LOUISIANA BLUE

Closure Devices for Patent Foramen Ovale and Atrial Septal Defects

Policy # 00016
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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Patent Foramen Ovale

Based on review of available data, the Company may consider the percutaneous transcatheter closure of a patent foramen ovale (PFO) using AMPLATZER PFO Occluder or the Gore Cardioform Septal Occluder to be **eligible for coverage**** to reduce the risk of recurrent ischemic stroke if individual meets all of the following criteria:

- Between 18 and 60 years of age; AND
- Diagnosed with patent foramen ovale with a right-to-left interatrial shunt confirmed by echocardiography with at least one of the following characteristics:
    - 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; AND
- Documented history of cryptogenic ischemic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude any other identifiable cause of stroke, including large vessel atherosclerotic disease and small vessel occlusive disease

AND none of the following are present:

- 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.

Atrial Septal Defect

Based on review of available data, the Company may consider transcatheter closure of secundum atrial septal defects (ASD) 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 to be **eligible for coverage**** when patient selection criteria are met.

Patient Selection Criteria

Three devices have been approved by the U.S. FDA 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:

- Individuals with echocardiographic evidence of ostium secundum atrial septal defect; AND either of the following
    - Clinical evidence of right ventricular volume overload (ie, 1.5:1 degree of left-to-right shunt or right ventricular enlargement); OR
    - Clinical evidence of paradoxical embolism.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers transcatheter closure of secundum atrial septal defects for all other indications not meeting criteria outlined above to be **investigational.***

Policy Guidelines

Four devices approved by the U.S. 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.

Background/Overview

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 patent foramen ovale (PFO) is a

common finding in 25% of asymptomatic adults. 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 patients 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 patients 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 patients who survive into their sixth decade are symptomatic; fewer than 50% of patients 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. Patients 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 consist of a single or paired wire mesh disc 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.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Patent Foramen Ovale Closure Devices
The U.S. Food and Drug Administration (FDA) has approved 2 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 1).

FDA product code: MLV.

In 2002, 2 transcatheter devices were cleared for marketing by the FDA through a humanitarian device exemption as a treatment for patients 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, 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 the closure of PFO to reduce the risk of recurrent stroke (see Table 1). The new indication was based on the results of the Reduction in the Use of Corticosteroids in Exacerbated COPD (REDUCE) pivotal clinical trial.

Table 1. Patent Foramen Ovale Closure Devices Approved by the U.S. Food and Drug Administration

Device	Manufacturer	PMA Approval Date	Indications
Amplatzer PFO Occluder (now Amplatzer Talisman PFO Occluder)	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 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.

Atrial Septal Defect Closure Devices

The FDA has approved 5 devices for ASD closure through the premarket approval process or a premarket approval supplement: the Amplatzer Septal Occluder, the GORE HELEX Septal Occluder (discontinued), GORE CARDIOFORM ASD Occluder, the GORE CARDIOFORM Septal Occluder, and Occlutech®‡ ASD Occluder (see Table 2).
FDA product code: MLV; OZG.

Table 2. Atrial Septal Defect Closure Devices Approved by the U.S. 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 • 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	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.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

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 a migraine. 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. 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.

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 multiple randomized controlled trials (RCTs) comparing device-based PFO closure with medical therapy, systematic reviews, meta-analyses, and observational studies. 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 (ITT) analyses in earlier trials (ie, 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 (ie, 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 3 RCTs of PFO closure, 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 endpoint 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 (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. 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 defects (ASD) and evidence of left-to-right shunt or right ventricular overload who receive ASD closure with a transcatheter device, the evidence includes systematic reviews, 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 patients with an indication for ASD closure. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

Clinical Input 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 2 academic medical centers (1 of which provided 2 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 patients with cryptogenic stroke or transient ischemic attack due to presumed paradoxical embolism through the PFO. There was a consensus that use of closure devices for PFO in patients with other conditions (eg, migraine, platypnea-orthodeoxia syndrome) is not medically necessary.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information’ 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 stroke:

"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 to 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 patients with stroke and PFO to address whether percutaneous closure of PFO is superior to medical therapy alone. 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 patients 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 to 0.67, I^2=12%) and an absolute risk reduction of 3.4% (95% CI, 2.0% to 4.5%) at 5 years,"
- "probably is associated with a periprocedural complication rate of 3.9% (95% CI, 2.3% to 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 to 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 to 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 patients with ischemic stroke or transient ischemic attack. The guidelines made the following recommendations for device-based closure for PFO:

- "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 anti-platelet 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. The treatment recommendations are summarized in Table 3. Recommendations for surgical closure versus transcatheter closure are dependent on the underlying condition.

Table 3. 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	IIa1/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	IIa1/C-LD2
ASD when net left-to-right shunt is ≥1.5:1, PA systolic pressure and/or pulmonary vascular resistance is greater than of one-third of systemic resistance	Percutaneous or surgical closure	IIb1/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).

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.
[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.

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.

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."*

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 4.

Table 4. Summary of Key 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	150	Aug 2027

	Transcatheter Closure of Patent Foramen Ovale for Relief of Migraine Headaches		
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[a]	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	Sep 2022

NCT: national clinical trial.
[a]Denotes industry sponsored or co-sponsored trial

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Policy History

Original Effective Date: 06/05/2002
Current Effective Date: 05/01/2025

04/18/2002	Medical Policy Committee review
06/05/2002	Managed Care Advisory Council approval
06/24/2002	Format revision
03/31/2004	Medical Director review
04/20/2004	Medical Policy Committee review. Format revision. Coverage eligibility unchanged.
04/26/2004	Managed Care Advisory Council approval
04/05/2005	Medical Director review
04/19/2005	Medical Policy Committee review. Coverage eligibility unchanged. Investigational statement added to policy to address the use of transcatheter closure devices in situations where patient selection criteria are not met.
05/23/2005	Managed Care Advisory Council approval
04/05/2006	Medical Director review
04/19/2006	Medical Policy Committee approval. Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
07/07/2006	Format revised. Investigational statements added to clarify coverage eligibility. Coverage eligibility unchanged.
04/04/2007	Medical Director review
04/18/2007	Medical Policy Committee approval. Coverage eligibility unchanged.
04/02/2008	Medical Director review
04/16/2008	Medical Policy Committee approval. No change to coverage eligibility.
04/02/2009	Medical Director review
04/15/2009	Medical Policy Committee approval. Closure of patent foramen ovale using a transcatheter approach is now considered to be investigational.
04/08/2010	Medical Policy Committee approval.
04/21/2010	Medical Policy Implementation Committee approval. No change to coverage.
04/07/2011	Medical Policy Committee approval.
04/13/2011	Medical Policy Implementation Committee approval. No change to coverage.
04/12/2012	Medical Policy Committee review
04/25/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Policy # 00016
Original Effective Date: 06/05/2002
Current Effective Date: 05/01/2025

04/04/2013	Medical Policy Committee review
04/24/2013	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/06/2014	Medical Policy Committee review
03/19/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/07/2015	Medical Policy Committee review
05/20/2015	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/05/2016	Medical Policy Committee review
05/18/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
07/06/2017	Medical Policy Committee review
07/19/2017	Medical Policy Implementation Committee approval. 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; policy statements otherwise unchanged.
08/09/2018	Medical Policy Committee review
08/15/2018	Medical Policy Implementation Committee approval. Criteria for PFO revised.
04/04/2019	Medical Policy Committee review
04/24/2019	Medical Policy Implementation Committee approval. Added the GORE CARDIOFORM Septal Occluder as FDA approved for PFO.
04/02/2020	Medical Policy Committee review
04/08/2020	Medical Policy Implementation Committee approval. No change to coverage.
04/01/2021	Medical Policy Committee review
04/14/2021	Medical Policy Implementation Committee approval. No change to coverage.
04/07/2022	Medical Policy Committee review
04/13/2022	Medical Policy Implementation Committee approval. No change to coverage.
04/06/2023	Medical Policy Committee review
04/12/2023	Medical Policy Implementation Committee approval. No change to coverage. Patients replaced with individuals.
04/04/2024	Medical Policy Committee review
04/10/2024	Medical Policy Implementation Committee approval. No change to coverage.
04/03/2025	Medical Policy Committee review
04/09/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 04/2026

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Louisiana Blue Medical Policy Coverage Guidelines is with Louisiana Blue and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Louisiana Blue Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Louisiana Blue Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	93580
HCPCS	C1817
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.