

FEP 2.02.09 Closure Devices for Patent Foramen Ovale and Atrial Septal Defects

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Related Policies: None

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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. 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 patients with a significant degree of left-to-right shunting. 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 migraine. 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 patients with cryptogenic stroke and PFO.

FDA REGULATORY STATUS

Patent Foramen Ovale Closure Devices

In 2002, 2 transcatheter devices were cleared for marketing by the U.S. Food and Drug Administration (FDA) through a humanitarian device exemption (HDE) as treatment for patients with cryptogenic stroke and patent foramen ovale (PFO): the CardioSEAL® Septal Occlusion System (NMT Medical; device no longer commercially available) and the Amplatzer® PFO Occluder (Amplatzer, now St. Jude Medical, St. Paul, MN). HDE approval is applicable to devices designed to treat a patient population of fewer than 4000 patients per year. This approval process requires the manufacturer to submit data on the safety and the probable clinical benefit. Clinical trials validating the device effectiveness are not required. The labeled indications of both limited the use of these devices to closure of PFO in patients with recurrent cryptogenic stroke due to presumed paradoxical embolism through a PFO and who have failed conventional drug therapy.

Following this 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 HDE.² As a result, in 2006, FDA withdrew the HDE approval for these devices.

In November 2016, the Amplatzer® PFO Occluder was approved by the FDA through the premarket approval (PMA) process for the following indication³:

“For percutaneous transcatheter closure of a patent foramen ovale (PFO) 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.”

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The PMA was based on analysis of the RESPECT trial, initial results of which were published in 2013. We discuss the FDA's analysis of the RESPECT trial data in the Rationale section below.

FDA product code: MLV.

Atrial Septal Defect Closure Devices

Three devices have been approved by the FDA through the PMA process or a PMA supplement for transcatheter atrial septal defect closure (see Table 1).

Table 1 ASD Closure Devices Approved by the Food and Drug Administration

Device	Manufacturer	PMA Approval Date	Indications
Amplatzer™ Septal Occluder	St. Jude Medical (Plymouth, MN)	Dec 2001	<ul style="list-style-type: none"> • Occlusion of ASDs in the secundum position • Use in patients who have had a fenestrated Fontan procedure who require closure of the fenestration • (Patients indicated for ASD closure have echocardiographic evidence of ostium secundum ASD and clinical evidence of right ventricular volume overload.)
GORE HELEX Septal Occluder ^a	W.L. Gore & Associates (Flagstaff, AZ)	Aug 2006	<ul style="list-style-type: none"> • Percutaneous, transcatheter closure of ostium secundum ASDs
GORE CARDIOFORM Septal Occluder	W.L. Gore & Associates (Flagstaff, AZ)	Oct 2016 (supp.)	<ul style="list-style-type: none"> • Percutaneous, transcatheter closure of ostium secundum ASDs

ASD: atrial septal defect; PMA: premarket approval.

^a Discontinued.

POLICY STATEMENT

Closure of patent foramen ovale using a transcatheter approach is considered **not medically necessary**.

Transcatheter closure of secundum atrial septal defects may be considered **medically necessary** when using a device that has been approved by the U.S. Food and Drug Administration for that purpose and used according to the labeled indications.

POLICY GUIDELINES

Three devices have been approved by the U.S. Food and Drug Administration for atrial septal defect closure: the Amplatzer™ Septal Occluder, the GORE HELEX Septal Occluder (discontinued), and the GORE CARDIOFORM Septal Occluder.

The labeled indications for these devices are similar and include:

- Patients with echocardiographic evidence of ostium secundum atrial septal defect; AND
- Clinical evidence of right ventricular volume overload (ie, 1.5:1 degree of left-to-right shunt or right ventricular enlargement).

Generally recognized indications for closure include a pulmonary-to-systemic flow ratio of greater than 1.5, right atrial and right ventricular enlargement, and paradoxical embolism.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

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RATIONALE

Summary of Evidence

For individuals who have patent foramen ovale (PFO) and cryptogenic stroke who receive PFO closure with a transcatheter device, the evidence includes 3 randomized controlled trials (RCTs) comparing device-based PFO closure with medical therapy, multiple nonrandomized comparative studies, and multiple systematic reviews and meta-analyses of these studies. Relevant outcomes are overall survival, morbid events, and treatment-related morbidity and mortality. None of the 3 trials reported statistically significant improvements on their main outcomes using intention-to-treat analysis. In all 3 trials, low numbers of outcome events in both groups limited the power to detect differences between groups. One trial showed a significant benefit for the closure group on per protocol analysis and another showed significant benefit on secondary outcomes. Meta-analyses of these trials have also come to different conclusions, with some reporting statistically significant reductions in recurrent events on pooled analysis and others reporting a trend for benefit that was not statistically significant. A high-quality meta-analysis reported a significantly lower risk of recurrent ischemic stroke with device therapy, but a higher risk of atrial fibrillation. While these results suggest that a benefit might be present, the evidence is not definitive and the risk-benefit ratio of transcatheter PFO closure as an alternative to medical therapy is not well-defined. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have PFO and migraines who receive PFO closure with a transcatheter device, the evidence includes 2 RCTs of PFO closure and multiple observational studies reporting on the association between PFO and migraine. Relevant outcomes are symptoms, quality of life, medication use, and treatment-related morbidity and mortality. The available sham-controlled randomized trial did not demonstrate significant improvements in migraine symptoms after PFO closure. A second RCT with blinded end point evaluation did not demonstrate improvements in migraine days after PFO closure, but likely it was underpowered. Nonrandomized studies have shown highly variable rates of migraine improvement after PFO closure. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have PFO and conditions associated with PFO other than cryptogenic stroke or migraine (eg, 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. The body of evidence only consists of small case series and case reports. Comparative studies are needed to evaluate outcomes in similar patient groups treated with and without PFO closure. The evidence is insufficient to determine the effects of the technology on health outcomes.

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. 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 patients with an indication for ASD closure. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

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 patent foramen ovale (PFO) and cryptogenic stroke⁷⁵:

“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, 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), 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 2016, the American Academy of Neurology (AAN) updated its evidence-based guidelines on the management of patients with stroke and PFO to address whether percutaneous closure of PFO is superior to medical therapy alone.⁷⁶ Following a systematic review of the literature and structured formulation of recommendations, AAN developed separate conclusions for the STARFlex and Amplatzer PFO Occluder devices. The conclusions of the systematic review were as follows:

For patients with cryptogenic stroke and PFO, percutaneous PFO closure with the STARFlex device:

- “Possibly does not provide a large benefit in preventing stroke in place of medical therapy alone—RD [risk difference] 0.13%, 95% CI -2.2-2.0%; possibly increases the risk of new-onset AF [atrial fibrillation]—RD 5%, 95% CI 2%-8% (1 Class I study, confidence downgraded to low for risk of bias relative to magnitude of effect);”
- “Probably is associated with a serious periprocedural complication risk of 3.2%, 95% CI 1.9%-5.2% (1 Class I study).”

For patients with cryptogenic stroke and PFO, percutaneous PFO closure with the Amplatzer PFO Occluder:

- “Possibly decreases the risk of recurrent stroke—RD -1.68%, 95% CI -3.18% to -0.19%;”
- “Possibly increases the risk of new-onset AF—RD 1.64%, 95% CI 0.07%–3.2% (2 Class I studies; confidence downgraded to low for risk of bias relative to magnitude of effect and imprecision);”
- “Is highly likely to be associated with a procedural complication risk of 3.4%, 95% CI 2.3%–5% (2 Class I studies).”

The guidelines concluded:

“Clinicians should not routinely offer percutaneous PFO closure to patients with cryptogenic ischemic stroke outside of a research setting (Level R). In rare circumstances, such as recurrent strokes despite adequate medical therapy with no other mechanism identified, clinicians may offer the AMPLATZER PFO Occluder if it is available (Level C).”

American Heart Association and American Stroke Association

In 2014, the American Heart Association (AHA) and American Stroke Association updated its guidelines on the prevention of stroke in patients with ischemic stroke or transient ischemic attack (TIA). The guidelines listed the following recommendations for device-based closure for PFO⁷⁷:

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- “For patients with a cryptogenic ischemic stroke or TIA and a PFO without evidence for DVT, available data do not support a benefit for PFO closure (Class III; Level of Evidence A).”
- “In the setting of PFO and DVT [deep vein thrombosis], PFO closure by a transcatheter device might be considered, depending on the risk of recurrent DVT (Class IIb; Level of Evidence C).”

American College of Cardiology and American Heart Association

Guidelines issued by the American College of Cardiology and AHA in 2008 on the management of congenital heart disease recommended closure of an atrial septal defect (ASD) by percutaneous or surgical methods for several indications.⁷⁸ For sinus venosus, coronary sinus, or primum ASD, however, surgery rather than percutaneous closure was recommended.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

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Force on Practice Guidelines (writing committee to develop guidelines on the management of adults with congenital heart disease). Circulation. Dec 2 2008;118(23):e714-833. PMID 18997169

POLICY HISTORY

Date	Action	Description
December 2011	New Policy	
December 2012	Update Policy	Policy updated with literature search. References 3, 6, 7, and 30 added. No change to policy statement.
December 2013	Update Policy	Policy updated with literature search. References 4-7 and 25 added. Policy summary revised with no change to intent.
December 2014	Update Policy	Policy updated with literature review through August 1, 2014. References 8-17, 21, 26, 33-37, 40, 48, 53-55, 58, and 59 added. No changes to policy statement.
March 2018	Update Policy	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 U.S. Food and Drug Administration [FDA] approval or clearance for this indication," removed from investigational statement for PFO closure devices due to Amplatzer FDA premarket approval and that policy statement was changed from "investigational" to "not medically necessary".

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