



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Transcatheter Closure of Septal Defects

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Table of Contents

Coverage Policy	1
General Background	2
Coding/Billing Information	10
References	11
Policy History	15

Hyperlink to Related Coverage Policies

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Coverage Policy

CIGNA covers transcatheter closure with a U.S. Food and Drug Administration (FDA)-approved device used according to FDA labeling as medically necessary for ANY of the following conditions:

- secundum atrial septal defect (ASD)
- patent ductus arteriosus (PDA)
- fenestration 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 individual is considered to be at high risk for standard transatrial or transarterial surgical closure.

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

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

General Background

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. 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). Ostium primum ASDs account for 15% of all ASDs and are located in the lower portion of the septum just above the atrioventricular valves. Sinus venosus or venous ASDs, which constitute 10% of all ASDs, occur at the junction of the superior vena cava and the right atrium. Moderate or large ASDs may be associated with significant left-to-right shunting and increase in pulmonary blood flow, and right ventricular volume overload. 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. Transcatheter closure using implantable occlusive devices has evolved as an alternative to open surgical intervention in selected patients with secundum septal defects. 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.

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 GORE HELEX[™] Septal Occluder (W.L. Gore & Associates, Flagstaff, AZ) received FDA approval through the PMA process on August 11, 2006, for the percutaneous transcatheter closure of ostium secundum atrial septal defects.

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.

Transcatheter closure of secundum ASDs 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, 2007).

Interventional Procedure Guidance issued by the National Institute for Clinical Excellence (United Kingdom) in 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.

Patent Foramen Ovale (PFO)

The foramen ovale, a remnant of the fetal circulation, is a tunnel-like space between the overlying septum secundum and septum primum. In fetal life, this interatrial communication directs blood flow from the umbilical vein to the left atrium. After birth, the left atrial pressure increases and the valve to the fossa ovalis closes. In approximately 25% of people, however, this fusion is not complete. This persistent communication is a variant of atrial septal defect (ASD), but differs from ASD in morphology and associated signs and symptoms. With ASD an actual hole exists between the left and right atria. This defect, especially when large, may result in significant left-to-right shunting and right ventricular volume overload, as described above. The flap-like opening seen with PFO however, is usually not clinically significant in healthy adults, and is generally 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. PFOs have been scrutinized for their implication in the mechanism of cryptogenic stroke (i.e. stroke with no other known cause of cerebral ischemia). Although basic principles linking PFO and stroke are plausible, this link has not been definitively established. It has been proposed that PFOs may serve as either a conduit for paradoxical embolization from the venous side to the systemic circulation, or as a point of origin for thrombus formation because of their tunnel-like structure and tendency for stagnant flow. A coordinated series of events is necessary for a paradoxical embolism through a PFO to occur, however. Therefore, even in patients with a history of cryptogenic stroke, the risk of recurrence may not be high (Libby: Braunwald's Heart Disease, 2007; Almekhlafi et al., 2009)

Antiplatelet therapy may be indicated for patients with PFO who have had a cryptogenic stroke or transient ischemic attack (TIA). 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, and has also been evaluated for treatment of patients with PFO and migraine (Messe, et al., 2004, reaffirmed 2007; Sacco et al., 2006, Valente and Rhodes, 2007)

U.S. Food and Drug Administration (FDA): No FDA-approved PFO closure devices have been available to market in the United States since October 31, 2006. Two devices had previously received FDA Humanitarian Device Exemption (HDE) approval. The CardioSEAL[®] Septal Occlusion System (Nitinol Medical Technologies, Inc., Boston, MA) had received FDA HDE approval on February 1, 2000 for closure of a 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[®] PFO Occluder (AGA Medical Corporation, Golden Valley, MN) had received HDE approval 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).

Since October 31, 2006, the Amplatzer PFO Occluder and the CardioSEAL Septal Occlusion System have been available in the United States only 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.

In 2007, the FDA convened a meeting of the Circulatory System Devices Panel (CSDP) to address several issues regarding PFO closure devices, and issued the following recommendations:

- Randomized controlled trials of PFO closure to prevent recurrent stroke are required.
- A “proof of principle” trial with pooled data demonstrating that PFO closure does prevent recurrent stroke could allow this question to be answered in a timely fashion, if sponsors are amenable to cooperating and sharing data. “Proof of device” trials demonstrating that an individual device effectively closes a PFO could be done separately.
- “Off-label” closure should be discouraged. Enrollment in ongoing trials should be encouraged.
- Patients and physicians should be educated about the lack of evidence of benefit of closure and the need for completion of trials. (Slottow et al., 2007)

Literature Review: Almedhlafi et al. (2009) conducted a systematic review and meta-analysis of the literature to estimate the absolute risk of recurrent cerebrovascular events in medically treated patients with PFO, and to evaluate their relative risk of recurrent events compared to patients without a PFO. Of 15 identified eligible studies, four included a non-PFO comparison group. In these four studies, the pooled relative risk of recurrent ischemic stroke or TIA in patients with vs. without a PFO was 1.1. For ischemic stroke alone, the absolute relative risk was 0.8. The absolute rate for recurrent events in all 15 studies was also calculated. The pooled absolute rate of recurrent ischemic stroke or TIA in patients with PFO was 4.0 events per 100 person years, and the rate of recurrent ischemic stroke alone was 1.6 events per 100 person years. The authors concluded that the available evidence does not support an increased relative risk of recurrent ischemic events in those with vs. without a PFO, and that PFO closure in these patients cannot be recommended until the results of ongoing clinical trials are reported.

Harms et al. (2007) conducted a case series to evaluate clinical outcomes and closure status following transcatheter PFO closure for prevention of recurrent stroke (n=237). The duration of follow-up was 568 ± 364 days. There were six deaths unrelated to the procedure or the presence of PFO, and one death due to a new neurologic event. Eight of 237 patients (3.4%) experienced clinically and radiographically confirmed strokes after PFO closure. All eight patients were taking aspirin at the time of recurrent stroke; two were taking clopidogrel and aspirin, and three were taking warfarin and aspirin. There was a significant difference in the rate of recurrent stroke based on age (≤ 55 years, 1.4%; > 55 years, 6.6%; $P=0.03$). In the overall group, three devices were explanted due to malalignment and large, persistent right-to-left shunt that required surgical closure. Complete closure or minimal residual right-to-left shunting was achieved in 66% of patients.

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.

Transcatheter closure of PFO has also been evaluated in the treatment of migraine. Migraine with aura has been associated with PFO and with other causes of right-to-left shunts. Dowson et al. (2008) conducted a prospective, double-blind, randomized controlled trial to evaluate the effectiveness of PFO closure in patients with migraine with aura who experienced frequent migraine attacks, had failed \geq two classes of prophylactic treatments, and had moderate to large right-to-left shunts consistent with the presence of PFO. Patients were randomized to transcatheter closure with the STARFlex implant (NMT Medical, Inc., Boston MA) (n=74) or to a sham procedure (n=73). The primary efficacy endpoint was migraine headache cessation 91–180 days after the procedure. There was no significant difference in the primary outcome between the two groups; in the treatment group, 3 of 74 patients experienced headache cessation, compared to 3 of 73 patients in the sham group.

Schwedt et al. (2008) conducted a systematic review to evaluate the association of PFO and migraine and to assess the effect of PFO closure on migraine. Six retrospective studies met the inclusion criteria for the effect of PFO closure on migraine. The authors stated that the low-to-moderate grade of evidence from observational studies supports an apparent association between PFO and migraine, and that although PFO closure seemed to have a favorable effect on migraine patterns, the very low grade of available evidence to support this association precludes definitive conclusions.

Interventional Procedure Guidance issued by the National Institute for Clinical Excellence (NICE) (United Kingdom) in 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. As detailed above in the U.S. Food and Drug Administration (FDA) section, there are currently no FDA-approved devices for transcatheter closure of PFO.

Professional Societies/Organizations: A science advisory on percutaneous device closure of patent foramen ovale for secondary stroke prevention was issued by the American Heart Association/American Stroke Association and the American College of Cardiology, and was affirmed by the American Academy of Neurology (O’Gara et al., 2009). According to the advisory, the optimal therapy for prevention of recurrent stroke or transient ischemic attack in patients with cryptogenic stroke and patent foramen ovale has not been defined. Although a strong association between patent foramen ovale and cryptogenic stroke has been suggested by numerous observational studies, a causal relationship has not been convincingly established for the majority of affected patients. The advisory further states:

“The choice between medical therapy and percutaneous device closure has been the subject of intense debate over the past several years, albeit one that has not been adequately informed by randomized, prospective clinical trial data to permit an objective comparison of the relative safety and efficacy of these respective approaches. Enrollment in clinical trials has lagged considerably despite frequent calls for participation from the US Food and Drug Administration and major professional societies. Completion and peer review of ongoing trials are critical steps to establish an evidence base from which clinicians can make informed decisions regarding the best therapy for individual patients. The present advisory strongly encourages all clinicians involved in the care of appropriate patients with cryptogenic stroke and patent foramen ovale—cardiologists, neurologists, internists, radiologists, and surgeons—to consider referral for enrollment in these landmark trials to expedite their completion and help resolve the uncertainty regarding optimal care for this condition.”

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. Food and Drug Administration (FDA): On May 14, 2003, the Amplatzer Duct Occluder and 180° Delivery System (AGA Medical Corporation, Golden Valley, MN) 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 device trial. The device was not implanted in 45 patients because the PDA was too small or because of elevated pulmonary resistance. The Amplatzer occluder 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 Amplatzer duct occluder, 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 (Libby: Braunwald's Heart Disease, 2007).

NICE Interventional Procedure Guidance (United Kingdom) published 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 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.

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.

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.

U.S. Food and Drug Administration (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 Defect (VSD)

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. 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. Surgical closure of congenital and acquired ventricular septal defects is associated with high surgical morbidity and mortality. Transcatheter closure has evolved as a less invasive alternative to surgical closure of VSDs.

U.S. Food and Drug Administration (FDA): The CardioSEAL[®] Septal Occlusion System with QuikLoad[™] (Nitinol Medical Technologies, Inc., Boston, MA) 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

A modified version of the CardioSEAL device, to be marketed under the trade name STARFlex® Septal Occlusion System, received FDA PMA approval on March 5, 2009. The device as modified is indicated for use in patients with a complex ventricular septal defect of a significant size to warrant closure but that, based on location, cannot be closed with standard transatrial or transarterial approaches.

The Amplatzer Muscular VSD Occluder (AGA Medical Corporation, Golden Valley, MN) 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.

Literature Review: 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 ($p=0.028$).

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.

Thanopoulos and Rigby (2005) 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.

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.

Interventional Procedure Guidance issued by the National Institute for Clinical Excellence (NICE) (United Kingdom) in 2004, updated in 2010, 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 states that patient selection is important, especially in children and asymptomatic patients, and that for children, the procedure should only be undertaken in specialized pediatric cardiology units. For all patients, the procedure should only be undertaken by cardiologists training in the technique, with access to emergency cardiac surgery by a surgeon experienced in the treatment of congenital heart disease.

Perventricular/Transmyocardial Closure of Ventricular Septal Defects: The use of a perventricular approach, also referred to as a transmyocardial approach, has been explored as an alternative to the transcatheter approach for ventricular septal defect (VSD) closure. This hybrid approach has been investigated in the treatment of patients for whom transcatheter closure is challenging, including small infants and patients with poor vascular access. A perventricular approach was 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).

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.

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

Moderate or large atrial septal defects in secundum position may be associated with significant left-to-right shunting, right heart dilation, or volume overload. Transcatheter closure of these defects has been shown to be a safe and effective alternative to surgical intervention in selected patients when the defect shows no signs of spontaneous closure.

Transcatheter closure has also been shown to be an effective alternative for closure of 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.

A paradoxical embolism that passes through a patent foramen ovale (PFO) has been associated with cryptogenic stroke, although a direct causal relationship has not been established between PFO and cryptogenic stroke. A high rate of recurrence of cerebrovascular events has not been demonstrated in patients with PFO who have experienced a cryptogenic stroke or TIA. This is likely due to the fact that a coordinated series of events is necessary for a paradoxical embolism to occur. Randomized controlled trials are needed to definitively determine whether PFO closure prevents recurrent stroke. In addition, 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 for treatment of secundum atrial septal defect, patent ductus arteriosus, or fenestration following a Fontan procedure (transcatheter closure is experimental, investigational or unproven and not covered for treatment of patent foramen ovale [PFO]):

CPT [®] * Codes	Description
93580 [†]	Percutaneous transcatheter closure of congenital interatrial communication (i.e., Fontan fenestration, atrial septal defect) with implant

ICD-9-CM Diagnosis Codes	Description
745.5	Ostium secundum type atrial septal defect-
747.0	Patent ductus arteriosus

Transcatheter closure is experimental, investigational or unproven and not covered for the following diagnoses:

ICD-9-CM Diagnosis Codes	Description
745.61	Ostium primum defect
745.8	Other bulbus cordis anomalies and anomalies of cardiac septal closure

Covered when medically necessary for treatment of ventricular septal defect:

CPT [®] * Codes	Description
93581	Percutaneous transcatheter closure of a congenital ventricular septal defect with implant

ICD-9-CM Diagnosis Codes	Description
745.2	Tetralogy of Fallot
745.4	Ventricular septal defect

Experimental/Investigational/Unproven/Not Covered:

CPT [®] * 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

ICD-9-CM Diagnosis Codes	Description
	All codes

*Current Procedural Terminology (CPT®) © 2010 American Medical Association: Chicago, IL.

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	11/15/2007	0011	Transcatheter Closure of Septal Defects

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