

MEDICAL POLICY – 2.02.09

Closure Devices for Patent Foramen Ovale and Atrial Septal Defects

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RELATED MEDICAL POLICIES:

None

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Introduction

The heart's two upper chambers are called atria. The septum is the thin wall of tissue that separates the atria. Sometimes there may be a congenital heart defect in which there is a hole in the septum between the two atria. This is called an atrial septal defect. Atrial septal defects may not cause any problems and might not even be diagnosed until adulthood. Larger atrial septal defects may cause problems and may need to be closed.

One way to treat an atrial septal defect is to use a catheter. A catheter is a long, thin tube which is threaded through a blood vessel in the groin to the heart. Once the catheter is in the correct location, a small device is put in place to seal the opening between the atria. This policy discusses when a catheter may be considered medically necessary to treat atrial septal defects.

The foramen ovale is an opening in the septum between the two atria that is normally found in a baby before it is born. This opening usually closes soon after birth. If a foramen ovale doesn't automatically close after the baby is born, it is called a patent foramen ovale (PFO). For most people a patent foramen ovale does not cause problems. In the small subset of people who have had a stroke where the cause is uncertain, using a new device to close the PFO may decrease the risk of a second stroke.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

FDA approved devices	Medical Necessity
Atrial septal defects (ASD) closure devices: <ul style="list-style-type: none"> Amplatzer Septal Occluder GORE CARDIOFORM Septal Occluder 	<p>Transcatheter closure of secundum atrial septal defects may be considered medically necessary when using a US Food and Drug Administration approved device according to the labeled indications, including the following:</p> <ul style="list-style-type: none"> Echocardiographic evidence of ostium secundum atrial septal defect is present <p>AND either ONE of the following:</p> <ul style="list-style-type: none"> Clinical evidence of right ventricular volume overload (i.e., 1.5:1 degree of left-to-right shunt or right ventricular enlargement) is present; OR Clinical evidence of paradoxical embolism is present (see Definition of Terms). <p>Transcatheter closure of secundum atrial septal defects is considered investigational for all other indications not meeting criteria outlined above.</p>
Patent foramen ovale (PFO) closure devices: <ul style="list-style-type: none"> AmplatzerPFO Occluder GORE CARDIOFORM Septal Occluder 	<p>Percutaneous transcatheter closure of a patent foramen ovale (PFO) may be considered medically necessary when using a US Food and Drug Administration approved device to reduce the risk of recurrent ischemic stroke when ALL of the following criteria are met:</p> <ul style="list-style-type: none"> The individual is between the ages of 18 and 60 Diagnosed with PFO with a right-to-left interatrial shunt confirmed by echocardiography with at least ONE of the following characteristics:

FDA approved devices	Medical Necessity
	<ul style="list-style-type: none"> ○ PFO with large shunt (defined as >30 microbubbles in the left atrium within 3 cardiac cycles, after opacification of the right atrium); OR ○ PFO associated with atrial septal aneurysm on transesophageal examination (septum primum excursion >10 mm) • Documented history of a cryptogenic ischemic stroke due to a presumed paradoxical embolism, as determined by the following: <ul style="list-style-type: none"> ○ A neurologist and cardiologist agree the stroke is cryptogenic ○ Evaluation has ruled out other identifiable cause of stroke, including large vessel atherosclerotic disease and small vessel occlusive disease AND • None of the following are present: <ul style="list-style-type: none"> ○ Uncontrolled vascular risk factors, including uncontrolled diabetes or uncontrolled hypertension ○ Other sources of right-to-left shunts, including an atrial septal defect and/or fenestrated septum ○ Active endocarditis or other untreated infections ○ Inferior vena cava filter

Documentation Requirements

The individual's medical records submitted for review should document that medical necessity criteria are met. The record should include clinical documentation of:

- Diagnosis/condition
- History and physical examination documenting the severity of the condition
- Results and/or reports from prior imaging or testing completed
- Any prior procedures
- Name of device to be used for closure

Coding

Code	Description
CPT	
93580	Percutaneous transcatheter closure of congenital interatrial communication (i.e., Fontan fenestration, atrial septal defect) with implant

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Diagnosing the Presence of Right-To-Left Shunt on Transthoracic Echocardiogram

The timing of bubble appearance in the left heart is important in making a correct shunt diagnosis (intracardiac vs. intrapulmonary). If shunting is occurring at the cardiac level, then contrast appears in the left heart usually within 3 cardiac cycles of the contrast entering the right heart. There is no widely accepted grading scheme for the assessment of the degree of left-to-right shunt from a PFO. Most determinations are made by the number of bubbles seen in a single still frame in the left atrium. One protocol uses 4 grades of shunt grading: grade 1: < 5 bubbles, grade 2: 5 to 25 bubbles, grade 3: > 25 bubbles, and grade 4: opacification of the chamber. Another study defined the degree of shunting of a PFO as: small as 3-9 contrast bubbles, moderate was 10-30 contrast bubbles and large if more than 30 contrast bubbles appeared in the left atrium.

Four devices approved by the US Food and Drug Administration for patent foramen ovale closure and/or atrial septal defect closure are currently marketed: the Amplatzer Septal Occluder (now Amplatzer Talisman PFO Occluder), the GORE CARDIOFORM Septal Occluder, GORE CARDIOFORM ASD Occluder, and Occlutech ASD Occluder. The GORE HELEX Septal Occluder has been discontinued.

Definition of Terms

Atrial septal aneurysm: Is a rare, but well-recognized cardiac abnormality in which there is an overabundant or weakened septal tissue allowing the septum to become very mobile and protrude or bulge into the right or left atrium of at least 10 mm to 15 mm. This can be visualized



at echocardiography and the degree of deviation can be measured. Atrial septal aneurysms are often associated with larger PFOs.

Cryptogenic stroke: A stroke that happens for an unknown reason after other causes such as cardiac, pulmonary, vascular or neurologic sources have been ruled out.

Ischemic stroke: A stroke that happens when a blood vessel that carries blood to the brain is blocked either due to arteries narrowed by atherosclerosis or a blood clot (thrombus).

Paradoxical embolism (PDE): is when a blood clot travels from the right side of the heart to the left without going through the lungs, which normally acts as a clot filter; this can then block blood flow to other parts of the body and can lead to a stroke, a heart attack, or a blood clot in an extremity,.

Septum primum: A septum in the embryonic heart, dividing the primitive atrium into right and left chambers from Latin, meaning 'first septum'.

Evidence Review

Description

Patent foramen ovale (PFO) and atrial septal defects (ASDs) are relatively common congenital heart defects that can be associated with a range of symptoms. PFOs may be asymptomatic but have been associated with higher rates of cryptogenic stroke. PFOs have also been investigated for a variety of other conditions, such as migraines. Depending on their size, ASDs may lead to left-to-right shunting and signs and symptoms of pulmonary overload. Repair of ASDs is indicated for individuals with a significant degree of left-to-right shunting. Transcatheter closure devices have been developed to repair PFO and ASDs. These devices are alternatives to open surgical repair for ASDs or treatment with antiplatelet and/or anticoagulant medications in individuals with cryptogenic stroke and PFO.

Background

Patent Foramen Ovale

The foramen ovale, a component of fetal cardiovascular circulation, consists of a communication between the right and left atrium that functions as a vascular bypass of the uninflated lungs. The

ductus arteriosus is another feature of the fetal cardiovascular circulation, consisting of a connection between the pulmonary artery and the distal aorta. Before birth, the foramen ovale is held open by the large flow of blood into the left atrium from the inferior vena cava. Over the course of months after birth, an increase in left atrial pressure and a decrease in right atrial pressure result in permanent closure of the foramen ovale in most individuals. However, a PFO is a common finding in 25% of asymptomatic adults.¹ In some epidemiologic studies, PFO has been associated with cryptogenic stroke, defined as an ischemic stroke occurring in the absence of potential cardiac, pulmonary, vascular, or neurologic sources. Studies have also shown an association between PFO and migraine headache.

Atrial Septal Defects

Unlike PFO, which represents the postnatal persistence of normal fetal cardiovascular physiology, atrial septal defects (ASDs) represent an abnormality in the development of the heart that results in free communication between the atria. ASDs are categorized by their anatomy. Ostium secundum describes defects located midseptally and are typically near the fossa ovalis. Ostium primum defects lie immediately adjacent to the atrioventricular valves and are within the spectrum of atrioventricular septal defects. Primum defects occur commonly in individuals with Down syndrome. Sinus venous defects occur high in the atrial septum and are frequently associated with anomalies of the pulmonary veins.

Ostium secundum ASDs are the third most common form of congenital heart disorder and among the most common congenital cardiac malformations in adults, accounting for 30% to 40% of these individuals older than age 40 years. The ASD often goes unnoticed for decades because the physical signs are subtle, and the clinical sequelae are mild. However, virtually all individuals who survive into their sixth decade are symptomatic; fewer than 50% of individuals survive beyond age 40 to 50 years due to heart failure or pulmonary hypertension related to the left-to-right shunt. Symptoms related to ASD depend on the size of the defect and the relative diastolic filling properties of the left and right ventricles. Reduced left ventricular compliance and mitral stenosis will increase left-to-right shunting across the defect. Conditions that reduce right ventricular compliance and tricuspid stenosis will reduce left-to-right shunting or cause a right-to-left shunt. Symptoms of an ASD include exercise intolerance and dyspnea, atrial fibrillation, and less commonly, signs of right heart failure. Individuals with ASDs are also at risk for paradoxical emboli.

Treatment of Atrial Septal Defects

Repair of ASDs is recommended for those with a pulmonary-to-systemic flow ratio ($Q_p: Q_s$) exceeding 1.5:1.0. Despite the success of surgical repair, there has been interest in developing a transcatheter-based approach to ASD repair to avoid the risks and morbidity of open heart surgery. A variety of devices have been researched. Technical challenges include minimizing the size of the device so that smaller catheters can be used, developing techniques to center the device properly across the ASD, and ensuring that the device can be easily retrieved or repositioned, if necessary.

Individuals with ASDs and a history of cryptogenic stroke are typically treated with antiplatelet agents, given an absence of evidence that systemic anticoagulation is associated with outcome improvements.

Transcatheter Closure Devices

Transcatheter PFO and ASD occluders typically consist of a single or paired wire mesh discs covered or filled with polyester or polymer fabric that are placed over the septal defect. Over time, the occlusion system is epithelialized. ASD occluder devices consist of flexible mesh discs delivered via catheter to cover the ASD.

Summary of Evidence

For individuals who have PFO and cryptogenic stroke who receive PFO closure with a transcatheter device, the evidence includes multiple randomized controlled trials (RCTs) comparing device-based PFO closure with medical therapy, systematic reviews, meta-analyses, and observational studies. The relevant outcomes are symptoms, change in disease status, overall survival, morbid events, and treatment-related morbidity and mortality. The RCTs comparing PFO closure with medical management have suggested that PFO closure is more effective than medical therapy in reducing event rates. Although these results were not statistically significant by intention-to-treat analyses in earlier trials (i.e., Amplatzer PFO Occluder with Medical Treatment in Patients with Cryptogenic Embolism [PC-Trial] and Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment [RESPECT; initial study]), they were statistically significant in later trials (i.e., RESPECT [extended follow-up], Reduction in the Use of Corticosteroids in Exacerbated COPD [REDUCE], and Patent Foramen Ovale Closure or Anticoagulants versus Antiplatelet Therapy to Prevent Stroke Recurrence [CLOSE]). Use of appropriate patient selection criteria to eliminate other

causes of cryptogenic stroke in RESPECT, REDUCE, and CLOSE trials contributed to findings of the superiority of PFO closure compared with medical management. Of note, higher rates of atrial fibrillation were reported in a few of the individual trials and in the meta-analysis that incorporated evidence from RESPECT, REDUCE, and CLOSE trials. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have PFO and migraines who receive PFO closure with a transcatheter device, the evidence includes three RCTs of PFO closure and multiple observational studies reporting on the association between PFO and migraine, and systematic reviews of these studies. Relevant outcomes are symptoms, quality of life, medication use, and treatment-related morbidity and mortality. Two sham-controlled randomized trials did not demonstrate significant improvements in migraine symptoms after PFO closure. A third RCT with blinded end point evaluation did not demonstrate reductions in migraine days after PFO closure compared to medical management, but likely was underpowered. Nonrandomized studies have shown highly variable rates of migraine reduction after PFO closure. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have PFO and conditions associated with PFO other than cryptogenic stroke or migraine (e.g., platypnea-orthodeoxia syndrome, myocardial infarction with normal coronary arteries, decompression illness, high-altitude pulmonary edema, obstructive sleep apnea) who receive PFO closure with a transcatheter device, the evidence includes small case series and case reports. Relevant outcomes are symptoms, change in disease status, morbid events, and treatment-related morbidity and mortality. Comparative studies are needed to evaluate outcomes in similar patient groups treated with and without PFO closure. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have atrial septal defect (ASD) and evidence of left-to-right shunt or right ventricular overload who receive ASD closure with a transcatheter device, the evidence includes nonrandomized comparative studies and single-arm studies. Relevant outcomes are symptoms, change in disease status, and treatment-related morbidity and mortality. The available nonrandomized comparative studies and single-arm case series have shown rates of closure using transcatheter-based devices approaching the high success rates of surgery, which are supported by meta-analyses of these studies. The percutaneous approach has a low complication rate and avoids the morbidity and complications of open surgery. In systematic reviews, the risk of overall mortality was similar with transcatheter device versus surgical closure, whereas in-hospital mortality was significantly reduced with transcatheter device closure. If the percutaneous approach is unsuccessful, ASD closure can be achieved using surgery. Because of the benefits of percutaneous closure over open surgery, it can be determined that transcatheter

ASD closure improves outcomes in individuals with an indication for ASD closure. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some currently ongoing trials that might influence this review are listed in [Table 1](#).

Table 1. Summary of Key Clinical Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT03309332^a	OBS Lead-AMPLATZER PFO Occluder New Enrollment Study	1214	Apr 2030
NCT04100135^a	GORE CARDIOFORM Septal Occluder Migraine Clinical Study: A Study to Evaluate the Safety and Efficacy of Transcatheter Closure of Patent Foramen Ovale for Relief of Migraine Headaches	150	Aug 2027
NCT05561660	Comparison of the Effect of Device Closure in Alleviating Migraine With Patent Foramen Oval (COMPETE-2)	460	Oct 2025
NCT04029233^a	Prospective, Open-label, Multicenter, Non-randomized Investigation on Percutaneous Patent Foramen Ovale (PFO) Closure Using the Occlutech PFO Occluder to Prevent Recurrence of Stroke in Patients With Cryptogenic Stroke and High Risk PFO	570	May 2024
Unpublished			
NCT02985684	GORE CARDIOFORM ASD Occluder Clinical Study: A Study to Evaluate Safety and Efficacy in the Treatment of Transcatheter Closure of Ostium Secundum Atrial Septal Defects (ASDs) - The Gore ASSURED Clinical Study	125	Sept 2022

NCT: national clinical trial

Clinical Input Received from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2016 Input

In response to requests, input was received from two academic medical centers (one of which provided two responses while this policy was under review in 2016). Input was mixed about the medical necessity of closure devices for patent foramen ovale (PFO) in individuals with cryptogenic stroke or transient ischemic attack due to presumed paradoxical embolism through the PFO. There was consensus that use of closure devices for PFO in individuals with other conditions (e.g., migraine, platypnea-orthodeoxia syndrome) is not medically necessary.

Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the policy conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Chest Physicians

In 2012, the American College of Chest Physicians updated its guidelines on antithrombotic therapy and the prevention of thrombosis, which made the following recommendations related to PFO and cryptogenic stroke⁴⁶:

We suggest that patients with stroke and PFO are treated with antiplatelet therapy following the recommendations for patients with noncardioembolic stroke... In patients with a history of noncardioembolic ischemic stroke or TIA [transient ischemic attack], we recommend long-term treatment with aspirin (75-100 mg once daily), clopidogrel (75 mg once daily), aspirin/extended release dipyridamole (25 mg/200 mg bid [twice daily]), or cilostazol (100 mg bid) over no antiplatelet therapy (Grade 1A), oral anticoagulants (Grade 1B), the combination of clopidogrel plus aspirin (Grade 1B), or triflusal (Grade 2B).

American Academy of Neurology

In 2020, the American Academy of Neurology updated its evidence-based guidelines on the management of individuals with stroke and PFO to address whether percutaneous closure of PFO is superior to medical therapy alone.⁴⁷ This update to the practice advisory published in 2016 was completed due to the approval of the Amplatzer PFO Occluder and the GORE CARDIOFORM Septal Occluder. Following a systematic review of the literature and structured formulation of recommendations, the Academy developed the following conclusions addressing percutaneous PFO closure as compared to medical therapy alone. For individuals with cryptogenic stroke and PFO, percutaneous PFO closure:

- "probably reduces the risk of stroke recurrence with an HR [hazard ratio] of 0.41 (95% CI [confidence interval], 0.25–0.67, $I^2 = 12\%$) and an absolute risk reduction of 3.4% (95% CI, 2.0%–4.5%) at 5 years "
- "probably is associated with a periprocedural complication rate of 3.9% (95% CI, 2.3%–5.7%), and "
- "probably is associated with the development of serious non-periprocedural atrial fibrillation, with a relative risk of 2.72 (95% CI, 1.30–5.68, $I^2 = 0\%$)."

The guidelines recommended:

In patients being considered for PFO closure, clinicians should ensure that an appropriately thorough evaluation has been performed to rule out alternative mechanisms of stroke, as was performed in all positive PFO closure trials (level B). In patients with a PFO detected after stroke and no other etiology identified after a thorough evaluation, clinicians should counsel that having a PFO is common; that it occurs in about 1 in 4 adults in the general population; that it is difficult to determine with certainty whether their PFO caused their stroke; and that PFO closure probably reduces recurrent stroke risk in select patients (level B).

In patients younger than 60 years with a PFO and an embolic-appearing infarct and no other mechanism of stroke identified, clinicians may recommend closure following a discussion of potential benefits (reduction of stroke recurrence) and risks (procedural complication and atrial fibrillation) (level C). PFO closure may be offered in other populations, such as for a patient who is aged 60–65 years with a very limited degree of traditional vascular risk factors (i.e., hypertension, diabetes, hyperlipidemia, or smoking) and no other mechanism of stroke detected following a thorough evaluation, including prolonged monitoring for atrial fibrillation (level C). PFO closure may be offered to younger patients (e.g., <30 years) with a single, small, deep stroke (<1.5 cm), a large shunt, and absence of any vascular risk factors that would lead to intrinsic small-vessel disease such as hypertension, diabetes, or hyperlipidemia (level C).

American Heart Association and American Stroke Association

In 2021, the American Heart Association and American Stroke Association updated their guidelines on the prevention of stroke in individuals with ischemic stroke or transient ischemic attack. The guidelines made the following recommendations for device-based closure for PFO⁴⁸:

- In patients 18 to 60 years of age with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a PFO with high-risk anatomic features* it is reasonable to choose closure with a transcatheter device and long-term antiplatelet therapy over antiplatelet therapy alone for preventing recurrent stroke (Class IIa; Level of Evidence B-Randomized)
- In patients 18 to 60 years of age with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a PFO without high-risk anatomic features,* the benefit of closure with a transcatheter device and long-term antiplatelet therapy over antiplatelet therapy alone for preventing recurrent stroke is not well established (Class IIb; Level of Evidence C-Limited Data)
- In patients 18 to 60 years of age with a nonlacunar ischemic stroke of undetermined cause despite a thorough evaluation and a PFO, the comparative benefit of closure with a transcatheter device versus warfarin is unknown (Class IIb; Level of Evidence C-Limited Data)

*The guideline notes that high-risk anatomic features are not uniformly described throughout the literature.

The guideline also defined the following relevant terms:

- **Cryptogenic stroke:** An imaging-confirmed stroke with unknown source despite thorough diagnostic assessment (including, at a minimum, arterial imaging, echocardiography, extended rhythm monitoring, and key laboratory studies such as a lipid profile and hemoglobin A1c [HbA1c]).
- **Embolic stroke of undetermined source (ESUS):** A stroke that appears nonlacunar on neuroimaging without an obvious source after a minimum standard evaluation (including arterial imaging, echocardiography, extended rhythm monitoring, and key laboratory studies such as a lipid profile and HbA1c) to rule out known stroke etiologies such as cardioembolic sources and atherosclerosis proximal to the stroke. A diagnosis of ESUS implies that the stroke is embolic in origin, given the nonlacunar location; however, the source of the embolus is unknown, despite a minimal standard evaluation. Although cryptogenic stroke similarly implies that the cause of the origin is unknown, the stroke is not necessarily embolic. Individuals with ESUS have cryptogenic stroke, but the converse is not always the case.

American College of Cardiology and American Heart Association

In 2018, the American College of Cardiology and American Heart Association updated guidelines on the management of adults with congenital heart disease.⁴⁹ The treatment recommendations are summarized in [Table 2](#). Recommendations for surgical closure versus transcatheter closure are dependent on the underlying condition.

Table 2. American College of Cardiology and American Heart Association Recommendations for Treating Atrial Septal Defect

Condition	Recommendation	COR ^a /LOE ^b
Symptomatic isolated secundum ASD, right atrial and/or RV enlargement, and net left-to-right shunt sufficiency large enough to cause physiological sequelae, without cyanosis at rest or during exercise	Transcatheter or surgical closure	I1/B-NR2
Symptomatic primum ASD, sinus venosus defect, or coronary sinus defect, right atrial and/or RV enlargement, and net left-to-right shunt sufficiency large enough to cause physiological sequelae, without cyanosis at rest or during exercise	Surgical closure unless precluded by comorbidities	I1/B-NR2

Asymptomatic isolated secundum ASD, right atrial and RV enlargement, and net left-to-right shunt sufficiency large enough to cause physiological sequelae, without cyanosis at rest or during exercise	Transcatheter or surgical closure	Ila1/C-LD2
Secundum ASD when a concomitant surgical procedure is being performed and there is a net left-to-right shunt sufficiently large enough to cause physiological sequelae, and right atrial and RV enlargement without cyanosis at rest or during exercise	Surgical closure	Ila1/C-LD2
ASD when net left-to-right shunt is $\geq 1.5:1$, PA systolic pressure and/or pulmonary vascular resistance is greater than of one-third of systemic resistance	Percutaneous or surgical closure	Ilb1/B-NR2
ASD with PA systolic pressure greater than two-thirds systemic, pulmonary vascular resistance greater than two-thirds systemic, and/or a net left-to-right shunt	ASD closure should not be performed	III-Harm1/C-LD2

Adapted from Stout et al (2019).⁴⁹

ASD: atrial septal defect; COR: class (strength) of recommendation; LOE: level (quality) of evidence; PA: pulmonary artery; RCT: randomized controlled trial; RV: right ventricular.

a COR key: I=strong; IIa=moderate; IIb=weak; III: No Benefit=weak; III: Harm=strong.⁴⁹

b LOE key: A=high quality from >1 RCT, meta-analyses of high-quality RCTs, ≥ 1 RCT corroborated by high-quality registry studies; B-R=randomized, moderate-quality evidence from ≥ 1 RCT or meta-analysis of moderate-quality RCTs; B-NR=nonrandomized, moderate-quality evidence from ≥ 1 well-designed, well-executed nonrandomized study, observational study, or registry study, or meta-analyses of such studies; C-LD: limited data, randomized or nonrandomized observational or registry studies with limitations of design or execution, meta-analyses of such studies, or physiological or mechanistic studies in human subjects; C-EO: expert opinion.⁴⁹

European Association of Percutaneous Cardiovascular Interventions

In 2021, the European Association of Percutaneous Cardiovascular Interventions Scientific Documents and Initiatives Committee invited 8 European scientific societies and international experts to develop interdisciplinary position statements on the management of PFO; 3 US-based experts were listed as authors on part II of the position paper.⁵⁰

For decompression sickness, authors note: "If behavioral and technical changes are not possible or not effective, PFO closure can be proposed with shared decision making underscoring the lack of evidence."

For migraines, authors note: "Consider PFO closure only in clinical trials or for compassionate use in migraine with aura."

Medicare National Coverage

There is no national coverage determination.

Regulatory Status

Patent Foramen Ovale (PFO) Closure Devices

The US Food and Drug Administration (FDA) has approved two devices for PFO closure through the premarket approval process or a premarket approval supplement: the Amplatzer PFO Occluder, and the GORE CARDIOFORM Septal Occluder (see [Table 2](#)) (FDA product code: MLV).

In 2002, two transcatheter devices were cleared for marketing by the FDA through a humanitarian device exemption as treatment for individuals with cryptogenic stroke and PFO: the CardioSEAL Septal Occlusion System (NMT Medical; device no longer commercially available) and the Amplatzer PFO Occluder (Amplatzer, now Abbott Cardiovascular). Following the limited FDA approval, use of PFO closure devices increased by more than 50-fold, well in excess of the 4000 per year threshold intended under the humanitarian device exemption,² prompting the FDA to withdraw the humanitarian device exemption approval for these devices in 2007. The Amplatzer PFO Occluder was approved through the premarket approval process in 2016.

In March 2018, the FDA granted an expanded indication to the Gore Cardioform Septal Occluder to include closure of PFO to reduce the risk of recurrent stroke (see [Table 3](#)). The new indication was based on results of the REDUCE pivotal clinical trial.³

Table 3. PFO Closure Devices Approved by the US Food and Drug Administration

Device	Manufacturer	PMA Approval Date	Indications
Amplatzer PFO Occluder (now	St. Jude Medical (now Abbott Cardiovascular)	Nov 2016	For percutaneous transcatheter closure of a PFO to reduce the risk of recurrent ischemic stroke in patients, predominantly between the ages of 18

Device	Manufacturer	PMA Approval Date	Indications
Amplatzer Talisman PFO Occluder)			and 60 years, who have had a cryptogenic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude known causes of ischemic stroke. ⁴
GORE CARDIOFORM Septal Occluder	W.L. Gore & Associates	Mar 2018 (supplement)	PFO closure to reduce the risk of recurrent ischemic stroke in patients, predominantly between the ages of 18 and 60 years, who have had a cryptogenic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude known causes of ischemic stroke

PFO: patent foramen ovale; PMA: premarket approval. FDA product code: MLV.

ASD Closure Devices

The FDA has approved five devices for ASD closure through the premarket approval process or a premarket approval supplement: the Amplatzer Septal Occluder, the GORE HELEX Septal Occluder (discontinued), the GORE CARDIOFORM ASD Occluder and the GORE CARDIOFORM Septal Occluder, and Occlutech ASD Occluder. (see [Table 4](#))

(FDA product code: MLV; OZG).

Table 4. ASD Closure Devices Approved by the US Food and Drug Administration

Device	Manufacturer	PMA Approval Date	Indications
Amplatzer Septal Occluder	St. Jude Medical (Abbott Medical)	Dec 2001	Occlusion of ASDs in the secundum position

Device	Manufacturer	PMA Approval Date	Indications
			<p>Use in patients who have had a fenestrated Fontan procedure who require closure of the fenestration</p> <p>Patients indicated for ASD closure have echocardiographic evidence of ostium secundum ASD and clinical evidence of right ventricular volume overload</p>
GORE HELEX Septal Occluder	W.L. Gore & Associates	Aug 2006 (discontinued)	Percutaneous, transcatheter closure of ostium secundum ASDs
GORE CARDIOFORM ASD Occluder	W.L. Gore & Associates	May 2019 (supplement)	Percutaneous, transcatheter closure of ostium secundum ASDs
GORE CARDIOFORM Septal Occluder	W.L. Gore & Associates	Apr 2015 (supplement)	Percutaneous, transcatheter closure of ostium secundum ASDs
OcclutechASD Occluder	Occlutech	Dec 2023	Percutaneous, transcatheter closure of ostium secundum ASDs

ASD: atrial septal defect; PMA: premarket approval. FDA product code: MLV.

References

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History

Date	Comments
09/07/99	Add to Medicine Section - New Policy
01/18/01	Replace policy - New information on patent foramen ovale; rest unchanged.
03/12/02	Replace policy - Revised; added requirements to policy statement patients with PFO must fail trial of oral anticoagulants. Noted FDA approval of Amplatzer device. Policy replaces 2.02.09.
08/13/02	Replace policy - Policy statement revised to indicate transcatheter treatment of ASD may be considered medically necessary. Replaces P2.02.100.
05/13/03	Replace policy - Policy reviewed; no change to policy statement; CPT codes updated.
05/26/06	Update Scope and Disclaimer - No other changes.
03/11/08	Cross Reference Update - No other changes.
10/14/08	Cross Reference Update - No other changes.
03/10/09	Replace policy - Policy updated with literature search; policy rationale extensively revised. Policy statement for PFO changed to investigational due to the FDA's withdrawal of the humanitarian device exemption approval. References added.
06/08/10	Replace policy - Policy updated with literature search; no change to the policy statement. References added.
10/11/11	Replace policy - Policy updated with literature search. Policy statements unchanged. References 5, 8, 15 and 25 added. ICD-10 codes added to policy.
11/27/12	Replace policy - Policy updated with literature search. References 3, 6, 7, and 30 added. No change to policy statement.

Date	Comments
12/04/13	Replace Policy. Policy guidelines reformatted for usability. Updated Regulatory Status with information about the FDA medical device alert issued 10/17/13 for the Amplatzer ASO. Rationale updated with literature search through July 31, 2013. References 4-7, 25 added; others renumbered/removed. Policy statement unchanged.
11/20/14	Annual Review. Policy updated with literature review through August 1, 2014. References 8-17, 21, 26, 33-37, 40, 48, 53-55, 58-59 added. Policy statement unchanged. ICD-9 and ICD-10 diagnosis codes removed; these are not utilized in adjudication of the policy.
06/09/15	Coding update: Correct ICD-10-PCS codes to support remediation efforts.
12/08/15	Annual Review. Policy updated with literature review through July 2015; references 16-19, 48, 55-56, and 67 added. Policy statements unchanged.
07/01/16	Annual Review, approved June 14, 2016. Policy statements unchanged. Clinical input received from physician specialty societies and academic medical centers added. No new literature added.
01/01/17	Interim review, approved December 13, 2016. Changed policy statement from investigational to medically necessary for closure of PFO in the presence of cryptogenic stroke due to paradoxical embolism using a PFO occluder device (Amplatzer PFO) when criteria are met. Updated Regulatory Status with information about the Amplatzer device for PFO. Policy updated with literature review through October 2016.
07/01/17	Annual Review, approved June 22, 2017. Policy moved into new format. Policy updated with literature review through March 23, 2017; references 3, 6-7, 9-10, 48-49, 51-52, 64, and 78 added. Statement, "There are currently no transcatheter devices with the US Food and Drug Administration [FDA] approval or clearance for this indication," removed from investigational statement for PFO closure devices; policy statements otherwise unchanged.
08/01/18	Annual Review, approved July 10, 2018. Policy updated with literature review through March 2018; references 9-11, 14-15, and 17 added. Policy statement changed to: The percutaneous transcatheter closure of a patent foramen ovale using AMPLATZER PFO Occluder may be considered medically necessary to reduce the risk of recurrent ischemic stroke if patient meets all of the specified criteria.
08/10/18	Corrected errors in the description of the heart anatomy discussed under Background, Patent Foramen Ovale on page 5.
04/01/19	Minor update, added Documentation Requirements section.
08/01/19	Annual Review, approved July 25, 2019. Policy updated with literature review through March 2019; references added. Added new FDA approved patent foramen ovale closure device: Gore Cardioform Septal Occluder. An investigational statement was added for situations not meeting criteria.



Date	Comments
04/01/20	Delete policy, approved March 10, 2020. This policy will be deleted effective July 2, 2020, and replaced with InterQual criteria for dates of service on or after July 2, 2020.
05/06/20	Interim Review, approved May 5, 2020. This policy is reinstated immediately and will no longer be deleted or replaced with InterQual criteria on July 2, 2020.
08/01/21	Annual Review, approved July 9, 2021. Policy updated with literature review through March 19, 2021; references added. Policy statements unchanged.
08/01/22	Annual Review, approved July 11, 2022. Policy updated with literature review through March 14, 2022; references added. Minor editorial corrections to policy statements; intent unchanged.
08/01/23	Annual Review, approved July 10, 2023. Policy updated with literature review through March 17, 2023; 1 reference added. Minor editorial refinements to policy statements; intent unchanged. Changed the wording from "patient" to "individual" throughout the policy for standardization.
08/01/24	Annual Review, approved July 8, 2024. Policy updated with literature review through March 13, 2024; no references added. Policy statements unchanged.

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