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

Policy Number: CS329NE.G
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Instructions for Use

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Related Policies

- Implantable Loop Recorders and Wearable Heart Rhythm Monitors (for Nebraska Only)
- Omnibus Codes (for Nebraska Only)

Application

This Medical Policy only applies to the State of Nebraska.

Coverage Rationale

Note: This policy does not apply to individuals < 18 years of age and does not apply to atrial septal defect closure.

Percutaneous patent foramen ovale (PFO) 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 PFO 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.

Medical Records Documentation Used for Reviews

Benefit coverage for health services is determined by the federal, state, or contractual requirements, and applicable laws that may require coverage for a specific service. Medical records documentation may be required to assess whether the member meets the clinical criteria for coverage but does not guarantee coverage of the service requested; refer to the guidelines titled Medical Records Documentation Used for Reviews.

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

CPT® is a registered trademark of the American Medical Association

Description of Services

A stroke occurs when there is a loss of blood flow to the brain causing damage and tissue death. 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. There are two types of strokes: 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 blood clot traveling through a patent foramen ovale (PFO).

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 PFO 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

Stroke

Eichelmann et al. (2024) studied the recurrence of stroke comparing PFO closure versus drug therapies for individuals over 60 years and a follow up of 5 years. Included in the study were 342 individuals who were over 60 years of age and suffered a cryptogenic stroke and were accepted for PFO closure procedure. A total of 143 individuals proceeded with the procedure (Group A). The average follow-up time was 5.5 ±1.5 years. All participants in Group B refused PFO occlusion and showed persistent shunt in the follow-up period (n = 199, 100%). In Group A, seven participants were diagnosed with residual shunt during echocardiography examination (5%). A new onset of atrial fibrillation occurred in seven people in Group A (5%) and six in Group B (3%), p = .117. Recurrent stroke occurred in 3 participants in Group A (2%) and 11 in Group B (6%), p = .021. One person died of unknown reason (1%) and two people were lost due to neurological death (1%) in Group B, whereas none in Group A died during the follow-up period. The study is limited by a lack of randomization, a small sample size, retrospective results, and a possible recall bias due to parts of the follow up being collected via telephone contact with individuals and doctors. The authors concluded that further large, randomized studies are needed to evidently recommend PFO closure for individuals > 60 years of age and those with other reasons for arterial embolism.

In a 2023 systematic review and meta-analysis of RCTs, Kolokathis and colleagues evaluated the net clinical benefit (NCB) between PFO closure and medical treatment. The outcomes measured were the NCB-1 (cumulative incidence of stroke, major bleeding, atrial fibrillation/flutter, and serious procedural or device complications), NCB-2, and NCB-3 (NCB-1 using a weighted factor of 0.5 and 0.25 for atrial fibrillation/flutter events, respectively). Each component outcome of NCB was measured as a secondary outcome. The review results showed no difference between PFO closure and

medical treatment according to NCB-1, NCB-2, and NCB-3 rates. A significant decrease in stroke was seen (44% [95% CI, 21-60%]), which favors the PFO closure arm. An increase in atrial fibrillation/flutter (4.04 times [95% CI, 1.57-8.89]) was seen in the PFO closure compared with the medical treatment group. The meta-regression analysis showed a reduction in NCB-1 with PFO closure, which increased as the proportion of individuals treated with the Amplatzer™ device increased (p = 0.02). A decrease in NCB-1, NCB-2, and NCB-3 was seen when PFO closure increased as the proportion of individuals treated with substantial PFO size increased (p = 0.03). The limitations of the study include NCB being calculated as a sum of events, which implies that duplication was not avoided for individuals with stroke/transient ischemic attack (TIA) and other events during the follow-up period. The weighted factors of 0.5 and 0.25 used to calculate NCB-2 and NCB-3 were arbitrary, and the sample size was relatively small. There was no standardization in the medical regimens applied in the medical treatment and postprocedural in the PFO closure arm. The limited number of RCTs should be interpreted cautiously, and the quality of evidence was low, with an increased risk for bias and imprecision problems. The authors concluded that there was no net clinical benefit of PFO closure vs. medical treatment. There was a significant relative decrease of 44% in stroke in the PFO closure arm.

In the 2022 meta-analysis, Krittanawong and associates sought to investigate the differences in outcomes of previous trials addressing the optimal treatment strategy for individuals with PFO. Included studies are as follows: RESPECT (Carroll et al., 2013) (NCT00465270), PC (Meier et al., 2013) (NCT00166257), CLOSER I (Furlan et al., 2012) (NCT00201461), DEFENSE-PFO (Lee et al., 2018) (NCT 01550588), REDUCE (Søndergaard et al., 2017) (NCT00738894), and CLOSE (Mas et al., 2017) (NCT00562289). Included in the six studies were 3,558 individuals (1,889 who underwent PFO closure and 1,669 who had medical therapy only). The results showed a median follow-up period of 3.8 years (range 2 to 5.9 years); 46.2% were female, 4.1% had diabetes mellitus, 24.8% were smokers, 24.4% had hypertension, and 25.6% had hypercholesterolemia. Recurrent TIA (risk ratio [RR] 0.63, 95% CI 0.37 to 1.07, p = 0.07, I^2 = 0.00%) and recurrent stroke (RR 0.38, 95% CI 0.13 to 1.11, p = 0.07, I^2 = 54.37%) were not statistically significantly different between PFO closure and optimal medical therapy (OMT) groups. Additionally, there was no significant difference between PFO closure and medical therapy on recurrent stroke in the subgroup of those with an atrial septal aneurysm and those with a significant shunt size. The limitations of the analysis include a small sample size, heterogeneity in inclusion criteria, and a focus on recurrent stroke/TIA with no analysis of bleeding or surgical complications. The authors concluded that the meta-analysis did not demonstrate superior clinical outcomes with PFO closure compared with OMT alone at the short and long-term follow-up.

In 2022, Tejada et al. sought to investigate the clinical practice of PFO and analyze the variables for decision-making on selecting individuals for this procedure through a prospective observational multicentric survey. Included were all the cases of cryptogenic strong/TIA associated with PFO, with the closure being analyzed according to age (≤/> 60 years) and the characteristics of the PFO. The exploration resulted in a group of 488 individuals ≤ 60 years 143 (29.3%) who underwent PFO closure, and a > 60-year group of 124 individuals, with 24 having PFO closure (19%). The variables included for the ≤ 60 groups were the detection of a high-risk PFO (OR 4.11; IC 2.6-6.5, p < .001), criteria for paradoxical embolism (OR 2.61; IC 1.28-5.28; p = .008) and previous use of antithrombotics (OR 2.67; IC 1.38-5.18; p = .009). The > 60 years group variables were history of pulmonary thromboembolism, predisposition to thromboembolic disease, paradoxical embolism criteria, and high-risk PFO. The limitations of the study include variability in the interpretation of some studies due to study design, potential for bias, small sample size, and short follow-up. A larger sample size may have achieved greater validity for specific groups (> 60 years, TIA, and low-risk PFO). The authors concluded that in clinical practice, the main factor for indicating percutaneous closure in patients with cryptogenic stroke associated with PFO is the detection of high-risk PFO (large shunt or interatrial septal aneurysm). Other important factors include a history of thromboembolic disease, meeting criteria for paradoxical embolism, and prior use of antithrombotics.

A systematic review and meta-analysis of RCTs compared the safety and efficacy of percutaneous PFO closure (with medical therapy) versus medical therapy alone for individuals with cryptogenic stroke or TIA. Among 3,627 people, 1,829 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)

Mas et al., 2017, Søndergaard et al., 2017, Saver et al., 2017, Meier et al., 2013, and Furlan et al., 2012 are all included in the 2023 systematic review and meta-analysis authored by Kolokathis et al.

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 for individuals 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.

In a 2018 Hayes Health Technology Assessment a comparative effectiveness review was conducted for transcatheter closure of patent foramen ovale for prevention of recurrent cryptogenic stroke. The results suggest that the transcatheter closure of a PFO may be as effective as medical therapy at preventing recurrent stroke or other cerebrovascular events in those with a PFO and cryptogenic stroke or TIA There is some evidence that PFO closure is associated with a lower recurrence of stroke or other cerebrovascular events than seen with medical therapy alone. The risk of developing device or procedure related complications is relatively low. PFO closure and medical therapy have similar rates of complications, with the exception of atrial fibrillation, which may occur more frequently in those treated with PFO closure (updated in 2022).

Migraine Prevention

There is insufficient evidence to support using PFO closure for treating migraines. Several randomized trials, especially shamed-controlled trials, have failed to reach their primary endpoint of cessation or reduction in migraine days. Observational studies included in the review below are subject to biases and confounding.

Silalahi & Hariyanto 2024, aimed to analyze the efficacy and safety of PFO closure for mitigating migraine symptoms through a systematic review and meta-analysis of randomized trials and observational studies. The review incorporates evidence that examines the comparison between PFO closure and control with outcome data related to migraine. The outcomes measured were (SMD) and odds ratio (OR) for presentation of the outcomes. The results of the meta-analysis showed higher reduction of monthly migraine attacks from baseline (SMD -0.34; 95% CI: -0.51, -0.18, $p < 0.0001$, $I2 = 19\%$) and monthly migraine days from baseline (SMD -0.30; 95% CI: -0.53, -0.08, $p = 0.009$, $I2 = 0\%$) among PFO closure than control. However, the complete resolution of migraine (especially based on the evidence from RCTs; $p = 0.24$), HIT-6 score ($p = 0.08$), and migraine disability assessment survey (MIDAS) score ($p = 0.15$) did not differ significantly between two groups of intervention. The majority of adverse events reported were atrial fibrillation and access site infection/bleeding that only occurred in small proportions of people (< 5%). The limitations of the study included a short follow up period (3-12 months) with the exception of one RCT which had an extended follow up period of up to 60 weeks. The review suggested efficacy of PFO closure in reducing monthly migraine attacks and monthly migraine days. However, PFO closure was not effective in achieving complete resolution of migraine and improving HIT-6 or MIDAS score, especially based on the findings from RCTs. In terms of safety, PFO closure demonstrates a commendable safety profile, with adverse events being documented in only a limited percentage of patients. Although, the study suggests better efficacy of PFO closure in reducing monthly migraine attacks and days with similar safety profile when compared to control it is recommended to conduct carefully designed RCTs with a substantial sample size and an extended period of follow-up in order to confirm the results of this study (Downson et al. 2009; Mattle et al. 2016; and Tobis et al. 2017 previously cited are included in this review).

In 2023, Tang et al. aimed to monitor the incidence of migraine non-remission after PFO closure and discuss the relevant risk factors through a retrospective analysis involving 139 individuals diagnosed with PFO and associated migraine who underwent PFO closure. Participants were evaluated using the Headache Impact Test (HIT-6™) and classified with a score higher than 55 points before closure. The HIT-6™ score was re-evaluated 1-6 months after the intervention. HIT-6™ was defined as headache remission (n = 93) and > 55 as headache non-remission (n = 46). A logistic regression model was developed to show the risk factors of headache non-remission after PFO closure. The authors concluded that age and serum phosphorus level were risk factors for continuous headache after PFO closure, where history of smoking, atrial fibrillation, platelet-to-lymphocyte ratio (PLR), and interventricular septal thickness (IVST) were independent risk factors. Migraineurs with such clinical characteristics have a higher risk of unremitting headaches after PFO closure. This study's findings may permit more precise identification of patients with migraines who can gain from PFO closure in future clinical works, which in turn could considerably improve the effectiveness of PFO closure for treating migraine. The limitations of the study include the limited size of samples included in the study and retrospective design. Prospective studies that include larger samples must be conducted in the future to obtain more reliable results and more reliable conclusions.

In a 2022 systematic review and meta-analysis conducted by Wang and associates, the association between PFO closure and reduction of migraine burden was explored. A total of 1,754 individuals from three randomized clinical trials and nine

case-control studies were eligible for inclusion. Out of the selected literature, seven reported non-recurrence of migraine, four reported reduced migraine frequency and days, five reported HIT-6™ score, and four reported MIDAS score. The results showed that there was a significant association of PFO closure with a reduced risk of migraine recurrence by 4.47 (95% CI, 2.94-6.80; I^2 = 12%), frequency of migraine by 0.35 (95% CI, 0.17-0.53; I^2 = 0%) and monthly migraine days by 0.28 (95% CI, 0.10-0.46), and decreased score of HIT-6™ (SMD 1.23, 95% CI 0.52-1.95, I^2 93%) with PFO closure. The limitations of the study include combination of experimental and observational studies, its retrospective nature, recall and reporting bias, heterogenicity, and a limited number of published studies. The authors concluded that the combined evidence confirmed that migraine could be efficiently improved after transcatheter PFO closure for those individuals at risk for paroxysmal embolism or visual aura. In order to confirm the prognostic values of PFO closure to improve migraine burden, more significant, multi-center prospective RCTs are needed.

In a 2022 publication, Zhang et al. conducted a systematic review and meta-analysis to assess the utility and safety of PFO closure in patients with migraine with and without aura. In total, three RCTs (MIST, PRIMA, and PREMIUM outlined below), one pooled study, and eight retrospective case series including 1,165 participants met the inclusion criteria. The results showed that PFO closure reduced monthly migraine attacks and days compared to control intervention. A subgroup analysis showed complete resolution of migraine of those with aura, particularly those with frequent aura. For individuals with migraines without aura, PFO closure did not significantly reduce migraine days or result in complete headache cessation. A low incidence of adverse events occurred in all three RCTs, and included pericardial effusion, retroperitoneal bleed, access-site bleeding, and device-related events that resulted in atrial fibrillation. These were transient and recoverable, and some were routine following occlusion surgery. The authors concluded that PFO closure is safe and effective, especially for migraine with aura. This study is limited by the retrospective nature of the majority of the included studies, heterogeneous post-surgical therapy, and protocols for assessing outcome, and different devices used.

Mojadidi et al. (2021) conducted a pooled analysis of individual-level data from two randomized migraine trials (the PRIMA and PREMIUM trials outlined below) to assess the efficacy and safety of percutaneous device closure as a therapy for episodic migraine with or without aura at 12 months. Three hundred thirty-seven total participants were randomized, 176 to device PFO closure and 161 to medical management only. Since the two trials used different endpoints, all were selected for the efficacy endpoints of this pooled analysis and included responder rate, mean reduction in monthly migraine days, defined as ≥ 50% reduction in monthly migraine attacks, mean reduction in monthly migraine attacks, and the percentage of those who experienced complete cessation of migraine. Additionally, a subgroup analysis was done on participants who have migraines with aura, particularly frequent aura (defined as aura occurring in 50% or more of the migraine attacks). The safety endpoint was major procedure and device-related adverse events. The results showed in the PFO closure group, a significant reduction in monthly migraine days at 12 months, with a mean reduction of monthly migraine days 1.2 greater than the control group, no statistical difference in responder rate, a significant mean reduction in migraine attacks, and a higher rate of complete migraine cessation when compared to medical therapy. In participants with migraine with aura and frequent aura compared to controls, there was a significant reduction in migraine days, and the responder rate was not significantly greater. Complete headache cessation occurred in 12 of 114 (11%) in the PFO closure group compared with 1 of 111 (0.9%) in the control group. In subjects without aura, complete headache cessation occurred in 2 of 43 (5%) in the PFO closure group compared with none in the control group. There was a total of nine procedure related, and four device-related adverse events. Procedure-related adverse events would be expected with any right heart catheterization, including hematoma and transient hypotension. The most common device-related adverse event was paroxysmal atrial fibrillation. All of the events were transient. The authors concluded that despite the clinical trials failing to reach primary endpoints, individual data supports PFO as reducing migraine burden in select individuals at 12 months, and it is not known if the benefit extends beyond this time. This pooled analysis increases the power of the two trials assessed, and PFO closure for treating migraine, especially with frequent aura, warrants further evaluation. The findings are limited by the inclusion of selected studies.

In the CLOSE-MIG study, Mas et al. (2021) conducted a planned sub-study of individuals with migraines enrolled in the CLOSE randomized controlled trial. Of 473 participants randomized to PFO closure or antiplatelet therapy, 145 had migraines (75 with aura and 70 without aura). Sixty-seven individuals were randomized to PFO closure and antiplatelet therapy and 78 to antiplatelet therapy alone. The primary outcome was the mean annual number of migraine attacks. Secondary outcomes were the proportion of those with cessation of migraine attacks during the follow-up period, the proportion of individuals who used migraine-preventive treatment during follow-up, and the proportion of those with substantial to severe migraine-related disability at two years. During a mean follow-up of about five years, PFO closure plus antiplatelet therapy did not significantly reduce the mean annual number of migraine attacks compared to antiplatelet therapy alone for individuals with migraine both with and without aura. There were also no statistically significant differences between treatment groups regarding cessation of migraine attacks, migraine-related disability at two years, and use of migraine-preventive drugs.

In the PREMIUM study, Tobis et al. (2017) randomly assigned individuals 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 one 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 (included in the 2022 Wang et al. systematic review and meta-analysis).

In the multicenter, prospective, randomized, open-label, international PRIMA trial, Mattle et al. (2016) investigated the effect of percutaneous PFO closure for individuals 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 the 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 participants (40 Occluder, 43 control) completed a 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 the control group. In those with refractory migraine with aura and PFO, closure did not reduce overall monthly migraine days (included in the 2022 Wang et al. systematic review and meta-analysis).

In the MIST study, Dowson et al. (2009) evaluated the effectiveness of PFO closure to resolve refractory migraine headaches. One hundred forty-seven participants were randomized to transcatheter PFO closure with the STARFlex implant (n = 74) or to a sham procedure (n = 73). Participants were followed up for six months. The primary efficacy endpoint was the cessation of migraine headache 91 to 180 days after the procedure. No significant difference between implant and sham groups was observed in the primary endpoint of migraine headache cessation (3 of 74 versus 3 of 73, respectively). Secondary endpoints also were not achieved (included in the 2022 Wang et al. systematic review and meta-analysis).

Clinical Practice Guidelines

American Academy of Neurology (AAN)

An AAN practice advisory (Messé et al., 2020) makes the following recommendations for transcatheter patent foramen ovale (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 the presence of a large shunt probably is associated with the benefit from closure. Conversely, there is probably less likelihood of the 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 those a patient who are 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 diseases 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 the risk of stroke recurrence and risk of adverse events. Level B

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

Level C represents a recommendation that may be made. 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 secondary prevention of stroke state that it is reasonable to percutaneously close a PFO in individuals who meet each of the following criteria: age 18-60 years of age, nonlacunar stroke, no other identified cause, and high-risk PFO features (Kleindorfer et al., 2021).

The AHA/ASA guidelines for the primary prevention of stroke state that given the uncertainties and relatively low risk of initial stroke caused by PFO and the potential risk of antithrombotic therapy or invasive treatments, no treatment is recommended for the primary prevention of stroke in people with PFO (Meschia et al., 2014).

American Society of Echocardiography

In 2023, the American Society of Echocardiography stated that percutaneous closure of a PFO is indicated for select individuals with an embolic-appearing ischemic stroke and no other specific cause or mechanism after a thorough evaluation (Little et al., 2023).

National Institute for Health and Care Excellence (NICE)

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 of its efficacy is adequate (NICE, 2013).

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 participants) (NICE, 2010).

Society for Cardiovascular Angiography and Interventions (SCAI)

The evidence-based 2022 SCAI Guidelines for the Management of PFO makes key recommendations for PFO closure to prevent PFO-associated stroke. Thirteen recommendations are made based on five clinical scenarios, including recommendations for those with and without a history of stroke, combined antiplatelet and anticoagulant therapy, as well as other less common conditions such as platypnea-orthodeoxia syndrome, thrombophilia, and diving-related decompression illness. SCAI also states that the decision to perform PFO closure on anyone for any clinical scenario should be highly individualized and nuanced in the context of a multi-disciplinary team. Furthermore, the following recommendations are made:

- PFO closure is recommended to prevent recurrent PFO-associated stroke (strong recommendation).
- In persons experiencing migraines without a prior PFO-associated stroke, the guidelines suggest against the routine use of PFO closure for the treatment of migraines (conditional recommendation, moderate certainty of evidence).
- In persons with systemic embolism and without a prior PFO-associated stroke, in whom other embolic etiologies have been excluded, the SCAI guideline panel suggests PFO closure rather than medical therapy alone (conditional recommendation, very low certainty of evidence).
- In persons with a history of transient ischemic attack (TIA) and without a prior PFO-associated stroke, the SCAI guideline panel suggests against PFO closure (conditional recommendation, very low certainty of evidence).

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 patent foramen ovale (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 (Abbott) received FDA premarket approval (P120021) on October 28, 2016. The device is indicated 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. Additional information is available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P120021. (Accessed October 9, 2024)

As a supplement to the original PMA, the Amplatzer™ Talisman™ PFO Occluder received FDA premarket approval (P120021, S020) on September 27, 2021. The device is a line extension of the current Amplatzer™ PFO Occluder product family.

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 October 9, 2024)

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Policy History/Revision Information

Date	Summary of Changes
11/01/2025	• Created state-specific policy version for the state of Nebraska (no change to coverage guidelines)
06/01/2025	**Related Policies** • Updated reference link to reflect the current Medical Policy title for *Implantable Loop Recorders and Wearable Heart Rhythm Monitors* **Medical Records Documentation Used for Reviews** • Updated reference link to the guidelines titled *Medical Records Documentation Used for Reviews*
04/01/2025	**Medical Records Documentation Used for Reviews** • Added language to indicate: ○ Benefit coverage for health services is determined by federal, state, or contractual requirements, and applicable laws that may require coverage for a specific service

Date	Summary of Changes
	○ Medical records documentation may be required to assess whether the member meets the clinical criteria for coverage but does not guarantee coverage of the service requested; refer to the protocol titled Medical Records Documentation Used for Reviews **Supporting Information** • Updated *Clinical Evidence* and *References* sections to reflect the most current information • Archived previous policy version CS329.F

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.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.