Medical Policy

Subject:	Transcatheter Closure of Patent Foramen Ovale and Left Atrial Appendage for Stroke Prevention		
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Description/Scope

This document addresses the transcatheter approach for closure of patent foramen ovale and left atrial appendage (LAA) when performed to prevent stroke using cardiac occlusion devices, which are deployed under transesophageal echocardiographic or fluoroscopic guidance as a nonsurgical alternative to open heart surgery.

Note: This document does not address the percutaneous transcatheter closure of atrial septal defects (ASDs).

Note: Please see the following related document for additional information:

- SURG.00096 Surgical and Ablative Treatments for Chronic Headaches

Position Statement

Medically Necessary:

Transcatheter closure of a patent foramen ovale (PFO) using a U.S. Food and Drug Administration (FDA) approved device approved for that indication is considered **medically necessary** for:

A. the prevention of subsequent stroke in individuals with a history of cryptogenic stroke who have failed conventional drug therapy, (for example, warfarin), or who are not candidates for conventional drug therapy; **or**
B. in individuals 60 years old and younger with a history of cryptogenic stroke and either a) have an atrial septal aneurysm or b) have large interatrial shunt (*see definition section*).

Investigational and Not Medically Necessary:

Transcatheter closure of a patent foramen ovale for the prevention of stroke is considered **investigational and not medically necessary** when the criteria above are not met.

Transcatheter closure of a left atrial appendage is considered **investigational and not medically necessary** for all indications.

Rationale

Transcatheter Closure of Patent Foramen Ovale (PFO)

A transcatheter PFO occluder is a permanently implanted device that provides a non-surgical method for PFO closure, blocking clots from passing from the right atrium to the left atrium. There was limited early evidence to support the net benefit of transcatheter closure of a PFO, in individuals with a history of cryptogenic stroke who have failed, or who are not candidates for medical anticoagulation therapy, mostly in the form of case series. These studies reported that the risk of an embolic event after transcatheter closure was comparable to open surgical closure, with minimal complications. An advisory article by O'Gara and colleagues (2009) reviewed studies of participants that underwent transcatheter closure for the treatment of PFO for stroke prevention. There is no clear objective evidence to demonstrate that either medical therapy (antiplatelet agents or vitamin K antagonists), transcatheter closure, or open surgical closure are superior treatment options for the prevention of transient ischemic attack (TIA) or recurrent stroke in individuals with cryptogenic stroke. Randomized controlled trials are needed to establish the safety and efficacy, as well as to determine the benefits, of one treatment option over another. Therefore, the Advisory identified a need for clinicians to refer individuals with cryptogenic stroke and PFO to one of the ongoing clinical trials (O'Gara, 2009). Ongoing studies include the randomized evaluation of recurrent stroke comparing PFO to established current standard of care treatment (RESPECT) and phase III/IV clinical trials that are comparing device closure to medical therapy in individuals who have cryptogenic stroke with high risk PFO.

On October 28, 2016 the FDA granted premarket approval for the AMPLATZER™ PFO Occluder (St. Jude Medical, Plymouth, MN). The device is indicated for percutaneous transcatheter closure of a PFO to reduce the risk of recurrent ischemic stroke in individuals (predominantly between ages 18 to 60 years of age) 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.

The AMPLATZER PFO Occluder approval was based on unpublished results from the RESPECT trial, a prospective, multi-center, randomized, unblinded study that enrolled 980 participants (aged 18 to 60 years old) with a PFO who had a cryptogenic stroke (stroke from unknown cause) within the last 270 days. Participants were randomized (1:1) to either the device group with PFO closure using the AMPLATZER PFO Occluder (n=499) or the medical management group (n=481) with four medical regimens allowed (aspirin alone, Coumadin alone, clopidogrel alone, or aspirin combined with dipyridamole). While the rate of new strokes in both treatment groups was very low, there was a clinically meaningful 50% relative risk reduction in the rate of new strokes in participants using the AMPLATZER PFO Occluder plus blood-thinning medications compared to participants taking only blood-thinning medications. The safety evaluation performed during the study found an acceptable rate of adverse events. Procedure-related risks include atrial fibrillation, access site bleeding, cardiac perforation, and deep vein thrombosis. In participants undergoing an AMPLATZER PFO Occluder implantation the risk of device or implantation procedure-related serious adverse events was 4.2% with no device related deaths. The RESPECT PFO trial results showed that the AMPLATZER PFO Occluder is superior to current standard of care medical treatment in prevention of recurrent embolic stroke; the FDA concluded that probable benefits of the device outweigh the probable risks (AMPLATZER PFO Occluder Product Information, 2016).

A study by Saver and colleagues (2017) reported long-term results from the ongoing RESPECT PFO trial (NCT00465270) that compared PFO closure with AMPLATZER PFO Occluder (PFO closure group) to medical therapy alone (that is, aspirin, warfarin, clopidogrel, or aspirin combined with extended-release dipyridamole) for individuals at risk of recurrence of ischemic stroke who had cryptogenic stroke. The main contraindication to oral anticoagulation therapy included work-related and athletic activities that posed increased risk of bleeding. Median follow-up was 5.9 years with a greater dropout rate in the medical therapy only group. In the intent-to-treat

population, there were 18 participants in the PFO closure group that had recurrent ischemic stroke and in the medical therapy alone group there were 28 participants. Ten participants in the PFO closure group and 23 participants in the medical therapy alone group had recurrent ischemic stroke of undetermined cause. The authors found that:

> The rate of venous thromboembolism in both groups exceeded that in healthy populations, which suggests that persons who have had a cryptogenic stroke and also have a PFO have a mildly elevated long-term risk of venous thromboemboli. In our trial, the lower intensity of antithrombotic therapy, including the less common agents, in the PFO closure group than in the medical-therapy group may have contributed to the higher rate of venous thromboembolism in the PFO closure group.

In summary, the authors found that during the follow-up period, participants with a history of cryptogenic stroke due to PFO that underwent PFO closure had a lower rate of recurrent ischemic strokes than those that received medical therapy alone.

In 2017, Mas and colleagues reported results from the CLOSE study (NCT00562289), a multicenter, randomized (1:1:1), open-label study that evaluated participants who had cryptogenic stroke attributed to PFO with atrial septal aneurysm (defined as redundant interatrial tissue, diagnosed on the basis of a septum primum excursion greater than 10 mm on transesophageal echocardiography [TEE]) or large interatrial shunt (defined as presence of more than 30 microbubbles in the left atrium within three cardiac cycles after opacification of the right atrium, based on transthoracic echocardiography [TTE] or TEE). Participants (16 to 60 years of age) were assigned to either PFO closure plus long term antiplatelet therapy (PFO group; n=238), anticoagulation alone group (n=187), or antiplatelet-only group (n=235); participants that had identified contraindication to anticoagulation therapy or PFO closure were assigned to alternative noncontraindicated treatment or to antiplatelet therapy. There were no reported strokes among the PFO group, 14 strokes occurred among the antiplatelet-only group (HR, 0.03; 95% CI, 0 to 0.26; P<0.001). Procedural complications were reported in 14 (5.9%) participants in the PFO closure group. Among the groups, adverse events did not differ significantly. The authors concluded that:

> In conclusion, among patients 16 to 60 years of age who had had a recent cryptogenic stroke attributed to PFO with an associated atrial septal aneurysm or large interatrial shunt, the rate of stroke recurrence was lower among those assigned to PFO closure plus long-term antiplatelet therapy than with antiplatelet therapy alone. The effects of oral anticoagulant therapy as compared with antiplatelet therapy on the risk of stroke recurrence could not be determined.

In April 2018, the FDA granted premarket approval for the GORE® CARDIOFORM Septal Occluder (W.L. Gore & Associates, Inc., Flagstaff, AZ), a permanently implanted device indicated in PFO to reduce the risk of recurrent ischemic stroke in individuals (predominantly between 18-60 years of age) 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. The device is contraindicated in individuals who are unable to take antiplatelet or anticoagulation therapy. The FDA approval is based on data reported by Sondergaard and colleagues (2017) from the REDUCE (NCT00738894) study, an ongoing, international, prospective, randomized (2:1 ratio), controlled, open-label trial that evaluated participants who underwent PFO closure plus antiplatelet therapy (PFO group; n=441) or received antiplatelet therapy alone (antiplatelet-only group; n=223). During a median follow-up of 3.2 years, 6 participants (1.4%) in the PFO group and 12 participants (5.4%) in the antiplatelet-only group had a

clinical ischemic stroke (HR, 0.23; 95% CI, 0.09 to 0.62; P=0.002). There was a lower incidence of brain infarctions reported in the PFO group (n=22; 5.7%) versus the antiplatelet group only (n=20; 11.3%). Fewer serious adverse events were reported among the PFO group than the antiplatelet-only group, 23.1% versus 27.9% respectively. The authors concluded that:

> In conclusion, among patients who had cryptogenic stroke most likely attributed to PFO, the risk of recurrent stroke and now brain infarction were significantly lower with closure of the PFO plus antiplatelet therapy than with antiplatelet therapy alone.

Lee and colleagues (2018) reported results from the DEFENSE PFO (Device Closure Versus Medical Therapy for Cryptogenic Stroke Patients with High-Risk Patent Foramen Ovale) trial. The study enrolled 120 participants with history of cryptogenic stroke and high-risk PFO, and participants underwent randomization and were divided between PFO closure group and medication-only group. The study primary endpoint was a composition of stroke, vascular death, or thrombosis in myocardial infarction (TIMI) - defined major bleeding during a 2-year follow-up period. All participants in the PFO group had a successful PFO closure, therefore no event of primary endpoint occurred in the PFO closure group. The primary endpoint occurred in 6 of 60 participants in the medication-only group; 2-year event rate: 12.9% (95% CI), 2-year rate of ischemic stroke: 10.5% (p=0.023). "The events in the medication-only group included ischemic stroke (n=2), and transient ischemic attack (n=1). Nonfatal procedural complications included development of atrial fibrillation (n=2), pericardial effusion (n=1), and pseudoaneurysm (n=1)."

> In patients who had a recent cryptogenic stroke attributed to PFO with a large PFO, atrial septal aneurysm, or hypermobility, the rate of primary composite endpoint as well as stroke recurrence was lower with combined PFO closure in combination with medication than with medication therapy alone.

Transcatheter Closure of Left Atrial Appendage (LAA)

Transcatheter closure of an LAA is a new treatment strategy that prevents travel of an LAA thrombus out of the LAA in individuals with non-valvular atrial fibrillation (AF). The LAA closure system is introduced in the right atrium and then passed into the left atrium through a PFO or through a puncture hole. The Holmes and colleagues (2009) randomized, non-inferiority trial compared LAA closure using the WATCHMAN™ LAA Closure Device (Boston Scientific, Marlborough, MA) versus warfarin therapy for prevention of stroke in individuals with AF. The study evaluated efficacy between the interventional group and the warfarin group based upon the primary endpoint of reported cardiovascular death (n=5 vs. n=10), all types of stroke (n=16 vs. n=12), and systemic embolism (n=2 vs. n=0). Researchers reported a higher occurrence of primary safety events in the interventional group compared to the warfarin therapy group; serious adverse events included major bleeding, pericardial effusion and device embolization. The authors concluded:

> Thus, our strategy for closing the LAA was non-inferior to warfarin therapy in terms of primary efficacy endpoint of all stroke, cardiovascular death, and systemic embolism. Although there is a higher initial safety event rate for device implantation, adverse events were without long term sequelae for most patients. Closure of the LAA might provide an alternative strategy to chronic warfarin therapy for stroke prophylaxis in patients with non-valvular atrial fibrillation.

A study by Reddy and colleagues (2011) reported on preliminary outcomes from the Watchman LAA System for Embolic Protection in Patients with AF (PROTECT AF) trial and Continued Access PROTECT AF Registry (CAP Registry). Although with improved procedural experience there was a decline in safety events reported, there remains a higher risk of complications. The FDA granted PMA approval March 2015 for the WATCHMAN LAA Closure Device in individuals with non-valvular AF in facilities equipped for heart surgery as an alternative option to long-term warfarin therapy. According to the manufacturer, Boston Scientific Corporation:

> WATCHMAN is indicated to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who are at increased risk for stroke and systemic embolism based on $CHADS_2$ or CHA_2DS_2-VASc scores, are deemed by their physicians to be suitable for warfarin; and have an appropriate rationale to seek a non-pharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared to warfarin.

Reddy and colleagues (2014) reported long-term outcomes of the PROTECT AF trial. The randomized, multicenter study enrolled 707 participants with nonvalvular AF and at least one additional stroke risk factor ($CHADS_2$ score greater than or equal to 1) who were randomized 2:1 to undergo left atrial appendage closure with the WATCHMAN LAA Closure Device (n=463, treatment group) or warfarin therapy (n=244, control group). The trial demonstrated a noninferior rate of cardiovascular death, stroke or systemic embolism, compared with warfarin alone. The authors concluded:

> After 3.8 years of follow-up among patients with nonvalvular AF at elevated risk for stroke, percutaneous LAA closure met criteria for both noninferiority and superiority, compared with warfarin, for preventing the combined outcome of stroke, systemic embolism, and cardiovascular death, as well as superiority for cardiovascular and all-cause mortality.

A multicenter, randomized, clinical trial PREVAIL assessed safety and efficacy of the WATCHMAN LAA Closure device versus long-term warfarin in individuals with nonvalvular AF who had a $CHADS_2$ score of 2 or more ($CHADS_2$ score of 1 and another risk factor were eligible) (Holmes, 2014). Exclusion criteria included contraindication to warfarin or aspirin, stroke/transient ischemic attack within the last 90 days, symptomatic carotid disease, PFO or atrial septal defect (ASD), thromboembolism or bleeding. PREVAIL enrolled 407 participants, assigned randomly (2:1 ratio) to the device group (n=269) or control group (n=138). Unlike the PROTECT AF trial the PREVAIL did not demonstrate noninferiority in overall efficacy. The authors report that:

> At 18 months, the rate of the first co primary efficacy endpoint (composite of stroke, systemic embolism [SE], and cardiovascular/unexplained death was 0.064 in the device group versus 0.063 in the control group (rate ratio 1.07 [95% credible interval (Crl): 0.57 to 1.89]) and did not achieve the pre-specified criteria noninferiority (upper boundary of 95% Crl ≥1.75). The rate for the second co-primary efficacy endpoint (stroke or SE > 7 days' post randomization) was 0.0253 versus 0.0200 (risk difference 0.0053 [95% Crl: -0.0190 to 0.0273], achieving noninferiority. Early safety events occurring in 2.2% of the Watchman arm, significantly lower than in PROTECT AF, satisfying the pre-specified safety performance goal. Using a broader, more inclusive definition of adverse events, these still were lower in PREVAIL (Watchman LAA Closure Device in Patients With Atrial Fibrillation Versus Long Term Warfarin Therapy) trial than in PROTECT AF (4.2% vs. 8.7%; p=0.004). Pericardial effusions requiring surgical repair decreasing from 1.6% to 0.4% (p=0.36), although the number of events was small.

> LAA occlusion was noninferior to warfarin for ischemic stroke prevention or SE >7 days post-procedure. Although noninferiority was not achieved for overall efficacy, event rates were low and numerically comparable in both arms. Procedural safety has significantly improved. This trial provides additional data that LAA occlusion is a reasonable alternative to warfarin therapy for stroke prevention in patients with NVAF who do not have an absolute contraindication to short-term warfarin therapy.

Two randomized controlled trials have compared use of the WATCHMAN device for LAA closure in individuals with AF eligible for anticoagulation therapy. The peer-reviewed published literature suggests that the WATCHMAN is associated with an increased periprocedural ischemic stroke risk. There is limited evidence supporting the net benefit of transcatheter closure of an LAA with the WATCHMAN LAA Closure device, in individuals with non-valvular AF who are deemed eligible for systemic anticoagulation. Further studies are needed to determine if the long-term risk of systemic anticoagulation exceeds the periprocedural risk of device implantation.

Reddy and colleagues (2017) reported final results from the PREVAIL trial and as part of a meta-analysis with PROTECT AF trial followed for 5 years. Participants underwent LAAC with the WATCHMAN or treatment with warfarin. The authors reported results:

> For the PREVAIL trial, the first composite coprimary endpoint of stroke, systemic embolism (SE), or cardiovascular/unexplained death did not achieve noninferiority (posterior probability for noninferiority = 88.4%), whereas the second coprimary endpoint of post-procedure ischemic stroke/SE did achieve noninferiority) posterior probability for noninferiority = 97.5%); the warfarin arm maintained an unusually low ischemic stroke rate (0.73%). In the meta-analysis, the composite endpoint was similar between groups (hazard ratio [HR]: 0.820; p=0.27), as were all-stroke/SE (HR: 0.961; p=0.87). The ischemic stroke/SE rate was numerically higher with LAAC, but this difference did not reach statistical significance (HR: 1.71; p=0.080). However, differences in hemorrhagic stroke, disabling/fatal stroke, cardiovascular/unexplained death, all-cause death, and post-procedure bleeding favored LAAC (HR: 0.20; p=0.0022; HR: 0.45; p=0.03; HR: 0.59; p=0.027; HR: 0.73; p=0.0003, respectively).

The 2019 American Heart Association (AHA)/ American College of Cardiology (ACC)/ Heart Rhythm Society (HRS) focused update of the 2014 AHA/ACC/HRS guidelines for the management of atrial fibrillation issued a category IIb recommendation, indicating "percutaneous LLA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term anticoagulation" (January, 2019). The authors further concluded:

> Oral anticoagulation remains the preferred therapy for stroke prevention for most patients with AF and elevated stroke risk. However, for patients who are poor candidates for long-term oral anticoagulation (because of the propensity for bleeding or poor drug tolerance or adherence), the Watchman device provides an alternative… A number of unresolved issues remain, including the optimal patient selection and periprocedural antithrombotic regimen.
>
> The current FDA labeling specifies that patients should be deemed suitable for anticoagulation and, in particular, a period of periprocedural anticoagulation. Patients unable to take oral anticoagulation were excluded from the Watchman RCTs. However, there is increasing experience outside the United States

with LAA closure in oral anticoagulation–ineligible patients using an antiplatelet regimen only, and this is the focus of an ongoing RCT.

Boersma and colleagues (2019) reported periprocedural, 2-year outcome data from the prospective, multicenter, multinational EWOLUTION registry (Evaluating Real-life Clinical Outcomes in Atrial Fibrillation Patients Receiving the WATCHMAN Left Atrial Appendage Closure Technology). Overall safety and efficacy data are presented in a subgroup of participants who are at very high-risk of stroke or bleeding, including those with a history of ischemic and hemorrhagic stroke and those with prior bleeding episodes. In total, 1020 participants (age 73.4±8.9 years) underwent implantation with the WATCHMAN device. While 72 percent of participants were deemed unsuitable for oral anticoagulation by their physicians, data was not readily provided on the reason for contraindication to anticoagulation therapy. At the time of hospital discharge, after successful WATCHMAN placement, 94% of participants were on some form of anticoagulation, and by study-end, 86% were using some form of anticoagulation therapy (8% were using oral anticoagulation, 7% were on dual antiplatelet therapy and 71% were on single antiplatelet therapy). At 2-year follow-up, 16.4% (n=161) of participants that underwent a WATCHMAN LAAC had died; 4.5% (n=46) had a cardiovascular reason (most commonly reported was heart failure) and 1% (n=10) were from fatal bleeding (6 were gastrointestinal bleeds while the other 4 were cerebral; only 1 participant was not taking an anticoagulant at time of death). The composite risk of ischemic stroke/TIA/embolic event was 2.0/100 patient-years (46 thromboembolic events in 35 patients, of which 22 were ischemic stroke (5 disabling), 23 were TIA, and one was an systemic embolism), which the authors compare to a historical rate of 10.0/100 patient-years based on CHA_2DS_2-VASc (congestive heart failure, hypertension, 75 years of age and older, diabetes mellitus, previous stroke or transient ischemic attack, vascular disease 65 to 74 years of age, female; left ventricular ejection fraction) score. In 835 participants with imaging of the LAA, a total of 34 cases of device-related thrombus (4.1%) were observed, resulting in 21 participants initiating treatment, and 1 major GI bleed which resolved. By study-end, resolution occurred in all but 1 participant (6 were lost to followed-up), no subsequent reports of embolic events were reported. Stroke and bleeding rates did not appear to differ by anticoagulation treatment strata, although it is difficult to draw conclusions based on the registry nature of the study.

In summary, the study is limited by its registry design; determining the absolute or relative benefit and risks of the WATCHMAN device versus standard treatment in the population studied is unclear given the lack of a randomized comparable prospective treatment arm. A high number of participants enrolled in EWOLUTION also died during the two-years of follow-up. Furthermore, a majority of individuals remained on some form of anticoagulation therapy despite being deemed unsuitable for short- or long-term oral anticoagulation at the time of implant, thus continued use of any form of oral anticoagulation may play a role in thromboembolic event prevention.

Ongoing trials include the PREVAIL (CAP2) continued access trial (NCT01760291) evaluating the long-term safety and efficacy of the WATCHMAN LAA Closure Device up to 5 years in 578 participants, with estimated study completion in 2019. The ASAP-TOO (assessment of the WATCHMAN device in patients unsuitable for oral anticoagulation) trial is a multicenter prospective randomized trial designed to establish the safety and effectiveness of the WATCHMAN LAAC device in individuals with nonvalvular AF that are considered ineligible for oral anticoagulants (NCT02928497); the estimated study completion date is December 2023 (Holmes, 2017). Another trial is evaluating the safety and effectiveness of the WATCHMAN LAA Closure Device compared to single antiplatelet therapy or no therapy at the discretion of the study physician and one comparing the WATCHMAN LAA Closure Device to the LARIAT Suture Delivery Device (SentreHEART®, Redwood City, CA) used as LAA

device occlusion for the treatment of AF, with estimated study completion in late 2018. Presently, no other LAA closure system has been granted final approval by the FDA for this indication.

In conclusion, oral anticoagulation remains the preferred therapy for stroke prevention for most individuals with AF and elevated stroke risk. While those who are poor candidates for long-term oral anticoagulation have been proposed as eligible candidates for WATCMAN device placement, observational data suggests that most individuals remain on anticoagulant therapy nonetheless, and the relative benefit versus harms of WATCMAN implantation versus standard care are unclear. Long-term follow-up is required to determine the safety of left atrial appendage occlusion.

Background/Overview

Patent Foramen Ovale (PFO)
PFO describes the persistence of a component of the fetal circulation between the right and left atrium. Although PFOs are found in 10-15% of adults, they are typically clinically insignificant. However, they may be associated with paradoxical embolus, in which an embolus arising in the venous circulation gains access to the arterial circulation through the PFO. It is estimated that individuals with a history of PFO and paradoxical embolism have a 3.4% and 3.8% yearly risk of recurrent stroke or transient ischemic attack. Therefore, there has been interest in either open surgery or transcatheter approaches to close the PFO, in individuals with a history of embolic stroke of unknown cause. Treatment alternatives include chronic warfarin therapy, based, in part, on the theory that clotting disorders may be present in individuals with embolic stroke. To date, the AMPLATZER PFO Occluder is the only device which has received FDA approval for transcatheter closure of a PFO to reduce risk of stroke in individuals who had cryptogenic stroke due to presumed paradoxical embolism, after a comprehensive clinical evaluation (by neurologist and cardiologist) has been conducted to rule out other causes of stroke. Contraindications for the AMPLATZER PFO Occluder include: individuals with active endocarditis, untreated infection, other heart defects, or a tumor or blood clot in the vessels along the path of the heart. The GORE® HELEX® Septal Occluder/ GORE® Septal Occluder (W.L. Gore & Associates, Inc., Flagstaff, AZ) provide another potential treatment option for PFO closure in individuals who had a cryptogenic stroke.

Left Atrial Appendage
In the U.S., AF is the most prevalent sustained cardiac arrhythmia, resulting in significantly greater risk of stroke due to migration of clots that may form in the LAA. As confirmed by echocardiography and autopsy, LAA is identified as a leading source of thrombi in individuals with non-valvular AF. By closing off the LAA, the occlusion device is designed to reduce risk of stroke and other cardiovascular complications. The WATCHMAN LAA Closure Device is the first of its kind treatment giving individuals with non-valvular AF an alternative option to long-term warfarin therapy. The AMPLATZER™ Cardiac Plug (ACP) (St. Jude Medical, St. Paul, MN) and LARIAT® Suture Delivery Device and Accessories provide other potential alternatives to closure, currently being studied as alternatives to standard anticoagulation therapy.

The CHADS (cardiac failure, hypertension, age, diabetes, stroke) score is a risk assessment tool that is based on a point system, in which 2 points are assigned for a history of stroke or TIA, and 1 point each is assigned for age over 75 and a history of hypertension, diabetes or recent HF. The adjusted stroke rate can be assessed based on the CHADS score. For example, a CHADS score of 2 is associated with an adjusted stroke rate of 4% per year (Fuster, 2006).

Definitions

Atrial fibrillation: A condition where there is disorganized electrical conduction in the atria, resulting in ineffective pumping of blood into the ventricle.

Atrial septal aneurysm: Redundant interatrial tissue, diagnosed on the basis of a septum primum excursion greater than 10 mm on TEE.

Cryptogenic stroke: A stroke or transient ischemic attack of obscure or unknown origin.

Large interatrial shunt: Presence of more than 30 microbubbles in the left atrium within three cardiac cycles after opacification of the right atrium, based on TTE or TEE.

Left atrial appendage (LAA): A muscular pouch attached to the upper portion of the left atrium.

Patent foramen ovale (PFO): A component of the fetal circulation that consists of a communication between the left and right atria that generally closes after birth; if an opening remains after birth, the possibility of an embolus (blood clot that breaks free in the blood) getting to the brain exists, resulting in a stroke or transient ischemic attack.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services may be Medically Necessary when criteria are met:

CPT

93580	Percutaneous transcatheter closure of congenital interatrial communication (ie, Fontan fenestration, atrial septal defect) with implant [when specified as closure of patent foramen ovale]

ICD-10 Procedure

02U53JZ	Supplement atrial septum with synthetic substitute, percutaneous approach [when specified as closure of patent foramen ovale]

ICD-10 Diagnosis

G45.9	Transient cerebral ischemic attack, unspecified
I25.3	Aneurysm of heart
I51.0	Cardiac septal defect, acquired
I63.81-I63.89	Other cerebral infarction
I63.9	Cerebral infarction, unspecified
Q21.1	Atrial septal defect [when specified as patent foramen ovale]

Z86.73	Personal history of transient ischemic attack (TIA), and cerebral infarction without residual deficits

When services are Investigational and Not Medically Necessary:
For the procedure and diagnosis codes listed above when criteria are not met, or when the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

When services are also Investigational and Not Medically Necessary:
When the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT	
33340	Percutaneous transcatheter closure of the left atrial appendage with endocardial implant, including fluoroscopy, transseptal puncture, catheter placement(s), left atrial angiography, left atrial appendage angiography, when performed, and radiological supervision and interpretation
ICD-10 Procedure	
02L73DK	Occlusion of left atrial appendage with intraluminal device, percutaneous approach
ICD-10 Diagnosis	
	All diagnoses

References

Peer Reviewed Publications:

1. Bartus K, Han FT, Bednarek J, et al. Percutaneous left atrial appendage suture ligation using the LARIAT device in patients with atrial fibrillation: initial clinical experience. J Am Col Cardiol. 2013; 62(2):108-118.
2. Boersma LV, Ince H, Kische S, et al. Evaluating real-world clinical outcomes in atrial fibrillation patients receiving the WATCHMAN left atrial appendage closure technology. Final 2-year outcome data of the EWOLUTION trial focusing on history of stroke and hemorrhage. Cir Arrhythm Electrophysiol. 2019; 12:e006841.
3. Holmes DR, Doshi SK, Kar S, et al. Left atrial appendage closure as an alternative to warfarin for stroke prevention in atrial fibrillation. A patient-level meta-analysis. J Am Coll Cardiol. 2015; 65(24):2614-2623.
4. Holmes DR, Kar S, Price MJ, et al. Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. J Am Coll Cardiol. 2014; 64(1):1-12.
5. Holmes DR, Reddy VY, Buchbinder M, et al. The assessment of the Watchman Device in patients unsuitable for oral anticoagulation (ASAP-TOO) trial. Am Heart J. 2017; 189:68-74.
6. Holmes DR, Reddy VY, Turi ZG, et al.; PROTECT AF Investigators. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomized non-inferiority trial. Lancet. 2009; 374(9689):534-542.
7. Kapadia SR. Patent foramen ovale closure: historical perspective. Cardiol Clin. 2005; 23(1):73-83.
8. Kay JD, O'Laughlin MP, Ito K, et al. Five-year clinical and echocardiographic evaluation of the Das Angel Wings atrial septal occluder. Am Heart J. 2004; 147(2):361-368.

9. Kuijpers T, Spencer FA, Siemieniuk RA, et al. Patent foramen ovale closure, antiplatelet therapy or anticoagulation therapy alone for management of cryptogenic stroke? A clinical practice guideline. Brit J Med. 2018; 362:k2515.
10. Lee PH, Song JK, Kim JS, et al. Cryptogenic stroke and high-risk patent foramen ovale: the DEFENSE-PFO trial. J Am Coll Cardiol. 2018; 71(20):2335-2342.
11. Mas JL, Derumeaux B, Guillon E, et al. Patent foramen ovale closure or anticoagulation vs. antiplatelets after stroke. N Eng J Med. 2017; 377(11):1011-1021.
12. O'Gara PT, Messa SR, Tuzcu EM, et al. Percutaneous device closure of patent foramen ovale for secondary stroke prevention: a call for completion of randomized clinical trials. A science advisory from the American Heart Association/American Stroke Association and the American College of Cardiology Foundation. J Am Coll Cardiol. 2009; 53(21):2014-2018.
13. Onorato E, Melzi G, Casilli F, et al. Patent foramen ovale with paradoxical embolism: mid-term results of transcatheter closure in 256 patients. J Interv Cardiol. 2003; 16(1):43-50.
14. Patel HT, Hijazi ZM. Pediatric catheter interventions: a year in review 2004-2005. Curr Opin Pediatr. 2005; 17(5):568-573.
15. Pisters R, Lane DA, Nieuwlaat R, et al. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation. The Euro heart survey. Chest. 2010; 138(5):1093-1100.
16. Price MJ, Reddy VY, Valderrabano M, et al. Bleeding outcomes after left atrial appendage closure compared with long-term warfarin. JACC. 2015; 8(15):1925-1932.
17. Reddy VY, Doshi SK, Kar S, et al. 5-Year outcomes after left atrial appendage closure. From the PREVAIL and PROTECT AF trials. J Am Coll Cardiol. 2017; 70(24):2964-2975.
18. Reddy VY, Doshi SK, Sievert H, et al. Percutaneous left atrial appendage closure for stroke prophylaxis in patients with atrial fibrillation: 2.3-year follow-up of the PROTECT AF (Watchman Left Atrial Appendage System for embolitic protection in patients with atrial fibrillation) Trial. Stroke. 2013; 127(6):720-729.
19. Reddy VY, Holmes D, Doshi SK, et al. Safety of percutaneous left atrial appendage closure: results from the Watchman left atrial appendage system for embolic protection in patients with AF (PROTECT AF) clinical trial and the Continued Access Registry. Circulation. 2011; 123(4):417-424.
20. Reddy VY, Mobius-Winkler S, Miller MA, et al. Left atrial appendage closure with the Watchman device in patients with a contraindication for oral anticoagulation: the ASAP study (ASA Plavix Feasibility Study with Watchman Left Atrial Appendage Closure Technology). J Am Coll Cardiol. 2013; 61(25):2551-2556.
21. Reddy VY, Sievert H, Halperin J, et al. Percutaneous left atrial appendage closure vs warfarin for atrial fibrillation: a randomized clinical trial. JAMA. 2014; 312(19):1988-1998.
22. Ries M, Kampmann C, Rupprecht HJ, et al. Nickel release after implantation of the Amplatzer occluder. Am Heart J. 2003; 145(4):737-741.
23. Rome JJ, Kreutzer J. Pediatric interventional catheterization: reasonable expectations and outcomes. Pediatr Clin North Am. 2004; 51(6):1589-1610, viii.
24. Saver JL, Carrol JD, Thaler DE, et al. Long-term outcomes of patent foramen ovale closure or medical therapy after stroke. N Engl J Med. 2017; 377(11):1022-1032.
25. Sondergaard L, Kasner SE, Rhodes JF, et al. Patent foramen ovale closure or antiplatelet therapy for cryptogenic stroke. N Eng J Med. 2017; 377(11):1033-1042.
26. Windecker S, Wahl A, Chatterjee T, et al. Percutaneous closure of patent foramen ovale in patients with paradoxical embolism: long term risk of recurrent thromboembolic events. Circulation. 2000; 101(8):893-898.

Government Agency, Medical Society, and Other Authoritative Publications:

1. AGA Medical Corporation. Respect PFO Clinical Trial. NCT00465270. Last updated February 19, 2019. Available at: http://www.clinicaltrials.gov/ct2/show/study/NCT00465270?term=respect+and+pfo&rank=1. Accessed on September 23, 2019.
2. Boston Scientific Corporation. Continued access to PREVAIL (CAP2). NLM Identifier: NCT01760291. Last updated on July 31, 2019. Available at: https://clinicaltrials.gov/ct2/show/NCT01760291?term=PREVAIL+WATCHMAN&rank=2. Accessed on September 23, 2019.
3. Boston Scientific Corporation. Evaluation of the WATCHMAN LAA Closure Device in patients with atrial fibrillation versus long term warfarin therapy (PREVAIL). NLM Identifier: NCT01182441. Last updated on July 26, 2018. Available at: https://clinicaltrials.gov/ct2/show/NCT01182441?term=PREVAIL+WATCHMAN&rank=1. Accessed on September 23, 2019.
4. Boston Scientific Corporation. WATCHMAN Left Atrial Appendage System for embolic PROTECTion in patients with atrial fibrillation. NLM Identifier: NCT00129545. Last updated on May 15, 2015. Available at: https://clinicaltrials.gov/ct2/show/NCT00129545?term=PROTECT+AF&rank=1. Accessed on September 23, 2019.
5. Dhanunjaya Lakkireddy, MD, FACC, University of Kansas Medical Center Research Institute. Safety and Efficacy of Left Atrial Appendage Occlusion Devices. NCT01695564. Last updated May 2, 2019. Available at: http://clinicaltrials.gov/ct2/show/NCT01695564?term=LARIAT&rank=1. Accessed on September 23, 2019.
6. Fuster V, Rydén LE, Cannom DS, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation): developed in collaboration with the European Heart Association and the Heart Rhythm Society. Circulation. 2006; 114(7):e257-e354. Available at: http://circ.ahajournals.org/content/114/7/e257.long. Accessed on September 23, 2019.
7. Jae-Kwan Song. Device Closure versus medical therapy for cryptogenic stroke patients with high-risk patent foramen ovale (DEFENSE-PFO). NLM Identifier: NCT01550588. Last updated June 29, 2017. Available at: https://clinicaltrials.gov/ct2/show/NCT01550588. Accessed on September 23, 2019.
8. January CT, Wann S, Alpert JS, et al. 2014 AHA/ACC/HRS practice guideline. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. A report of the American College of Cardiology/American Heart Association Task force on Practice Guidelines and the Heart Rhythm Society. Circulation. 2014; 130:e199-e267.
9. January CT, Wann SL, Calkins H, et al. 2019 AHA/ACC/HRS Focused updated of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation. A report of the American College of Cardiology/American Heart Association Task force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2019; pii: S0735-1097(19)30209-8.
10. Lip GY, Andreotti F, Fauchier L, et al. Bleeding risk assessment and management in atrial fibrillation patients: a position document from the European Heart Rhythm Association, endorsed by the European Society of Cardiology Working Group on Thrombosis. Europace. 2011; 13(5):723-746.
11. Masoudi FA, Caukins H, Kavinsky CJ, et al. 2015 ACC/HRS/SCAI left atrial appendage occlusion device societal overview: a professional societal overview from the American College of Cardiology, Heart Rhythm Society, and Society for Cardiovascular Angiography and Interventions. Catheter Cardiovasc Interv. 2015; 86(5):791-807.

12. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics- 2015 update: a report from the American Heart Association. Circulation. 2015; 131:e29-e322.
13. St. Jude Medical. AMPLATZER Cardiac Plug (ACP) registry-long term follow-up protocol (ACPR). NLM Identifier: NCT01786486. Last updated on February 04, 2019. Available at: https://clinicaltrials.gov/ct2/show/NCT01786486?term=AMPLATZER+AND+left+atrial+appendage&rank=1. Accessed on September 23, 2019.
14. St. Jude Medial. RESPECT PFO clinical trial. NLM Identifier: NCT00465270. Last updated on February 18, 2019. Available at: https://www.clinicaltrials.gov/ct2/show/NCT00465270?term=NCT00465270&rank=1. Accessed on September 23, 2019.
15. U.S. Food and Drug Administration (FDA). Premarket Approval (PMA). AMPLATZER PFO Occluder. No. P120021. Rockville, MD: FDA. October 28, 2016. Accessible at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P120021. Accessed on September 23, 2019.
16. U.S. Food and Drug Administration (FDA) Premarket Approval (PMA). GORE® CARDIOFORM Septal Occluder. No. P050006/S060. Rockville, MD: FDA. March 30, 2018. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P050006S060. Accessed on September 23, 2019.
17. U.S. Food and Drug Administration (FDA). Premarket Approval (PMA). Watchman™ Left Atrial Appendage Closure Device. No. P130013. Rockville, MD: FDA. March 13, 2015. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf13/p130013b.pdf. Accessed on September 23, 2019.
18. W.L. Gore & Associates. Gore® Helex® septal occlude/GORE® CARDIOFORM Septal Occlude for patent foramen ovale (PFO) closure in stroke patients - the Gore REDUCE clinical study (HLX 06-03). NLM Identifier: NCT00738894. Last updated August 9, 2018. Available at: https://clinicaltrials.gov/ct2/show/NCT00738894. Accessed on September 23, 2019.

Websites for Additional Information

1. American Heart Association. Patent foramen ovale (PFO). Revised March 31, 2017. Available at: http://www.heart.org/HEARTORG/Conditions/More/CardiovascularConditionsofChildhood/Patent-Foramen-Ovale-PFO_UCM_469590_Article.jsp. Accessed on September 23, 2019.
2. American Heart Association website. Available at: http://www.heart.org. Accessed on April 8, 2019.
3. Centers for Disease Control and Prevention. Atrial fibrillation fact sheet. Last updated August 22, 2017. Available at: https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_atrial_fibrillation.htm. Accessed on September 23, 2019.

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AMPLATZER PFO Occluder
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LAA
LARIAT Suture Delivery Device
Left Atrial Appendage

Patent Foramen Ovale
PFO
Starflex
WATCHMAN LAA Closure Device

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Revised	11/07/2019	Medical Policy & Technology Assessment Committee (MPTAC) review. Clarified age and size of interatrial shunt in MN criteria for transcatheter closure of PFO. Updated Rationale, Definitions, References and Websites sections.
Reviewed	06/06/2019	MPTAC review. Updated Rationale, References and Websites sections. Updated Coding section; removed ICD-10-PCS 02L73CK (not applicable)
Revised	07/26/2018	MPTAC review. Revised MN statement for transcatheter closure of PFO using FDA approved device for individuals with a history of cryptogenic stroke who are under age 60 when criteria met. Updated Rationale, References and Websites sections. Updated Coding section to include 10/01/2018 ICD-10-CM changes (added I63.81-I63.89 replacing I63.8).
Revised	05/03/2018	MPTAC review. The document header wording updated from "Current Effective Date" to "Publish Date." Note added to description to clarify that the document does not address the percutaneous transcatheter closure of atrial septal defects (ASDs). Revised MN statement for transcatheter PFO closure, removing information on specific device. Updated Description, Rationale, Background, References and Websites sections.
Reviewed	08/03/2017	MPTAC review. Updated Rationale, References and Websites sections.
Revised	02/02/2017	MPTAC review. Clarified MN criteria for transcatheter closure of a PFO. Updated Rationale, Background, Index, References and Websites sections.
	01/01/2017	Updated Coding section with 01/01/2017 CPT changes; removed 0281T deleted 12/31/2016.
Reviewed	02/04/2016	MPTAC review. Updated References and Websites sections.
Reviewed	11/05/2015	MPTAC review. Updated Background, Index and Reference sections. Removed ICD-9 codes from Coding section.
Reviewed	08/06/2015	MPTAC review. Description, Rationale, Background, Index, References and Websites sections updated.
Reviewed	02/05/2015	MPTAC review. Updated Rationale, Reference, Websites and Index sections.
Reviewed	02/13/2014	MPTAC review. Updated Websites.
Reviewed	02/14/2013	MPTAC review. Description, Rationale, Background, Index, References and Websites Updated.
Reviewed	02/16/2012	MPTAC review. Updated References and Websites.
	01/01/2012	Updated Coding section with 01/01/2012 CPT changes.

Revised	02/17/2011	MPTAC review. Title change. Position statements for PFO clarified, Added investigational and not medically necessary statement for LAA. Removed position statements for patent ductus arteriosus, fenestrated Fontan procedure, atrial and ventricular defects. Transferred content addressing Transmyocardial/Perventricular transcatheter device closure of ventricular septal defects to a new medical policy, SURG.00123. Updated Description, Rationale, Definitions, Coding, Index, References and Websites.
Revised	08/19/2010	MPTAC review. Clarified medically necessary statement addressing transcatheter closure of ventricular septal defect (VSD) and secundum atrial septal defect (ASD). Updated Websites and References.
Revised	05/13/2010	MPTAC review. Changed title to "Transcatheter Closure of Cardiac Defects". Removed "complex" from ventricular septal defect (VSD) medically necessary criteria. Transcatheter closure investigational and not medically necessary position statement clarified. Definition, Websites and References updated.
Reviewed	02/25/2010	MPTAC review. Rationale, Background, Coding and References updated.
Reviewed	02/26/2009	MPTAC review. References updated.
Reviewed	02/21/2008	MPTAC review. Updated references. The phrase "investigational/not medically necessary" was clarified to read "investigational and not medically necessary." This change was approved at the November 29, 2007 MPTAC meeting.
Revised	03/08/2007	MPTAC review. A position statement was added to state that transmyocardial/perventricular device closure of VSDs is considered investigational/not medically necessary. Rationale section was also updated to include the FDA withdrawal of HDE marketing approval for the CardioSEAL STARFlex and AMPLATZER PFO occluders. Coding was also updated to add the new CPT Category III codes (0166T, 0167T) effective 01/01/2007.
Reviewed	06/08/2006	MPTAC review. References were updated, including information regarding current FDA-approved devices.
Revised	7/14/2005	MPTAC review. Revision based on Pre-merger Anthem and Pre-merger WellPoint Harmonization.

Pre-Merger Organizations	Last Review Date	Document Number	Title
Anthem, Inc.	01/28/2004	SURG.00032	Transcatheter Closure of Patent Ductus Arteriosus, Foramen Ovale, Closure of a Fenestrated Fontan Procedure, and Atrial and Ventricular Septal Defects
WellPoint Health Networks, Inc.	09/23/2004	3.04.04	Catheter Closure for Atrial Septal Defect and Patent Foramen Ovale
	06/24/2004	3.04.25	Transcatheter Closure for Patent Ductus Arteriosus