounding the defect is considered one of the most important preselection criteria for catheter closure. Many of the studies that evaluated the efficacy of transcatheter closure of septal defects excluded patients with insufficient rims, as measured by transthoracic or transesophageal echocardiography. One small controlled study was designed to evaluate the safety of implanting the Amplatzer device in patients with insufficient rims. Du et al. (2002) compared outcomes of 48 patients with sufficient rims (> 5 mm), serving as the control group, to 23 patients with deficient rims (< 5 mm). Both groups underwent transcatheter closure with the Amplatzer device. Of the 23 patients with deficient rims, 74% had immediate complete closure compared to 92% with sufficient rims. At 24-hour and six-month follow-up, the complete closure rates were not significantly different between the two groups. While the results of this study were promising, the authors acknowledge that additional data are needed to assess the long-term safety and efficacy of performing this procedure on patients with insufficient rims.

Transcatheter closure of secundum ASDs with the Amplatzer device has been evaluated in several case series (Berger, et al., 1999; Chessa, et al., 2002; Fischer, et al., 2003). The consensus in these studies was that transcatheter closure is safe and effective in the majority of cases. Complications and complete closure rates were comparable to those seen with surgical closure, and transcatheter closure offered the advantages of less morbidity and shorter hospitalizations.

Although the indications for the procedure are the same as for surgical closure, the selection criteria are stricter in terms of defect size and surrounding rim tissue. This technique is generally precluded in patients with anomalous pulmonary venous connection or with proximity of the defect to the AV valves, coronary sinus or systemic venous drainage. Major complications occur in less than 1% of patients, and clinical closure is achieved in more than 80% of patients. Device closure of an ASD improves functional status in symptomatic patients and exercise capacity in asymptomatic and symptomatic patients, although long-term follow-up data is not yet available. Device closure of secundum ASDs percutaneously under fluoroscopy and transesophageal electrocardiography (TEE) or with intracardiac echo guidance is the therapy of choice when appropriate (Braunwald's Cardiology, 2005).

Interventional Procedure Guidance issued by the National Institute for Clinical Excellence (NICE) (2004) states that current evidence on the safety and efficacy of endovascular closure of atrial septal defects appears adequate to support the use of this procedure, provided that the normal arrangements are in place for consent, audit and clinical governance. The guidance also states that the procedure should be performed in units where there are arrangements for cardiac surgical support in the event of complications.

**Ostium Primum ASDs:** Ostium primum ASDs account for 15% of all ASDs and are located in the lower portion of the septum just above the atrioventricular valves. They are generally associated with a cleft in the anterior leaflet of the mitral valve and considered part of the atrioventricular septal defects group. Mitral regurgitation is common, and defect size does not typically decrease with time. Primum ASDs are formed when growth of the endocardial cushion is deficient.

**Sinus Venosus ASDs:** Sinus venosus or venous ASDs, which constitute 10% of all ASDs, occur at the junction of the superior vena cava and the right atrium. They are associated with partial anomalous pulmonary venous return, and defect size does not decrease over time. Sinus venosus ASDs are formed by incomplete septation of the upper portion of the atrial division.

Transcatheter closure is not an option for ostium primum and sinus venosus ASDs. These defects are located at the very lower and upper edges of the atrial septum, respectively, and are often associated with other valve abnormalities. The presence of these defects has typically constituted exclusion criteria in studies of transcatheter closure of ASDs. Surgical closure of ostium primum, sinus venosus, as well as secundum defects with unsuitable anatomy can be performed by primary suture closure or by using a pericardial or synthetic patch.

### **Patent Foramen Ovale**

Patent foramen ovale (PFO) is a variant of ostium secundum ASD that results from a persistent opening between the atrial septum primum and secundum at the location of the fossa ovalis. The foramen ovale allows fetal circulation to bypass the uninflated lungs in utero. This opening normally closes shortly after birth when pulmonary circulation is established. The presence of a patent foramen ovale is usually not clinically significant in healthy adults and usually not treated unless conditions such as pulmonary hypertension, chronic obstructive pulmonary disease or pulmonary embolism are present. These conditions may cause the right atrial pressure to be elevated, causing an increased potential for right-to-left shunting through the PFO. A thrombus in the right atrium could therefore be carried directly into the left atrium and create an embolus to the brain or coronary arteries

Antiplatelet therapy may be indicated for patients with PFO who have had a stroke or transient ischemic attack (TIA) with no other known cause of cerebral ischemia (i.e., cryptogenic stroke). Warfarin may be recommended for patients with other indications for oral anticoagulation, including patients with an underlying hypercoagulation state, or those with evidence of venous thrombosis. There is no clear evidence to demonstrate whether warfarin or aspirin is superior in preventing recurrent stroke or death. It is also unclear whether patients treated medically following a cryptogenic stroke are at increased risk for a subsequent stroke or death because of the presence of PFO. Transcatheter closure has been proposed as an alternative to medical therapy in patients with PFO associated with cryptogenic stroke (Messe, et al., 2004, reaffirmed 2007; Sacco et al., 2006)

**U.S. FDA:** On February 1, 2000, the CardioSEAL<sup>®</sup> Septal Occlusion System received FDA Humanitarian Device Exemption (HDE) approval for closure of a patent foramen ovale (PFO) in patients with recurrent cryptogenic stroke due to presumed paradoxical embolism through the patent foramen ovale and who have failed conventional drug therapy.

The Amplatzer<sup>®</sup> PFO Occluder received HDE approval from the FDA on April 5, 2002, for the nonsurgical closure of a PFO in patients with recurrent cryptogenic stroke due to presumed paradoxical embolism through a PFO and who have failed conventional drug therapy.

In order to receive HDE approval, a manufacturer must first be granted a Humanitarian Use Device (HUD) exemption by demonstrating that the device is designed to treat or diagnose a disease or condition that affects fewer than 4,000 people in the U.S. per year. Although data demonstrating the safety and probable clinical benefit are required for HDE approval, clinical trials evaluating the effectiveness of the device are not required. Following HDE approval, the hospital or health care facility institutional review board (IRB) must also approve the use of the device at that institution before the device may be used in a patient.

On August 14, 2006, the manufacturers of the Amplatzer PFO Occluder and the CardioSEAL Septal Occlusion System agreed to voluntarily withdraw their HDEs, effective October 31, 2006. The FDA had notified the manufacturers of its intent to formally propose to withdraw HDE approvals for these two devices because they no longer met the HDE criteria. The FDA determined that the target patient population described by the approved indication (i.e., patients with recurrent cryptogenic stroke due to presumed paradoxical embolism through a PFO and who have failed conventional drug therapy) is significantly in excess of 4,000 patients in the U.S. per year. These devices therefore are no longer eligible for HDE designation and no longer eligible for marketing under an HDE. Because of the larger number of patients eligible for these devices, the FDA concluded that a demonstration of reasonable assurance of both safety and effectiveness is required, as is the case with all class III (highest risk) devices not eligible for HDE status (FDA Information Sheet, Center for Devices and Radiological Health, Aug. 16, 2006).

Although the Amplatzer PFO Occluder and the CardioSEAL Septal Occlusion System will not be available for marketing after October 31, 2006, the devices will still be available to patients who meet the previously approved HDE indication through an FDA-approved Investigational Device Exemption (IDE). An IDE allows an investigational device to be used in a clinical study in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application submission to the FDA. A device being marketed through an IDE is not approved by the FDA or other appropriate regulatory agency to be lawfully marketed for the proposed use. An investigational device may also be available through an FDA compassionate use provision for a patient who does not meet the requirements for inclusion in clinical investigations, when the physician believes the device may provide a benefit in treating a serious disease or condition and no alternative treatments exist. The FDA uses its regulatory discretion to determine whether such investigational device use should occur. Prior FDA approval is needed before compassionate use occurs.

There are several clinical trials in progress comparing implantation of a PFO closure device to drug therapy. When one or more of these trials is completed, the FDA expects to review an associated PMA under expedited timelines in order to allow wider availability of devices that have been shown to be safe and effective. According to the FDA information sheet regarding HDE withdrawal, there are no new safety concerns regarding previously placed devices.

**Literature Review:** Hung et al. (2000) conducted a multicenter comparative case series evaluating the efficacy of different occlusion devices for the closure of PFO following paradoxical embolism. Data were collected for 63 patients following PFO closure with the Clamshell™, CardioSEAL or Buttoned devices at two centers. In the Clamshell (n=28) and CardioSEAL (n=13) groups, effective closure at the time of placement was achieved in 86% of patients, with moderate residual shunting occurring in two patients in the CardioSEAL group. Four recurrent embolic events and a device failure rate of 38% were reported.

Martin et al. (2002) reported on the immediate and long-term outcomes of 110 consecutive patients who underwent transcatheter closure of a PFO because of paradoxical embolism. Procedure success was defined as successful deployment of the device, and effective occlusion (no or trivial shunt after placement) was achieved in 100% of the patients. Data analysis showed a freedom from recurrent embolic events and re-intervention of 96% and 90% at one and five years, respectively.

Demkow et al. (2004) evaluated the short- and mid-term results of transcatheter closure of PFO in 32 consecutive patients with a history of cryptogenic ischemic stroke. The procedure was effective in all patients, and no complications were observed. During a mean follow-up period of 25.9 months (>12 months in 22 patients), no new neurological events were recorded. Control TEE was performed in 28 patients a mean 22.3 months after the procedure and confirmed the correct positioning of the occluder. A significant residual shunt was detected in two patients. One patient developed episodes of paroxysmal supraventricular tachycardia which were effectively resolved by radiofrequency ablation. The researchers concluded that transcatheter closure of PFO is safe, effective and devoid of side effects connected with extracorporeal circulation.

NICE Interventional Procedure Guidance (2004) states that current evidence suggests that there are no major safety concerns and that percutaneous closure of PFO for the prevention of cerebral embolic stroke is efficacious in achieving closure of the foramen. However, its efficacy in preventing future strokes has not been clearly shown.

Although several studies have demonstrated positive outcomes for transcatheter PFO closure, there are currently no closure devices with FDA approval to market, either through the HDE or PMA process. As stated above, devices previously available through an HDE are now available only through an IDE for investigational use in the context of a clinical trial.

### **Patent Ductus Arteriosus (PDA)**

The ductus arteriosus is the vessel leading from the bifurcation of the pulmonary artery to the aorta, just distal to the left subclavian artery. Under normal circumstances, this channel is open in the fetus and closes spontaneously during the first few days of life. PDA results from the failure of this duct to close following birth. It is a common finding in premature infants and progressively decreases in frequency with increasing gestational age. In premature infants with compromised respiratory status, closure may be

attempted using fluid restriction, diuresis, maintenance of good oxygenation, medications such as indomethacin or by surgical ligation. In full-term infants, surgical ligation and transection is generally indicated if heart failure occurs.

**U.S. FDA:** On May 14, 2003, the Amplatzer Duct Occluder and 180° Delivery System received FDA approval through the PMA process for the nonsurgical closure of patent ductus arteriosus (PDA).

**Literature Review:** Butera et al. (2004) conducted a case series (n=197) to analyze the safety and efficacy of percutaneous closure of PDA using the Amplatzer Duct Occluder in very young symptomatic children. Physical examinations and echocardiograms were performed before the surgery and at follow-up (three, six and twelve months) and yearly thereafter. No deaths or major complications occurred. Two patients experienced mild inguinal hematomas, and one patient had femoral artery thrombosis successfully treated with intravenous urokinase. The mean follow-up was 12.8 months. Patients with recurrent respiratory infections had no significant recurrences, and children who had failed to thrive had significantly increased growth. The authors concluded that in experienced hands, percutaneous closure of moderate to large PDA in very young symptomatic children is safe, effectively closes the PDA and solves clinical problems.

A multicenter case series (n=484) by Pass et al. (2004) reported initial and one-year efficacy and safety results of the USA Amplatzer ductal occluder (ADO) device trial. The ADO was not implanted in 45 patients because the PDA was too small or because of elevated pulmonary resistance. The ADO was successfully implanted in 435 of the 439 remaining patients. Angiographic demonstration of occlusion was seen in 329 (76%) of 435 patients, increasing to 384 (89%) of 433 patients on post-catheterization day one. Occlusion was documented in 359 (99.7%) of 360 patients at one year. There were two cases of partial left pulmonary artery occlusion after ADO implantation and no cases of significant aortic obstruction. The researchers concluded that moderate-to-large PDAs can be effectively and safely closed using the ADO device, with excellent initial and one-year results.

Interventional Procedures Guidance issued by the National Institute for Clinical Excellence (NICE) in 2004 states that current evidence on the safety and efficacy of endovascular closure of PDA appears adequate to support the use of this procedure.

The safety and efficacy of transcatheter device closure for ducts smaller than 8 mm has been established over the past 20 years, with complete ductal closure achieved in more than 85% of patients by one year with a mortality rate of less than 1%. Transcatheter closure has become the method of choice in centers with appropriate resources and experience. Although surgical closure has a marginally greater closure rate than device closure, the surgical mortality in adults is 1–3.5%, due to the presence of pulmonary arterial hypertension and difficult ductal morphology (e.g., calcified or aneurismal) frequently seen in adults. Surgical closure is therefore generally reserved for patients in whom the PDA is too large for device closure or centers without access to device closure (Braunwald's Heart Disease, 2005).

NICE Interventional Procedure Guidance (2004) states that current evidence on the safety and efficacy of endovascular closure of PDA appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. The guidance also states that the procedure should be performed in units where there are arrangements for cardiac surgical support in the event of complications.

The Amplatzer Duct Occluder is currently the only device to have received FDA approval for closure of PDA, although several additional devices have been in use and are in various stages of investigation. The Gianturco Coil is made of flexible loops of stainless steel with an attached mesh of Dacron fibers to enhance occlusion. The Gianturco-Grifka Vascular Occlusion Device consists of a nylon sack attached to an end-hole catheter. A wire is advanced through the catheter into the sack, and the wire coils filling the sack occlude the vessel and provide transmural pressure to maintain the sack position.

### **Fenestration Following Fontan Procedure**

The Fontan procedure is a palliation procedure that involves separating the pulmonary and systemic blood flows in patients with single ventricular defects. The technique reduces the mixing of unoxygenated and oxygenated blood by directing blood flow from the right atrium to the pulmonary artery, excluding the

ventricle from right-sided circulation. The procedure is intended to produce a normal workload on the ventricle. One component of this procedure involves leaving a hole or fenestration in the septum of the repaired section of the heart, allowing for some mixing of blood for patients who are unable to tolerate the change in venous pressure. The size of the fenestration varies, and smaller holes can close spontaneously. Some patients require the creation of larger holes and, in many of these patients, the fenestration will remain patent.

In patients with cyanosis in the setting of a fenestrated Fontan, surgical or preferably transcatheter closure of the fenestration can be attempted (Braunwald's Heart Disease, 2005). Postoperative closure of Fontan fenestrations using a test occlusion and subsequent permanent closure with an intracardiac device evolved based on growing experience with transcatheter techniques to close various intracardiac defects. Early and late closure after test occlusion has been reported to reduce mortality and morbidity after the Fontan procedure, especially in high-risk patients (Goff, et al., 2000).

**U.S. FDA:** The CardioSEAL Septal Occlusion System (Nitinol Medical Technologies, Inc., Boston, MA) received humanitarian device exemption (HDE) approval from the FDA on September 8, 1999, for the treatment of patients with complex single ventricle physiology who have undergone a fenestrated Fontan palliation procedure and required closure of the fenestration.

As stated above, the Amplatzer Septal Occluder received FDA approval through the PMA process on December 5, 2001, for the occlusion of secundum atrial septal defects and also for patients who have undergone a fenestrated Fontan procedure and require closure of the fenestration. According to the FDA approval order, the Amplatzer system is indicated for patients who have echocardiographic evidence of ostium secundum atrial septal defect and clinical evidence of right ventricular volume overload (i.e., 1.5:1 degree of left-to-right shunt or right ventricle enlargement).

**Literature Review:** The FDA PMA submission for the Amplatzer Septal Occluder included registry data that evaluated the safety and effectiveness in patients with fenestrated Fontan. According to the Summary of Safety and Effectiveness, the effectiveness of the device was demonstrated by results consistent with those obtained for treatment of ASD and by the primary efficacy at 12 months' follow-up. There was no need for additional surgical repair in the 32 patients. In addition, the adverse events rates at 12 months were within the protocol-defined acceptable limits. The mortality rate was zero, and the major adverse event rate was 4.2%.

Goff et al. (2000) published a multicenter registry study of patients who underwent catheter closure of a fenestrated Fontan with either the Clamshell (n=91) or CardioSEAL (n=63) device. All 63 patients who had their fenestrations treated with the CardioSEAL device achieved successful implantation. Late closure of the fenestration (at greater than six months after surgery) was followed by improved oxygenation, reduced need for anticongestive medication, and improved somatic growth at follow-up.

Because of the relative rarity of this condition, published studies that evaluate transcatheter closure for closure of fenestration following Fontan procedure are limited. There is sufficient evidence, however, to indicate that transcatheter septal occlusion is safe and effective for closure of a fenestration following a Fontan procedure in patients with single ventricle physiology.

### **Ventricular Septal Defects (VSDs)**

Congenital VSDs can occur in isolation and as one part of a combination of cardiac anomalies. The natural history of congenital VSDs may include spontaneous closure, development of pulmonary vascular obstruction, right ventricle outflow tract obstruction, aortic regurgitation, infective endocarditis, cardiomegaly, congestive cardiac failure and death in infancy. Many infants experience growth failure. Management of VSDs is largely dependent on the size and pathophysiology of the defect. Children with defects considered tiny or small with no associated cardiovascular symptoms typically receive well childcare and prophylaxis with antibiotics when clinically appropriate. Patients with large defects and pulmonary hypertension are those at greatest risk of developing pulmonary vascular obstruction as well as respiratory infections. Large defects require correction early in life when pulmonary vascular disease is still reversible. Medical treatment may include diuretics, digitalis, and treatment of respiratory infections, as well as increased caloric density of feedings.

Acquired VSDs can occur post-myocardial infarction (MI), as well as following multiple trauma. It has been estimated that there is an 80–90% mortality rate within the first two months of the occurrence of a post-MI VSD with medical treatment alone. Rupture of the intraventricular septum is an uncommon but often fatal complication of acute MI or traumatic injury. Treatment involves surgical closure of the defect.

Surgical closure of congenital and acquired ventricular septal defects is associated with high surgical morbidity and mortality and is generally not recommended for patients with normal pulmonary arterial pressures with small shunts. Surgery is indicated when there is a moderate to large left-to-right shunt with a pulmonary to systemic flow ratio of greater than 1.5:1 or 2.0:1, in the absence of prohibitively high levels of pulmonary vascular resistance. Transcatheter closure has been proposed as an alternative because of the high morbidity and mortality associated with surgical closure of VSDs.

**U.S. FDA:** The CardioSEAL® Septal Occlusion System with QuikLoad™ received FDA approval through the Premarket Approval (PMA) process on December 5, 2001, for use in patients with complex VSDs of significant size to warrant closure and who are considered at high risk for standard transatrial or transarterial surgical closure based on anatomical conditions and/or overall medical condition. According to the FDA approval order, high-risk anatomical factors for transatrial or transarterial surgical closure include:

- patients requiring a left ventriculotomy or an extensive right ventriculotomy
- patients with a failed previous VSD closure
- patients with multiple apical and/or anterior muscular VSDs ("Swiss cheese septum")
- patients with posterior apical VSDs covered by trabeculae

The CardioSEAL system consists of two components: the CardioSEAL permanent implant, constructed of a metal framework to which polyester fabric is attached, and the delivery catheter, a coaxial polyurethane catheter designed to facilitate attachment, loading, delivery and deployment of the occluder to the defect.

The Amplatzer Muscular VSD Occluder received FDA approval through the PMA process on September 7, 2007. The device is indicated for use in patients with a complex VSD of significant size to warrant closure (large volume, left to right shunt, pulmonary hypertension and/or clinical symptoms of congestive heart failure) who are considered to be at high risk for standard transatrial or transarterial surgical closure based on anatomical conditions and/or based on overall medical condition. The approval letter lists the same high-risk anatomical factors included in the approval letter for the CardioSEAL Septal Occlusion System with QuikLoad™, listed above. The device consists of a delivery system and a permanent implant. The implant is a self-expandable double disc made from wire mesh and polyester fabric.

**Literature Review:** Unpublished data from a prospective uncontrolled trial conducted at Children's Hospital in Boston, MA were submitted to the FDA during the approval process for the CardioSEAL device. The trial included patients with VSDs as well as several other types of defect. A total of 57 VSD patients were studied, with 84% of the patients reported to have successful closure and shunt reduction at six months. The CardioSEAL Septal Occlusion System with QuikLoad is currently the only FDA-approved device for transcatheter closure of VSDs, although other devices such as the Amplatzer VSD Occluder and the STARFlex device are being investigated.

Chessa et al. (2002) reported the combined preliminary experience of two cardiac centers in the transcatheter closure of both congenital and acquired VSDs using the Amplatzer device. A total of 32 patients underwent attempted VSD closure. The study included 19 patients with congenital defect, 12 with post-MI defects, and one had acquired VSD following surgical repair of hypertrophic cardiomyopathy. The device was successfully implanted in 30 of 32 patients, but only 16 had complete closure, and 13 had residual shunting. Among the 30 implanted patients, three died in the hospital, and two died within a month of discharge. Follow-up data was reported up to 29 months post-procedure.

Thanopoulos et al. (2003) evaluated the efficacy of the Amplatzer device in closing perimembranous VSDs in a small case series (n=10). There was no residual shunt in nine of ten patients. A trivial residual shunt that was noted in one patient disappeared at the three-month follow-up. Three patients developed transient complete left bundle branch block. The authors concluded that the Amplatzer device appears to

be promising, but further studies are required to document its efficacy, safety, and long-term results in a larger patient population.

Holzer et al. (2004) published registry data evaluating closure of muscular ventricular septal defects using the Amplatzer VSD Occluder. Data was collected from 83 procedures involving 75 patients who underwent an attempt at percutaneous device placement. The device was implanted successfully in 72 of 83 procedures. In 17 of 83 procedures, multiple devices were implanted (i.e., 2–3). Procedure-related major complications occurred in eight of 75 patients. Device embolization occurred in two patients and cardiac perforation in one patient. There were two procedure-related deaths. The 24-hour post-procedural complete closure rate was 47.2%, increasing to 69.6% at six months and 92.3% at 12 months. The authors concluded that device closure using the Amplatzer device should be considered an important alternative to the surgical approach in treating congenital muscular VSDs, but acknowledge that because of study limitations, including lack of randomization and incomplete follow-up data, long-term conclusions cannot be made.

Thanopoulos and Rigby evaluated the Amplatzer VSD Occluder in the treatment of muscular ventricular septal defects in a series of 30 patients aged four months to 16 years. The stretched diameter of the defects ranged from 6–14 mm. The communication was completely occluded in 28 of 30 patients (93% closure rate). One four-month-old patient with sustained complete left bundle branch block after the procedure went on to develop complete heart block one year later. No other complications were observed during a mean follow-up of 2.2 years (range 0.25–4.5 years). The authors concluded that the Amplatzer VSD Occluder is an efficient prosthesis that can be safely used in the majority of patients with a single muscular VSD.

A Phase I trial evaluated transcatheter closure using the Amplatzer VSD Occluder (Fu, et al., 2006) in patients with perimembranous VSDs. The attempt to place the device was successful in 32 (91%) patients. The complete closure rate by echocardiography at ten minutes, 24 hours, one month and six months was 47% (15/32), 63% (20/32), 78% (25/32) and 96% (27/28), respectively. Three patients (8.6%) had serious adverse events of complete heart block, peri-hepatic bleeding, and rupture of tricuspid valve chordae tendinae. The authors concluded that transcatheter closure of a perimembranous ventricular septal defect is technically feasible and seems safe enough in children over eight kg in weight to warrant continuation of clinical trials to assess the long-term safety and efficacy.

Arora, et al. (2004) reported results of a series of 149 patients, age three to 28 years, who underwent transcatheter closure of congenital VSD using various devices. Device deployment was achieved in all 50 of the patients with trabecular muscular defects. The Rashkind umbrella device was deployed in two patients and the Amplatzer VSD Occluder was used in 48 patients. No patients had residual shunt, new aortic regurgitation, or tricuspid regurgitation. Transient complete heart block after 24 hours was seen in one patient. On follow-up at two to 90 months, the device was in position in all patients. The authors concluded that transcatheter closure of muscular VSD is safe and efficacious, and should be considered as a procedure of choice as an alternative to surgery that avoids cardiopulmonary bypass.

Masura et al. (2005) conducted a case series to evaluate the Amplatzer membranous septal occluder in 186 patients age 3–51 years (average age 15.9 years) with an average weight of 43.5 kg. Patients were divided into three groups: single defects without aneurysm; single defects with aneurysm; and multiple defects with aneurysm. Immediate closure rates achieved in the three groups were 90%, 98%, and 89%, respectively. Complete closure rates at one year were 100%, 98%, and 89%, respectively. Complications included left anterior hemiblock, complete right bundle branch block, and incomplete right bundle branch block. Two patients developed complete heart block following the procedure but converted to sinus rhythm with left anterior hemiblock. The authors stated that these conduction abnormalities are comparable to those seen with surgery, but long-term follow-up studies are needed to determine late arrhythmia disturbances. The authors also recommended prospective studies of patients after surgery and transcatheter treatment of VSD.

Interventional Procedure Guidance issued by NICE (2006) states that current evidence on the safety and efficacy of endovascular closure of perimembranous VSD appears adequate to support the use of this procedure, provided that the normal arrangements are in place for consent, audit and clinical governance. The NICE guidance also stated that patient selection is important, especially in children and

asymptomatic patients, and that the procedure should only be undertaken in specialist pediatric cardiology units with on-site surgical facilities.

Butera et al. (2007) evaluated the safety and efficacy of transcatheter closure of perimembranous VSD in 104 patients who were treated between 1999 and 2006. The inclusion criteria were clinical and/or echocardiographic evidence of a significant left-to-right shunt through a perimembranous VSD. Two Amplatzer devices were used: the muscular VSD occluder, and the perimembranous VSD occluder. The latter device has not yet received FDA approval. The mean age at closure was 14 years. The device was successfully placed in 100 patients (96.2%). The total occlusion rate was 47% at the completion of the procedure and increased to 84% at discharge and 99% at follow-up. Early complications occurred in 13 patients (11.5%), but were transient in 11 patients. The median follow-up was 38 months. Complete atrioventricular (AV) block requiring pacemaker implantation occurred in six patients—two in the early phase and four during the follow-up period. The authors stated that the only variable that was significantly associated with complete AV block was age at the time of the procedure; all patients who experienced this complication were less than six years old ( $p=0.028$ ).

The use of a perventricular approach, also referred to as a transmyocardial approach, has been explored as an alternative to the transcatheter approach for VSD closure. This hybrid approach has been investigated in the treatment of patients for whom transcatheter is challenging, including small infants and patients with poor vascular access. Bacha et al. (2007) described a perventricular hybrid approach, combining surgical and interventional techniques, utilized in a series of 12 patients with muscular VSD. Using a sternotomy or subxyphoid approach, the right ventricle free wall was punctured under transesophageal echocardiography guidance. A guide wire was introduced across the largest defect, and a short delivery sheath was positioned in the left ventricle cavity. An Amplatzer muscular VSD occluder was deployed across the VSD. Cardiopulmonary bypass was required only for repair of concomitant lesions. At a median follow-up of 12 months, all patients were asymptomatic, and two patients had mild residual ventricular level shunts.

A perventricular approach was also reported in five of 55 patients included in the first report of the multicenter CardioSEAL VSD registry. The registry was created following FDA approval of the CardioSEAL VSD Occluder in order to track the device's safety in closing high-risk, complex, muscular VSDs. The five patients who were treated with perventricular implantation all weighed  $\leq$  seven kg. Four of these procedures were reported to be successful by the implanting center. One perventricular implant failed because the right ventricular arms of the device protruded the right ventricular free wall (Lim, et al., 2007).

Transcatheter closure of VSDs is a complex and challenging procedure that requires technical expertise and precise delineation of the defect and its relation to other cardiac structures. Chordae tendinae, aortic and tricuspid valves, a high pressure in the left ventricle, and disparity of the interventricular tissue are obstacles to successful device attachment. Complications include ventricular arrhythmias and conduction delays (e.g., complete heart block, bundle branch block), and new aortic or tricuspid regurgitation (Arora, et al., 2002; Hein, et al., 2005; NICE, 2006).

Several case studies have demonstrated successful short- and mid-term outcomes of transcatheter closure of ventricular septal defects. Given the complexity, potential for clinically significant complications, and lack of long-term outcomes, however, this technique should only be considered in carefully selected patients. Transcatheter closure of VSDs may be a reasonable alternative to surgical closure with cardiopulmonary bypass in patients with a VSD of significant size to warrant closure and who are considered to be at high risk for standard transatrial or transarterial surgical closure. There is insufficient evidence in the published medical literature to demonstrate the safety and efficacy of perventricular (transmyocardial) closure of VSD. In addition, no devices have received FDA approval for this application.

## Summary

Transcatheter closure has been shown to be a safe and effective alternative for closure of septal defects in selected patients who require closure of ostium secundum atrial septal defects (ASDs), patent ductus arteriosus (PDA), and for patients who require fenestration closure following the Fontan procedure. There is also sufficient evidence to demonstrate that this technique is a reasonable alternative for carefully selected patients with a ventricular septal defect (VSD) of significant size to warrant closure and who are

considered to be at high risk for standard transatrial or transarterial surgical closure. Long-term outcome data for transcatheter closure of ventricular septal defects is needed, however, prior to broader application of this technique. There is insufficient evidence in the published medical literature to demonstrate the safety and efficacy of perventricular (transmyocardial) VSD closure.

Although several studies have demonstrated positive outcomes for transcatheter patent foramen ovale (PFO) closure, there are currently no closure devices with FDA approval to market. Devices for PFO closure are available only through an Investigational Device Exemption (IDE) for investigational use in the context of a clinical trial or through an FDA compassionate use provision for patients who do not meet the criteria for inclusion in a clinical trial.

There is insufficient evidence in the published medical literature to demonstrate the safety and efficacy of transcatheter closure for ostium primum or sinus venosus ASDs.

## Coding/Billing Information

**Note:** This list of codes may not be all-inclusive.

### Covered when medically necessary:

CPT <sup>®</sup> * Codes	Description
37204	Transcatheter occlusion or embolization (eg, for tumor destruction, to achieve hemostasis, to occlude a vascular malformation), percutaneous, any method, non-central nervous system, non-head or neck
93580	Percutaneous transcatheter closure of congenital interatrial communication (i.e., Fontan fenestration, atrial septal defect) with implant
93581	Percutaneous transcatheter closure of a congenital ventricular septal defect with implant

HCPCS Codes	Description
	No specific codes

ICD-9-CM Diagnosis Codes	Description
429.71	Acquired cardiac septal defect
745.2	Tetralogy of Fallot
745.4	Ventricular septal defect
745.5	Ostium secundum type atrial septal defect (patent or persistent foramen ovale, ostium secundum, atrium secundum defect, fossa ovalis)
747.0	Patent ductus arteriosus

### Experimental/Investigational/Unproven/Not Covered:

CPT <sup>®</sup> * Codes	Description
0166T	Transmyocardial transcatheter closure of ventricular septal defect, with implant; without cardiopulmonary bypass
0167T	Transmyocardial transcatheter closure of ventricular septal defect, with implant; with cardiopulmonary bypass

HCPCS Codes	Description
	No specific codes

ICD-9-CM Diagnosis Codes	Description
	Multiple/varied

\*Current Procedural Terminology (CPT®) © 2006 American Medical Association: Chicago, IL.

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