Percutaneous Patent Foramen Ovale (PFO) Closure (for Louisiana Only)

Policy Number: CS329LA.A
Effective Date: TBD

➲ Instructions for Use

Table of Contents **Page**

Application

This Medical Policy only applies to the state of Louisiana.

Coverage Rationale

Note: This policy does not apply to individuals < 18 years of age.

Percutaneous patent foramen ovale closure for the prevention of recurrent ischemic stroke is proven and medically necessary when used according to U.S. Food and Drug Administration (FDA) labeled indications, contraindications, warnings and precautions and ALL of the following criteria are met:

- **History of cryptogenic stroke confirmed by imaging; and**
- **A cardiologist and a neurologist agree that the stroke is likely embolic in nature; and**
- **Other causes of ischemic stroke have been ruled out including, but not limited to, carotid disease, hypercoagulable states or atrial fibrillation; and**
- **Individual is 18-60 years of age**

Due to insufficient evidence of efficacy, percutaneous patent foramen ovale closure is unproven and not medically necessary for all other stroke or related neurological indications including, but not limited to, primary prevention of stroke, transient ischemic attacks, and migraine prevention.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

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

Description of Services

A stroke occurs when there is a loss of blood flow to the brain causing damage and tissue death. There are two types of stroke: ischemic and hemorrhagic. An ischemic stroke is caused by a blood clot that blocks a blood vessel in the brain. A hemorrhagic stroke is caused by a blood vessel that breaks and bleeds into the brain. A cryptogenic stroke is a type of ischemic stroke in which a specific cause is not found. In some individuals, the cause of a cryptogenic stroke may be due to a patent foramen ovale (PFO). A transient ischemic attack (TIA) occurs when the blood supply to the brain is blocked or interrupted for a short period of time but causes no permanent damage.

A PFO is a normal opening in the heart that is present in all people during fetal development. The opening is in the septal wall separating the left and right atria of the heart. Typically, this opening closes on its own after birth, but in some cases, the opening remains opened throughout adulthood. For the majority of people with a PFO, the condition does not cause any problems and requires no treatment. However, in some people with a PFO, small blood clots that form in the peripheral venous system may cross from the right to the left circulation and cause ischemic stroke if they reach the cerebral arterial circulation. Prevention of recurrent cryptogenic stroke in people with a PFO may be achieved through antithrombotic/anticoagulation therapy, surgery or percutaneous closure. While surgery is theoretically one treatment option, it is rarely used for this indication due to the inherent risks of surgery. Additionally, surgery has not been studied in comparison to percutaneous closure (American Heart Association, 2017).

Percutaneous or transcatheter PFO closure devices use catheter technology to access the heart and close the PFO without the need for open-heart surgery and cardiopulmonary bypass. Once in place, the device prevents blood, and potentially blood clots, from flowing between the heart's right and left atria.

Clinical Evidence

A systematic review and meta-analysis of randomized controlled trials compared the safety and efficacy of percutaneous PFO closure (with medical therapy) versus medical therapy alone in patients with cryptogenic stroke or TIA. Among 3627 patients, 1829 were allocated to PFO closure and 1798 to medical treatment. The mean follow-up was 3.7 years. Results showed a significant reduction in ischemic stroke recurrence using the two currently FDA approved PFO closure devices. One study using the older STARFlex device

showed no improvement. Combined data across all studies showed no significant reduction in all-cause mortality or TIA. New-onset atrial fibrillation occurred more frequently (five-fold) in the PFO group but resolved in 72% of cases within 45 days (Ntaios et al., 2018).

The following studies were included in the review:

- CLOSE (Mas et al., 2017) – used several PFO closure devices including the two currently FDA approved devices.
- REDUCE (Søndergaard et al., 2017) – Gore® Helex® (product discontinued) or Gore® Cardioform Septal Occluder
- RESPECT (Carroll et al., 2013; Saver et al., 2017) – Amplatzer™ PFO Occluder
- PC Trial (Meier et al., 2013) – Amplatzer™ PFO Occluder
- CLOSURE I (Furlan et al., 2012) – STARFlex (no longer on the market)

Two other meta-analyses reached similar conclusions (Garg et al., 2018; Turc et al., 2018).

In a small randomized controlled trial (DEFENSE-PFO) published after the Ntaois et al. (2018) meta-analysis, Lee et al. (2018) reported that device closure in addition to medical therapy prevented secondary stroke events following cryptogenic stroke in patients with high-risk PFO. High-risk PFO was defined as PFO with atrial septal aneurysm, hypermobility or PFO size ≥2 mm. ClinicalTrials.gov number NCT01550588.

A Hayes report concluded that there is some evidence that PFO closure is associated with a lower risk of recurrent stroke or other cerebrovascular events than that seen with medical therapy alone. However, the report is less definitive in its conclusions as it included older devices no longer on the market and showed less benefit (Hayes, 2018; updated 2020).

A NICE report concluded that evidence on the safety of percutaneous PFO closure to prevent recurrent cerebral embolic events shows serious but infrequent complications. Evidence on its efficacy is adequate (NICE, 2013).

Migraine Prevention

The evidence is insufficient to support the use of PFO closure for treating migraines. Several randomized trials have failed to reach their primary endpoint of cessation or reduction in migraine days.

In the PREMIUM study, Tobis et al. (2017) randomly assigned patients who had a PFO and medically intractable migraine with or without aura to undergo closure with the Amplatzer PFO Occluder (n=123) or a sham procedure (n=107). Both groups also received medical therapy. The procedure was generally safe, with only one device-related serious adverse event occurring during 1 year of follow-up. There was no difference between the groups in the percentage of responders (primary efficacy endpoint), defined as those having at least a 50% reduction in migraine attacks per month in months 10 through 12 after randomization. However, the PFO closure group had a lower mean number of headache days per month.

In the multicentre, prospective, randomized, open-label, international PRIMA trial, Mattle et al. (2016) investigated the effect of percutaneous PFO closure in patients with migraines refractory to medical treatment. Participants were randomized to PFO closure using the Amplatzer PFO Occluder (n=53) or medical treatment (n=54). The primary endpoint

was reduction in monthly migraine days during months 9-12 after randomization compared with a 3-month baseline phase. The trial was terminated prematurely because of slow enrollment. Eighty-three patients (40 occluder, 43 control) completed 12-month follow-up. Mean migraine days at baseline were 8 (±4.7 SD) in the closure group and 8.3 (±2.4) in controls. Findings on the primary endpoint were inconclusive with -2.9 days after PFO closure versus -1.7 days in control group. In patients with refractory migraine with aura and PFO, closure did not reduce overall monthly migraine days.

A NICE report concluded that evidence on the efficacy of percutaneous PFO closure for recurrent migraine is inadequate in quality and quantity. The evidence on safety shows a small incidence of well-recognized but sometimes serious adverse events, including device embolization and device prolapse (each reported in less than 1% of patients) (NICE, 2010).

In the MIST study, Dowson et al. (2009) evaluated the effectiveness of PFO closure to resolve refractory migraine headache. One hundred forty-seven patients were randomized to transcatheter PFO closure with the STARFlex implant (n=74) or to a sham procedure (n=73). Patients were followed up for 6 months. The primary efficacy end point was cessation of migraine headache 91 to 180 days after the procedure. No significant difference was observed in the primary end point of migraine headache cessation between implant and sham groups (3 of 74 versus 3 of 73, respectively). Secondary end points also were not achieved.

Clinical Practice Guidelines

American Academy of Neurology (AAN)

An AAN practice advisory (Messé et al., 2020) makes the following recommendations for transcatheter PFO closure:

- 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
- Clinicians may inform patients that presence of a large shunt probably is associated with benefit from closure. Conversely, there probably is less likelihood of benefit in patients with a small shunt or a non-embolic-appearing single, small, deep infarct, and it is uncertain whether atrial septal aneurysm in the absence of a large shunt influences the likelihood of benefitting from PFO closure. Level C
- PFO closure may be offered in other populations, such as for a patient who is 60–65 years old 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
- In a patient for whom PFO closure is being considered, a shared decision-making approach between clinicians and the patient should be used, exploring how well the patient's attributes match those included in the positive PFO closure trials and the patient's preferences and concerns regarding risk of stroke recurrence and risk of adverse events. Level B

Level B indicates a recommendation that should be done. In most circumstances, adherence to the recommendation will likely improve health-related outcomes.

Level C represents a recommendation that may be done. In some circumstances, adherence to the recommendation might improve health-related outcomes.

American Heart Association/American Stroke Association (AHA/ASA)

The AHA/ASA guidelines for the prevention of stroke in patients with stroke and TIA (Kernan et al., 2014) make the following recommendations regarding PFO closure:

- **For patients with an ischemic stroke or TIA and a PFO who are not undergoing anticoagulation therapy, antiplatelet therapy is recommended**
- **For patients with an ischemic stroke or TIA and both a PFO and a venous source of embolism, anticoagulation is indicated depending on stroke characteristics. When anticoagulation is contraindicated, an inferior vena cava filter is reasonable**
- **For patients with a cryptogenic ischemic stroke or TIA and a PFO without evidence for deep vein thrombosis, available data does not support a benefit for PFO closure**
- **In the setting of PFO and deep vein thrombosis, PFO closure by a transcatheter device might be considered, depending on the risk of recurrent deep vein thrombosis**

(The evidence base for these guidelines does not include recently published studies.)

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Transcatheter PFO closure is a procedure and, therefore, is not subject to FDA regulation. However, the devices designed for PFO occlusion are subject to FDA regulation. These devices are regulated by the premarket approval process and are classified as transcatheter septal occluders (product code MLV).

The Amplatzer™ PFO Occluder (SJM/Abbott) received FDA premarket approval (P120021) on October 28, 2016. The device is indicated 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. Additional information is available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P120021. (Accessed February 19, 2021)

The Gore® Cardioform Septal Occluder (W.L. Gore) received FDA premarket approval (P050006/S060) on July 31, 2017. The device is indicated for the percutaneous, transcatheter closure of the following defects of the atrial septum:

- **Ostium secundum atrial septal defects**
- **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.**

Additional information is available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P050006S060. (Accessed February 19, 2021)

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Policy History/Revision Information

Date	Summary of Changes
TBD	▪ New policy

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

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