



# Louisiana

## Percutaneous Left-Atrial Appendage Closure Devices for Stroke Prevention in Atrial Fibrillation

**Policy #** 00296

**Original Effective Date:** 05/18/2011

**Current Effective Date:** 10/17/2018

*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.*

Based on review of available data, the Company may consider the use of a device with U.S. Food and Drug Administration (FDA) approval for percutaneous left atrial appendage closure (eg, the Watchman)<sup>™‡</sup> for the prevention of stroke in patients with atrial fibrillation (AF) to be **eligible for coverage** when the following criteria are met:

### Patient Selection Criteria

Coverage eligibility will be considered when the following criteria has been met:

- There is an increased risk of stroke and/or systemic embolism based on CHADS<sub>2</sub> score (≥ 2) or CHA<sub>2</sub>DS<sub>2</sub>-VASc score (≥ 2), and systemic anticoagulation therapy is recommended; AND
- The long-term risks of systemic anticoagulation outweigh the risks of the device implantation (e.g., HAS-BLED score ≥ 3)

### **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 the use of a device with FDA approval for percutaneous left atrial appendage closure (eg, the Watchman) for stroke prevention in patients who do not meet the above criteria to be **investigational**.\*

Based on review of available data, the Company considers the use of other percutaneous left atrial appendage closure devices, including but not limited to the Lariat<sup>®‡</sup>, and Amplatzer<sup>®‡</sup> devices, for stroke prevention in patients with atrial fibrillation (AF) to be **investigational**.\*

### **Policy Guidelines**

The balance of risks and benefits associated with implantation of the Watchman device for stroke prevention, as an alternative to systemic anticoagulation with warfarin, must be made on an individual basis.

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Bleeding is the primary risk associated with systemic anticoagulation. A number of risk scores have been developed to estimate the risk of significant bleeding in patients treated with systemic anticoagulation. An example is the HAS-BLED score, which is validated to assess the annual risk of significant bleeding in patients with AF treated with warfarin (Pisters et al, 2010). Scores range from 0 to 9, based on a number of clinical characteristics (see Table PG1).

**Table PG1. Clinical Components of the HAS-BLED Bleeding Risk Score**

Letter	Clinical Characteristics	Points Awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile international normalized ratios	1
E	Elderly (>65 y)	1
D	Drugs or alcohol (1 point each)	1 or 2

Adapted from Pisters et al (2010).

Risk of major bleeding in patients with scores of 3, 4, and 5 has been reported at 3.74 per 100 patient-years, 8.70 per 100 patient-years, and 12.5 per 100 patient-years, respectively. Scores of 3 or greater are considered to be associated with high risk of bleeding, potentially signaling the need for closer monitoring of patients for adverse risks, closer monitoring of international normalized ratio, or differential dose selections of oral anticoagulants or aspirin (January et al, 2014).

### **Background/Overview**

#### **STROKE**

Stroke is the most serious complication of AF. The estimated incidence of stroke in nontreated patients with AF is 5% per year. Stroke associated with AF is primarily embolic, tends to be more severe than the typical ischemic stroke, and causes higher rates of mortality and disability. As a result, stroke prevention is a main goal of AF treatment.

Stroke in AF occurs primarily as a result of thromboembolism from the left atrium. The lack of atrial contractions in AF leads to blood stasis in the left atrium, and this low flow state increases the risk for thrombosis. The area of the left atrium with the lowest blood flow in AF, and, therefore, the highest risk of thrombosis, is the left atrial appendage (LAA). It has been estimated that 90% of left atrial thrombi occur in the LAA.

#### **Treatment**

##### ***Pharmacologic***

The main treatment for stroke prevention in AF is anticoagulation, which has proven efficacy. The risk for stroke among patients with AF is evaluated using several factors. Two commonly used scores, the CHADS<sub>2</sub> score and the CHADS<sub>2</sub>-VASc score are described below in Table 1. Warfarin is the predominant agent in clinical use. A number of newer anticoagulant medications, including dabigatran, rivaroxaban, and

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apixaban, have received U.S. FDA approval for stroke prevention in nonvalvular AF and have demonstrated noninferiority to warfarin in clinical trials. While anticoagulation is effective for stroke prevention, it carries an increased risk of bleeding. Also, warfarin requires frequent monitoring and adjustments as well as lifestyle changes. Dabigatran does not require monitoring. However, unlike warfarin, the antithrombotic effects of dabigatran are not reversible with any currently available hemostatic drugs. Guidelines from the American College of Chest Physicians (2012) have recommended the use of oral anticoagulation for patients with AF who are at high risk of stroke (ie, CHADS<sub>2</sub> score ≥2), with more individualized choice of antithrombotic therapy in patients with lower stroke risk.

**Table 1. CHADS<sub>2</sub> and CHADS<sub>2</sub>-VASc Scores to Predict Ischemic Stroke Risk in Patients With Atrial Fibrillation**

Letter	Clinical Characteristics	Points Awarded
C	Congestive heart failure (signs/symptoms of heart failure confirmed with objective evidence of cardiac dysfunction)	1
H	Hypertension (resting blood pressure >140/90 mmHg on at least 2 occasions or current antihypertensive pharmacologic treatment)	1
A	Age ≥75 y	2
D	Diabetes (fasting glucose >125 mg/dL or treatment with oral hypoglycemic agent and/or insulin)	1
S	Stroke or transient ischemic attack (includes any history of cerebral ischemia)	2
V	Vascular disease (prior myocardial infarction, peripheral arterial disease, or aortic plaque)	1
A	Age 65-74 y	1
Sc	Sex category of female (female sex confers higher risk)	1

Adapted from You et al (2012)<sup>1</sup> and January et al (2014).

Bleeding is the primary risk associated with systemic anticoagulation. Risk scores have been developed to estimate the risk of significant bleeding in patients treated with systemic anticoagulation, such as the HAS-BLED score, which has been validated to assess the annual risk of significant bleeding in patients with AF treated with warfarin. The score ranges from 0 to 9, based on clinical characteristics, including the presence of hypertension, renal and liver function, history of stroke, bleeding, labile international normalized ratios, age, and drug/alcohol use. Scores of 3 or greater are considered to be associated with high risk of bleeding, potentially signaling the need for closer monitoring of patients for adverse risks, closer monitoring of international normalized ratios, or differential dose selections of oral anticoagulants or aspirin.

### **Surgery**

Surgical removal, or exclusion, of the LAA is often performed in patients with AF who are undergoing open heart surgery for other reasons. Percutaneous left atrial appendage closure (LAAC) devices have been developed as a nonpharmacologic alternative to anticoagulation for stroke prevention in AF. The devices may prevent stroke by occluding the LAA, thus preventing thrombus formation.

Several versions of LAA occlusion devices have been developed. The Watchman Left Atrial Appendage System (Boston Scientific) is a self-expanding nickel titanium device. It has a polyester covering and fixation barbs for attachment to the endocardium. Implantation is performed percutaneously through a catheter delivery system, using venous access and transseptal puncture to enter the left atrium. Following

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implantation, patients receive anticoagulation with warfarin or alternative agents for approximately 1 to 2 months. After this period, patients are maintained on antiplatelet agents (ie, aspirin and/or clopidogrel) indefinitely. The Lariat Loop Applicator is a suture delivery device intended to close a variety of surgical wounds in addition to LAAC. The Cardioblate<sup>®†</sup> closure device (Medtronic) is currently being tested in clinical studies. The Amplatzer cardiac plug (St. Jude Medical), is FDA-approved for closure of atrial septal defects but not for LAAC. A second-generation device, the Amplatzer Amulet, has been developed. The Percutaneous LAA Transcatheter Occlusion device (ev3) has also been evaluated in research studies but has not received FDA approval. The Occlutech<sup>®‡</sup> (Occlutech) Left Atrial Appendage Occluder has received a CE mark for coverage in Europe.

### Outcome Measures

The optimal study design for evaluating the efficacy of percutaneous LAAC for the prevention of stroke in AF is a randomized controlled trial that includes clinically relevant measures of health outcomes. The rate of ischemic stroke during follow-up is the primary outcome of interest, along with rates of systemic embolization, cardiac events, bleeding complications, and death. For the LAAC devices, the appropriate comparison group could be oral anticoagulation, no therapy (for patients who have a prohibitive risk for oral anticoagulation), or open surgical repair.

Although the Watchman device and other LAAC devices would ideally represent an alternative to oral anticoagulation for the prevention of stroke in patients with AF, during the postimplantation period, the device may be associated with increased thrombogenicity and, therefore, anticoagulation is used during the periprocedural period. Most studies evaluating the Watchman device have included patients who are eligible for anticoagulation.

### FDA or Other Governmental Regulatory Approval

#### U.S. Food and Drug Administration (FDA)

In 2002, the PLAATO system (ev3 Endovascular) was the first device to be approved by FDA for LAA occlusion. The device was discontinued in 2007 for commercial reasons, and intellectual property was sold to manufacturers of the Watchman system.

In 2015, the Watchman Left Atrial Appendage Closure Technology (Boston Scientific) was approved by FDA through the premarket approval process by the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients with Atrial Fibrillation (PROTECT AF) randomized controlled trial. This device is indicated to reduce the risk of thromboembolism from the LAA in patients with nonvalvular AF who:

- Are at increased risk for stroke and systemic embolism based on CHADS<sub>2</sub> or CHA<sub>2</sub>DS<sub>2</sub>-VASc scores and are recommended for anticoagulation therapy;
- Are deemed by their physicians to be suitable for warfarin; and
- Have an appropriate rationale to seek a nonpharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared with warfarin.

FDA product code: NGV.

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Several other devices are being evaluated for LAA occlusion but are not approved in the United States for percutaneous LAAC. In 2006, the Lariat<sup>®†</sup> Loop Applicator device (SentreHEART), a suture delivery system, was cleared for marketing by FDA through the 510(k) process. The intended use is to facilitate suture placement and knot tying in surgical applications where soft tissues are being approximated or ligated with a pretied polyester suture. The Amplatzer Amulet<sup>®†</sup> device (St. Jude Medical) and WaveCrest<sup>®†</sup> (Coherex Medical) have CE approval in Europe for LAAC but are not currently approved in the United States for this indication.

### Centers for Medicare and Medicaid Services (CMS)

As of 2016, the Centers for Medicare and Medicaid Services has a national coverage determination (NCD) under coverage with evidence development for percutaneous LAAC in AF, as follows:

“LAAC devices are covered when the device has received FDA Premarket Approval (PMA) for that device’s FDA-approved indication and meet all of the conditions specified below:

The patient must have:

- A CHADS2 score  $\geq 2$  (Congestive heart failure, Hypertension, Age  $> 75$ , Diabetes, Stroke/transient ischemia attack/thromboembolism) or CHA2DS2-VASc score  $\geq 3$  (Congestive heart failure, Hypertension, Age  $\geq 65$ , Diabetes, Stroke/transient ischemia attack/thromboembolism, Vascular disease, Sex category)
- A formal shared decision making interaction with an independent non-interventional physician using an evidence-based decision tool on oral anticoagulation in patients with NVAF [nonvalvular atrial fibrillation] prior to LAAC. Additionally, the shared decision making interaction must be documented in the medical record.
- A suitability for short-term warfarin but deemed unable to take long-term oral anticoagulation following the conclusion of shared decision making, as LAAC is only covered as a second line therapy to oral anticoagulants. The patient (preoperatively and postoperatively) is under the care of a cohesive, multidisciplinary team (MDT) of medical professionals. The procedure must be furnished in a hospital with an established structural heart disease (SHD) and/or electrophysiology (EP) program.

The procedure must be performed by an interventional cardiologist(s), electrophysiologist(s), or cardiovascular surgeon (s) that meet the following criteria:

- Has received training prescribed by the manufacturer on the safe and effective use of the device prior to performing LAAC; and,
- Has performed  $\geq 25$  interventional cardiac procedures that involve transseptal puncture through an intact septum; and,
- Continues to perform  $\geq 25$  interventional cardiac procedures that involve transseptal puncture through an intact septum, of which at least 12 are LAAC, over a 2-year period.”

Patients must be enrolled in approved registries that track outcomes for procedures and devices.

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### **Rationale/Source**

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

The evidence on the efficacy of LAAC devices consists of numerous case series of various occlusion devices, and 2 published RCTs of the Watchman device, the PROTECT AF and PREVAIL trials, that have compared LAAC with warfarin anticoagulation. Evidence on each device will be reviewed separately because the devices are not similar in design, and each may have its unique considerations.

### **WATCHMAN DEVICE**

The Watchman device is intended as an alternative to anticoagulation for patients with AF who are at increased risk for embolic stroke.

### **Systematic Reviews**

A TEC Assessment (2014) evaluated the use of the Watchman device for patients eligible and ineligible for anticoagulation therapy. The Assessment determined that the device did not meet TEC criteria. The Assessment made the following conclusions about the use of LAAC in patients without contraindications to anticoagulation:

“We identified 2 RCTs and 1 case series evaluating the Watchman device. The RCTs were noninferiority trials and compared LAAC with anticoagulation. The first trial showed a lower rate of a composite outcome (stroke, death, and embolism) in patients receiving LAAC and met noninferiority criteria compared with anticoagulation, but FDA review noted problems with patient selection, potential confounding with other treatments, and losses to follow-up. The second trial, which incorporated the first trial’s results as a discounted informative prior in a Bayesian analysis, showed similar rates of the same composite outcome but did not meet noninferiority criteria. The second trial met its second principal outcome noninferiority criteria in 1 of 2 analyses and a performance goal for

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short-term complication rate. When assessing the results of both trials, the relative performance of LAAC and anticoagulation is uncertain.”

A number of systematic reviews published after the TEC Assessment have combined the results of the available RCTs. Others have included RCTs and observational studies.

The most rigorous meta-analysis is the patient-level meta-analysis by Holmes et al (2015). This analysis included patient-level data from the industry-sponsored PROTECT AF and PREVAIL trials (described below), together with both studies' continued access registries. The PROTECT AF and PREVAIL registries were designed to include patients with similar baseline characteristics as their respective RCTs. The meta-analysis included 2406 patients, 1877 treated with the Watchman device and 382 treated with warfarin alone. Mean patient follow-up durations were 0.58 years and 3.7 years, respectively, for the PREVAIL continued access registry, and the PROTECT AF continued access registry. In a meta-analysis of 1114 patients treated in the RCTs, compared with warfarin, LAAC met the trial's noninferiority criteria for the primary composite efficacy end point of all-cause stroke, systemic embolization, and cardiovascular death (hazard ratio [HR], 0.79, 95% confidence interval [CI], 0.52 to 1.2;  $p=0.22$ ). All-cause stroke rates did not differ significantly between groups (1.75 per 100 patient-years for LAAC vs 1.87 per 100 patient-years for warfarin;  $HR=1.02$ ; 95% CI, 0.62 to 1.7;  $p=0.94$ ). LAAC-treated patients had higher rates of ischemic stroke (1.6 events per 100 patient-years vs 0.9 events per 100 patient-years;  $HR=1.95$ ,  $p=0.05$ ) when procedure-related strokes were included but had lower rates of hemorrhagic stroke (0.15 events per 100 patient-years vs 0.96 events per 100 patient-years;  $HR=0.22$ ; 95% CI, 0.08 to 0.61;  $p=0.004$ ).

A second patient-level meta-analysis of the 2 RCTs, reported by Price et al (2015), focused on bleeding outcomes. There were 54 episodes of major bleeding, with the most common types being gastrointestinal bleed (31/54 [57%]) and hemorrhagic stroke (9/54 [17%]). On combined analysis, the rate of major bleeding episodes over the entire study period did not differ between groups. There were 3.5 events per 100 patient-years in the Watchman group compared with 3.6 events per 100 patient-years in the anticoagulation group, for a rate ratio of 0.96 (95% CI, 0.66 to 1.40;  $p=0.84$ ). However, there was a reduction in bleeding risk for the Watchman group past the initial periprocedural period. For bleeding events occurring more than 7 days postprocedure, the event rates were 1.8 per 100 patient-years in the Watchman group compared with 3.6 per 100 patient-years in the anticoagulation group (rate ratio, 0.49; 95% CI, 0.32 to 0.75;  $p=0.01$ ). For bleeding events occurring more than 6 months postprocedure (the time at which antiplatelet therapy is discontinued for patients receiving the Watchman device), the event rates were 1.0 per 100 patient-years in the Watchman group compared with 3.5 per 100 patient-years in the anticoagulation group (rate ratio, 0.28; 95% CI, 0.16 to 0.49;  $p<0.001$ ).

Reddy et al (2017) presented final results of the PROTECT AF trial and PREVAIL AF trial and conducted a meta-analysis of 5-year outcomes using data from both trials. Meta-analytic results are summarized in Table 2, showing that the Watchman device is noninferior to warfarin alone in stroke prevention among patients with nonvalvular AF. Also, patients treated with the Watchman device experienced significantly lower bleeding and mortality.

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**Table 2. Five-Year Meta-Analytcs Results for the PROTECT AF and PREVAIL AF Trials**

Outcomes	Watchman, n (Rate per 100 PY), %	Warfarin Alone, n (Rate per 100 PY),%	HR (95% CI)	p
Composite stroke/SE/CV death	79 (2.8)	50 (3.4)	0.8 (0.6 to 1.2)	0.3
All stroke or SE	49 (1.7)	27 (1.8)	1.0 (0.6 to 1.5)	0.9
CV/unexplained death	39 (1.3)	33 (2.2)	0.6 (0.4 to 0.9)	0.03
All cause death	106 (3.0)	73 (4.9)	0.7 (0.5 to 1.0)	0.03
Major bleeding, all	85 (3.1)	50 (3.5)	0.9 (0.6 to 1.3)	0.6
Major bleeding, non-LAAC-related	48 (1.7)	51 (3.6)	0.5 (0.3 to 0.7)	<0.001

Adapted from Reddy et al (2017).  
CI: confidence interval; CV: cardiovascular; HR: hazard ratio; LAAC: left atrial appendage closure; PY: patient-years; SE: systemic embolism.

Additional systematic reviews have used network meta-analyses to compare Watchman with novel oral anticoagulants and vitamin K antagonists (6 RCTs, total N=59,627 subjects), and have compared percutaneous LAA occlusion (5 RCTs, total N=1285 subject) with standard anticoagulant or antiplatelet therapy with device-based surgical or percutaneous LAA exclusion.

### Randomized Controlled Trials

#### **PROTECT AF Trial**

The first RCT published was PROTECT AF, an unblinded randomized trial evaluating the noninferiority of an LAAC device compared with warfarin for stroke prevention in AF. The trial randomized 707 patients from 59 centers in the United States and Europe to the Watchman device or warfarin treatment in a 2:1 ratio. Mean follow-up was 18 months. The primary efficacy outcome was a composite end point of stroke (ischemic or hemorrhagic), cardiovascular or unexplained death, or systemic embolism. There was also a primary safety outcome, a composite end point of excessive bleeding (intracranial or gastrointestinal bleeding) and procedure-related complications (pericardial effusion, device embolization, procedure-related stroke).

The primary efficacy outcome occurred at a rate of 3.0 per 100 patient-years in the LAAC group compared with 4.9 per 100 patient-years in the warfarin group (rate ratio, 0.62; 95% credible interval [CrI], 0.35 to 1.25). Based on these outcomes, the probability of noninferiority was greater than 99.9%. For the individual components of the primary outcome (hemorrhagic stroke, cardiovascular/unexplained death) were higher in the warfarin group. By contrast, ischemic stroke was higher in the LAAC group at 2.2 per 100 patient-years compared with 1.6 per 100 patient-years in the warfarin group (rate ratio, 1.34; 95% CrI, 0.60 to 4.29).

The primary safety outcome occurred more commonly in the LAAC group, at a rate of 7.4 per 100 patient-years compared with 4.4 per 100 patient-years in the warfarin group (rate ratio, 1.69; 95% CrI, 1.01 to 3.19). The excess in adverse event rates for the LAAC group was primarily the result of early adverse events associated with device placement. The most frequent type of complication related to LAAC device placement was pericardial effusion requiring intervention, which occurred in 4.8% (22/463) of patients.





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Longer term follow-up from the PROTECT AF trial was reported by Reddy et al (2013). At a mean follow-up of 2.3 years, the results were similar to the initial report. The relative risk for the composite primary outcome in the Watchman group compared with anticoagulation was 0.71, and this met noninferiority criteria with a confidence greater than 99%. Complications were more common in the Watchman group, with an estimated rate of 5.6% per year, compared with 3.6% per year in the warfarin group.

Outcomes through 4 years of follow-up were reported by Reddy et al (2014). Mean follow-up was 3.9 years in the LAAC group and 3.7 years in the warfarin group. In the LAAC group, warfarin was discontinued in 345 (93.2%) of 370 patients by the 12-month follow-up evaluation. During the follow-up period, the relative risk for the composite primary outcome in the Watchman group compared with anticoagulation was 0.60 (8.4% in the device group vs 13.9% in the anticoagulation group; 95% CrI, 0.41 to 1.05), which met the noninferiority criteria with a confidence greater than 99.9%. Fewer hemorrhagic strokes (0.6% vs 4.0%; rate ratio, 0.15; 95% CrI, 0.03 to 0.49) and fewer cardiovascular events (3.7% vs 0.95%; rate ratio, 0.40; 95% CrI, 0.23 to 0.82) occurred in the Watchman group. Rates of ischemic stroke did not differ significantly between groups, but Watchman patients had lower all-cause mortality rates than anticoagulation patients (12.3% vs 18.0%; HR=0.66; 95% CI, 0.45 to 0.98; p=0.04).

Alli et al (2013) reported on quality-of-life parameters, as measured by change in the 12-Item Short-Form Health Survey (SF-12) scores from baseline to 12-month follow-up, for a subset of 547 subjects in the PROTECT AF trial. For the subset of PROTECT AF subjects included in the Alli analysis, at baseline, control group subjects had a higher mean CHADS<sub>2</sub> score (2.4 vs 2.2; p=0.052) and were more likely to have a history of coronary artery disease (49.5% vs 39.6%; p=0.028). For subjects in the Watchman group, the SF-12 total physical score improved in 34.9% and was unchanged in 29.9%; for those in the warfarin group, the total physical score improved in 24.7% and was unchanged in 31.7% (p=0.01).

Five-year follow-up results, published by Reddy et al (2017), indicated that the LAAC group had significantly lower rates of the composite efficacy end point (stroke, systemic embolism, cardiovascular death) compared with the warfarin-only group (p=0.04).

### **PREVAIL Trial**

A second RCT, the PREVAIL trial, was conducted after the 2009 FDA decision on the Watchman device to address some limitations of the PROTECT AF trial, including its inclusion of patients with low stroke risk (CHADS<sub>2</sub> scores of 1), high rates of adjunctive antiplatelet therapy use in both groups, and generally poor compliance with warfarin therapy in the control group. Results from the PREVAIL trial were published by Holmes et al (2014). In the PREVAIL trial, 461 subjects enrolled at 41 sites were randomized in a 2:1 fashion to the Watchman device or control, which consisted of either initiation or continuation of warfarin therapy with a target international normalized ratio of 2.0 to 3.0. Subjects had nonvalvular AF and required treatment for prevention of thromboembolism based on a CHADS<sub>2</sub> score of 2 or higher (or ≥1 with other indications for warfarin therapy based on American College of Cardiology, American Heart Association, and European Society of Cardiology joint guidelines) and were eligible for warfarin therapy. In the device group, warfarin and low-dose aspirin were continued until 45 days postprocedure; if a follow-up echocardiogram at

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45 days showed occlusion of the LAA, warfarin therapy could be discontinued. Subjects who discontinued warfarin were treated with aspirin and clopidogrel for 6 months after device implantation and with aspirin 325 mg indefinitely after that.

Three noninferiority primary efficacy end points were specified: (1) occurrence of ischemic or hemorrhagic stroke, cardiovascular or unexplained death, and systemic embolism (18-month rates); (2) occurrence of late ischemic stroke and systemic embolization (beyond 7 days postrandomization, 18-month rates); and (3) occurrence of all-cause death, ischemic stroke, systemic embolism, or device- or procedure-related events requiring open cardiac surgery or major endovascular intervention (eg, pseudoaneurysm repair, arteriovenous fistula repair, or other major endovascular repair) occurring within 7 days of the procedure or by hospital discharge, whichever was later. The 18-month event rates were determined using Bayesian statistical methods to integrate data from the PROTECT AF trial. All patients had a minimum follow-up of 6 months. For randomized subjects, mean follow-up was 11.8 months, and median follow-up was 12.0 months (range, 0.03-25.9 months).

For the first primary end point, the 18-month modeled rate ratio between the device and control groups was 1.07 (95% CrI, 0.57 to 1.89). Because the upper bound of the 95% CrI was above the preset noninferiority margin of 1.75, the noninferiority criteria were not met. For the second primary end point of late ischemic stroke and systemic embolization, the 18-month relative risk between the device and control groups was 1.6 (95% CrI, 0.5 to 4.2), with an upper bound of the 95% CrI above the preset noninferiority margin of 2.0. The rate difference between the device and control groups was 0.005 (95% CrI, -0.019 to 0.027). The upper bound of the 95% CrI was lower than the noninferiority margin of 0.0275, so the noninferiority criterion was met for the rate difference. For the third primary end point (major safety issues), the noninferiority criterion was met.

Five-year follow-up results, published by Reddy et al (2017), indicated that the Watchman device was noninferior to warfarin alone in the composite efficacy end point (stroke, systemic embolism, cardiovascular death) ( $p=0.5$ ).

### **Nonrandomized Studies**

Numerous case series and nonrandomized studies of the Watchman have been published. Several are notable in that they were conducted in patients not eligible for anticoagulation, a population not included in PROTECT AF and PREVAIL. Reddy et al (2013) conducted a multicenter, prospective, nonrandomized trial to evaluate the safety and efficacy of LAAC with the Watchman device in patients who had nonvalvular AF, with a CHADS<sub>2</sub> score 1 or higher, and were considered ineligible for warfarin. Postimplantation, patients received 6 months of clopidogrel or ticlopidine and lifelong aspirin therapy. Thirteen (8.7%) patients had a procedure- or device-related serious adverse event, most commonly pericardial effusion (3 patients). Over a mean follow-up of 14.4 months, all-cause stroke or systemic embolism occurred in 4 patients.

Chun et al (2013) compared the Watchman device with the Amplatzer cardiac plug among patients who had nonvalvular AF, were at high risk for stroke, and had a contraindication to or were unwilling to take oral

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anticoagulants. Eighty patients were randomized to LAA occlusion with the Watchman or the Amplatzer device. After device implantation, either preexisting oral anticoagulation therapy or dual-platelet inhibition with aspirin and clopidogrel was continued for 6 weeks. There were no statistically significant differences in procedure time, fluoroscopy time, or major safety events between the 2 groups. At a median follow-up of 364 days, there were no cases of stroke, transient ischemic attack, or other bleeding complications.

The EWOLUTION Watchman registry tracks procedural success, long-term outcomes, and adverse events in real-world settings. This registry compiles data from patients receiving the Watchman device at 47 centers in 13 countries. Analysis of the EWOLUTION registry data by Boersma et al (2016) reported on 30-day outcomes after device implantation in 1021 patients. The overall population had a risk of bleeding that was substantially higher than that for patients in the RCTs. Over 62% of patients included in the registry were deemed ineligible for anticoagulation by their physicians. Approximately one-third of patients had a history of major bleeding, and 40% had HAS-BLED scores of 3 or greater, indicating moderate-to-high risk of bleeding. Procedural success was achieved in 98.5% of patients, and 99.3% of implants demonstrated no blood flow or minimal residual blood flow postprocedure. Serious adverse events due to the device or procedure occurred at an overall rate of 2.8% (95% CI, 1.9% to 4.0%) at 7 days and 3.6% (95% CI, 2.5% to 4.9%) at 30 days. The most common serious adverse event was major bleeding.

### **Section Summary: Watchman Device**

The most relevant evidence on the use of the Watchman device for LAAC in patients eligible for anticoagulation derives from 2 industry-sponsored RCTs and a patient-level meta-analysis of those studies. After 5 years of follow-up, meta-analytic results showed that the ischemic stroke risk beyond 7 days did not differ between groups and that the hemorrhagic stroke risk remained significantly lower in the LAAC group. The results showed that the Watchman device is noninferior to warfarin alone in stroke prevention among patients with nonvalvular AF. Also, patients treated with the Watchman device experienced significantly lower bleeding and mortality.

### **OTHER CLOSURE DEVICES**

#### **Lariat Device**

A systematic review of studies on the Lariat device was published by Chatterjee et al (2016). No RCTs were identified. Five case series were included, with a total of 309 patients (range, 4-154 patients) treated. The combined estimate of procedural success was 90.3%. One (0.3%) death was reported and 7 (2.3%) patients required urgent cardiac surgery. Reviewers also searched the MAUDE database for adverse events and found 35 unique reports. Among the 35 reported complications, there were 5 deaths and 23 cases of emergency cardiac surgery.

Individual case series published since the systematic review included a large 2016 case series of 712 consecutive patients from 18 U.S. hospitals. This series reported a procedural (suture deployment) success rate of 95% and complete closure rate in 98%. The high success rate was attributed to the appropriate selection of patients for the procedure, which was determined by a screening computed tomography scan showing if the LAA anatomy was suitable for LARIAT deployment. There was 1 death, and emergent

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cardiac surgery was required in 1.4%. Cardiac perforations (overall and those needing surgery) and the number of patients needing blood transfusions decreased when providers altered the procedure from using large bore needles to micropuncture needles. Other individual case series are smaller, reporting success rates and complication rates in the same range.

### **Section Summary: Lariat Device**

There are no RCTs of the Lariat device for LAAC. The available case series are insufficient to draw conclusions about treatment efficacy.

### **Amplatzer Cardiac Plug Device**

The available evidence on the use of the Amplatzer device for left atrial occlusion consists of a number of case series. The largest series identified was by Nietlispach et al (2013), which included 152 patients from a single institution in Europe. Short-term complications occurred in 9.8% (15/152) of patients. The longer term adverse outcomes occurred in 7% of patients, including 2 strokes, 1 peripheral embolization, and 4 episodes of major bleeding. Device embolization occurred in 4.6% (7/152) of patients. Other reports of patients treated with the Amplatzer device include a series of 90 patients from Belgium (2013), 86 patients from Portugal (2012), 37 patients from Italy (2013), 35 patients from Spain (2013), 21 patients from Poland (2013), and 20 patients from China (2012). All series reported high procedural success rates, as well as various complications such as vascular events, air embolism, esophageal injury, cardiac tamponade, and device embolization.

Several other case series have reported on the use of the Amplatzer device in patients with a contraindication to oral anticoagulation therapy. The largest, by Santoro et al (2016), reported on outcomes up to 4 years postprocedure, for 134 patients with nonvalvular AF and a long-term contraindication to oral anticoagulation treated with the Amplatzer device. Patients had a median CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 4 and were generally considered at high risk for bleeding complications. Procedural success occurred in 93.3%, and 3 major procedure-related complications (2 cases of cardiac tamponade, 1 case of pericardial effusion requiring drainage or surgery) occurred. Over a mean follow-up of 680 days, observed annual rates of ischemic strokes and any thromboembolic events were 0.8% and 2.5%, respectively. Other case series have been published in this population, evaluating between 37 and 100 patients. They also reported high success rates and low procedural complications.

### **Section Summary: Amplatzer Cardiac Plug Device**

There are no RCTs of the Amplatzer device for LAAC. The available case series are insufficient to draw conclusions about treatment efficacy.

### **PLAATO Device**

The available evidence on outcomes following the use of the Percutaneous Left Atrial Appendage Transcatheter Occlusion (PLAATO) device for stroke prevention in AF comes from case series and cohort studies. Bayard et al (2010) reported on 180 patients with nonrheumatic AF, a contraindication to warfarin, and treatment with the PLAATO device. Placement was successful in 90% of patients. Two (1.1%) patients

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died within 24 hours of the procedure, and 6 (3.3%) patients had cardiac tamponade, with 2 requiring surgical drainage. Other case reports and small case series have found complications, including multiple reports of thrombus formation at the site of device placement.

### **Section Summary: PLAATO Device**

There are no RCTs of the PLAATO device for LAAC. Future trials seem unlikely because the PLAATO device is no longer manufactured.

### **SUMMARY OF EVIDENCE**

For individuals who have AF who are at increased risk for embolic stroke who receive the Watchman percutaneous LAAC device, the evidence includes 2 RCTs and meta-analyses of these trials. Relevant outcomes are overall survival, morbid events, and treatment-related morbidity. The most relevant evidence comes from 2 industry-sponsored RCTs that compared the Watchman device with anticoagulation alone. One trial reported noninferiority on a composite outcome of stroke, cardiovascular/unexplained death, or systemic embolism after 2 years of follow-up, with continued benefits with the Watchman device after 4 years of follow-up. The second trial did not demonstrate noninferiority for the same composite outcome but did demonstrate noninferiority of the Watchman device to warfarin for late ischemic stroke and systemic embolization. Patient-level meta-analyses at 5-year follow-up for the 2 trials reported that the Watchman device is noninferior to warfarin on the composite outcome of stroke, systemic embolism, and cardiovascular death. Also, the Watchman was associated with lower rates in major bleeding, particularly hemorrhagic stroke, and mortality over the long term. The evidence also indicates that the Watchman device is efficacious in preventing stroke in the subset of patients with AF who are at increased risk for embolic stroke. When it is determined on an individualized basis that the long-term risk of systemic anticoagulation exceeds the procedural risk of device implantation, the net health outcome will be improved. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have AF who are at increased risk for embolic stroke who receive a percutaneous LAAC device other than the Watchman device (eg, the Lariat—or Amplatzer), the evidence includes uncontrolled case series. Relevant outcomes are overall survival, morbid events, and treatment-related morbidity. Case series of these devices have reported high procedural success, but also numerous complications. Also, these devices do not have FDA approval for LAAC. The evidence is insufficient to determine the effects of the technology on health outcomes.

### **References**

1. Blue Cross and Blue Shield Association, Medical Policy Reference Manual. "Left-Atrial Appendage Closure Devices for Stroke Prevention in Atrial Fibrillation", 2.02.26, 05:2018.
2. You JJ, Singer DE, Howard PA, et al. Antithrombotic therapy for atrial fibrillation: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. Feb 2012;141(2 Suppl):e531S-575S. PMID 22315271
3. 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. Nov 2010;138(5):1093-1100. PMID 20299623

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Current Effective Date: 10/17/2018

4. January CT, Wann LS, Alpert JS, et al. 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*. Dec 2 2014;64(21):e1-76. PMID 24685669
5. Administration FaD. Approval Letter: WATCHMAN LAA Closure Technology. 2015; [http://www.accessdata.fda.gov/cdrh\\_docs/pdf13/p130013a.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf13/p130013a.pdf). Accessed June 1, 2015.
6. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Percutaneous left atrial appendage closure therapy for prevention of stroke. *TEC Assessments* 2014;29; Tab 5.
7. Bode WD, Patel N, Gehi AK. Left atrial appendage occlusion for prevention of stroke in nonvalvular atrial fibrillation: a meta-analysis. *J Interv Card Electrophysiol*. Jun 2015;43(1):79-89. PMID 25711953
8. Briceno DF, Villablanca P, Cyrille N, et al. Left Atrial Appendage Occlusion Device and Novel Oral Anticoagulants Versus Warfarin for Stroke Prevention in Nonvalvular Atrial Fibrillation: Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Circ Arrhythm Electrophysiol*. Oct 2015;8(5):1057-1064. PMID 26226997
9. Holmes DR, Jr., 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*. Jun 23 2015;65(24):2614-2623. PMID 26088300
10. Li X, Wen SN, Li SN, et al. Over 1-year efficacy and safety of left atrial appendage occlusion versus novel oral anticoagulants for stroke prevention in atrial fibrillation: A systematic review and meta-analysis of randomized controlled trials and observational studies. *Heart Rhythm*. Dec 24 2015. PMID 26724488
11. Lip GY, Lane DA. Stroke prevention in atrial fibrillation: a systematic review. *JAMA*. May 19 2015;313(19):1950-1962. PMID 25988464
12. Price MJ, Reddy VY, Valderrabano M, et al. Bleeding outcomes after left atrial appendage closure compared with long-term warfarin: a pooled, patient-level analysis of the WATCHMAN randomized trial experience. *JACC Cardiovasc Interv*. Dec 28 2015;8(15):1925-1932. PMID 26627989
13. Holmes DR, Reddy VY, Turi ZG, et al. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. *Lancet*. Aug 15 2009;374(9689):534-542. PMID 19683639
14. 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 Embolic Protection in Patients With Atrial Fibrillation) trial. *Circulation*. Feb 12 2013;127(6):720-729. PMID 23325525
15. Reddy VY, Sievert H, Halperin J, et al. Percutaneous left atrial appendage closure vs warfarin for atrial fibrillation: a randomized clinical trial. *JAMA*. Nov 19 2014;312(19):1988-1998. PMID 25399274
16. Alli O, Doshi S, Kar S, et al. Quality of life assessment in the randomized PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) trial of patients at risk for stroke with nonvalvular atrial fibrillation. *J Am Coll Cardiol*. Apr 30 2013;61(17):1790-1798. PMID 23500276
17. FDA. 2013 Meeting Materials of the Circulatory System Devices Panel. 2013; <http://www.fda.gov/advisorycommittees/committeesmeetingmaterials/medicaldevices/medicaldevicesadvisorycommittee/circulatorysystemdevicespanel/ucm342357.htm>. Accessed May 5, 2015.
18. Holmes DR, Jr., 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*. Jul 8 2014;64(1):1-12. PMID 24998121
19. Lam YY, Yip GW, Yu CM, et al. Left atrial appendage closure with AMPLATZER cardiac plug for stroke prevention in atrial fibrillation: initial Asia-Pacific experience. *Catheter Cardiovasc Interv*. Apr 1 2012;79(5):794-800. PMID 21542102
20. Montenegro MJ, Quintella EF, Damonte A, et al. Percutaneous occlusion of left atrial appendage with the Amplatzer Cardiac Plug™ in atrial fibrillation. *Arq Bras Cardiol*. Jan 31 2012;98(2):143-150. PMID 22286325
21. Park JW, Bethencourt A, Sievert H, et al. Left atrial appendage closure with Amplatzer cardiac plug in atrial fibrillation: initial European experience. *Catheter Cardiovasc Interv*. Apr 1 2011;77(5):700-706. PMID 20824765
22. 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*. Feb 1 2011;123(4):417-424. PMID 21242484
23. Swaans MJ, Post MC, Rensing BJ, et al. Percutaneous left atrial appendage closure for stroke prevention in atrial fibrillation. *Neth Heart J*. Jan 10 2012;20(4):161-166. PMID 22231152

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24. Reddy VY, Möbius-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. PMID
25. Chun KR, Bordignon S, Urban V, et al. Left atrial appendage closure followed by 6 weeks of antithrombotic therapy: a prospective single-center experience. *Heart Rhythm.* Dec 2013;10(12):1792-1799. PMID 23973952
26. Boersma LV, Schmidt B, Betts TR, et al. Implant success and safety of left atrial appendage closure with the WATCHMAN device: peri-procedural outcomes from the EWOLUTION registry. *Eur Heart J.* Jan 27 2016. PMID 26822918
27. Chatterjee S, Herrmann HC, Wilensky RL, et al. Safety and Procedural Success of Left Atrial Appendage Exclusion With the Lariat Device: A Systematic Review of Published Reports and Analytic Review of the FDA MAUDE Database. *JAMA Intern Med.* Jul 2015;175(7):1104-1109. PMID 25938303
28. Lakkireddy D, Afzal MR, Lee RJ, et al. Short and long-term outcomes of percutaneous left atrial appendage suture ligation: Results from a US multicenter evaluation. *Heart Rhythm.* May 2016;13(5):1030-1036. PMID 26872554
29. Price MJ, Gibson DN, Yakubov SJ, et al. Early safety and efficacy of percutaneous left atrial appendage suture ligation: results from the U.S. transcatheter LAA ligation consortium. *J Am Coll Cardiol.* Aug 12 2014;64(6):565-572. PMID 25104525
30. 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 Coll Cardiol.* Jul 9 2013;62(2):108-118. PMID 23062528
31. Bartus K, Bednarek J, Myc J, et al. Feasibility of closed-chest ligation of the left atrial appendage in humans. *Heart Rhythm.* Feb 2011;8(2):188-193. PMID 21050893
32. Stone D, Byrne T, Pershad A. Early results with the LARIAT device for left atrial appendage exclusion in patients with atrial fibrillation at high risk for stroke and anticoagulation. *Catheter Cardiovasc Interv.* Jul 2015;86(1):121-127. PMID 23765504
33. Massumi A, Chelu MG, Nazeri A, et al. Initial experience with a novel percutaneous left atrial appendage exclusion device in patients with atrial fibrillation, increased stroke risk, and contraindications to anticoagulation. *Am J Cardiol.* Jan 9 2013;111(6):869-873. PMID 23312129
34. Nietlispach F, Gloekler S, Krause R, et al. Amplatzer left atrial appendage occlusion: Single center 10-year experience. *Catheter Cardiovasc Interv.* Feb 14 2013;82(2):283-289. PMID 23412815
35. Kefer J, Vermeersch P, Budts W, et al. Transcatheter left atrial appendage closure for stroke prevention in atrial fibrillation with Amplatzer cardiac plug: the Belgian Registry. *Acta Cardiol.* Dec 2013;68(6):551-558. PMID 24579432
36. Guerios EE, Schmid M, Gloekler S, et al. Left atrial appendage closure with the Amplatzer cardiac plug in patients with atrial fibrillation. *Arq Bras Cardiol.* Jun 2012;98(6):528-536. PMID 22584492
37. Danna P, Proietti R, Sagone A, et al. Does left atrial appendage closure with a cardiac plug system reduce the stroke risk in nonvalvular atrial fibrillation patients? A single-center case series. *Pacing Clin Electrophysiol.* Mar 2013;36(3):347-353. PMID 23252940
38. Lopez-Minguez JR, Eldoayen-Gragera J, Gonzalez-Fernandez R, et al. Immediate and one-year results in 35 consecutive patients after closure of left atrial appendage with the Amplatzer Cardiac Plug. *Rev Esp Cardiol.* Feb 2013;66(2):90-97. PMID 22939161
39. Streb W, Szymala M, Kukulski T, et al. Percutaneous closure of the left atrial appendage using the Amplatzer Cardiac Plug in patients with atrial fibrillation: evaluation of safety and feasibility. *Kardiol Pol.* 2013;71(1):8-16. PMID 23348528
40. Santoro G, Meucci F, Stolicova M, et al. Percutaneous left atrial appendage occlusion in patients with non-valvular atrial fibrillation: implantation and up to four years follow-up of the AMPLATZER Cardiac Plug. *EuroIntervention.* Feb 20 2016;11(10):1188-1194. PMID 25354761
41. Meerkin D, Butnaru A, Dratva D, et al. Early safety of the Amplatzer Cardiac Plug for left atrial appendage occlusion. *Int J Cardiol.* Oct 9 2013;168(4):3920-3925. PMID 23890886
42. Wiebe J, Bertog S, Franke J, et al. Safety of percutaneous left atrial appendage closure with the Amplatzer cardiac plug in patients with atrial fibrillation and contraindications to anticoagulation. *Catheter Cardiovasc Interv.* Apr 1 2014;83(5):796-802. PMID 24327462
43. Urena M, Rodes-Cabau J, Freixa X, et al. Percutaneous left atrial appendage closure with the AMPLATZER cardiac plug device in patients with nonvalvular atrial fibrillation and contraindications to anticoagulation therapy. *J Am Coll Cardiol.* Jul 9 2013;62(2):96-102. PMID 23665098
44. Gloekler S, Shakir S, Doblies J, et al. Early results of first versus second generation Amplatzer occluders for left atrial appendage closure in patients with atrial fibrillation. *Clin Res Cardiol.* Aug 2015;104(8):656-665. PMID 25736061

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Current Effective Date: 10/17/2018

45. Bayard YL, Omran H, Neuzil P, et al. PLAATO (Percutaneous Left Atrial Appendage Transcatheter Occlusion) for prevention of cardioembolic stroke in non-anticoagulation eligible atrial fibrillation patients: results from the European PLAATO study. *EuroIntervention*. Jun 2010;6(2):220-226. PMID 20562072
46. Cruz-Gonzalez I, Martin Moreiras J, Garcia E. Thrombus formation after left atrial appendage exclusion using an amplatzer cardiac plug device. *Catheter Cardiovasc Interv*. Nov 15 2011;78(6):970-973. PMID 21523900
47. Viles-Gonzalez JF, Reddy VY, Petru J, et al. Incomplete occlusion of the left atrial appendage with the percutaneous left atrial appendage transcatheter occlusion device is not associated with increased risk of stroke. *J Interv Card Electrophysiol*. Jan 2012;33(1):69-75. PMID 21947786
48. Masoudi FA, Calkins H, Kavinsky CJ, et al. 2015 ACC/HRS/SCAI left atrial appendage occlusion device societal overview. *J Am Coll Cardiol*. Sep 29 2015;66(13):1497-1513. PMID 26133570
49. Sahay S, Nombela-Franco L, Rodes-Cabau J, et al. Efficacy and safety of left atrial appendage closure versus medical treatment in atrial fibrillation: a network meta-analysis from randomised trials. *Heart*. Jan 15 2017;103(2):139-147. PMID 27587437
50. Li X, Wen SN, Li SN, et al. Over 1-year efficacy and safety of left atrial appendage occlusion versus novel oral anticoagulants for stroke prevention in atrial fibrillation: A systematic review and meta-analysis of randomized controlled trials and observational studies. *Heart Rhythm*. Jun 2016;13(6):1203-1214. PMID 26724488
51. Wei Z, Zhang X, Wu H, et al. A meta-analysis for efficacy and safety evaluation of transcatheter left atrial appendage occlusion in patients with nonvalvular atrial fibrillation. *Medicine (Baltimore)*. Aug 2016;95(31):e4382. PMID 27495048
52. Tereshchenko LG, Henrikson CA, Cigarroa J, et al. Comparative effectiveness of interventions for stroke prevention in atrial fibrillation: a network meta-analysis. *J Am Heart Assoc*. May 20 2016;5(5). PMID 27207998
53. Bajaj NS, Kalra R, Patel N, et al. Comparison of approaches for stroke prophylaxis in patients with non-valvular atrial fibrillation: network meta-analyses of randomized controlled trials. *PLoS One*. 2016;11(10):e0163608. PMID 27706224
54. Hanif H, Belley-Cote EP, Alotaibi A, et al. Left atrial appendage occlusion for stroke prevention in patients with atrial fibrillation: a systematic review and network meta-analysis of randomized controlled trials. *J Cardiovasc Surg (Torino)*. Feb 17 2017. PMID 28215062
55. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. *Europace*. Nov 2016;18(11):1609-1678. PMID 27567465
56. Center for Medicare and Medicaid Services.. National Coverage Determination (NCD) for Percutaneous Left Atrial Appendage Closure (LAAC) (20.34). 2016; <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=367&nacdver=1&NCAId=281&bc=AAAAAAAACAAAAA%3d%3d&>. Accessed May 3, 2017
57. 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*. Dec 19 2017;70(24):2964-2975. PMID 29103847
58. Andrade JG, Macle L, Nattel S, et al. Contemporary atrial fibrillation management: a comparison of the current AHA/ACC/HRS, CCS, and ESC guidelines. *Can J Cardiol*. Aug 2017;33(8):965-976. PMID 28754397

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|------------|---|
| 05/05/2011 | Medical Policy Committee review   |
| 05/18/2011 | Medical Policy Implementation Committee approval. New policy.   |
| 05/03/2012 | Medical Policy Committee review   |
| 05/16/2012 | Medical Policy Implementation Committee approval. Coverage eligibility unchanged.                         |
| 05/02/2013 | Medical Policy Committee review   |
| 05/22/2013 | Medical Policy Implementation Committee approval. Coverage eligibility unchanged.                         |
| 05/01/2014 | Medical Policy Committee review   |
| 05/21/2014 | Medical Policy Implementation Committee approval. Percutaneous added to the title and coverage statement. |
| 06/04/2015 | Medical Policy Committee review   |
| 06/17/2015 | Medical Policy Implementation Committee approval. No change to coverage.                                  |
| 04/07/2016 | Medical Policy Committee review   |

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# Louisiana

## Percutaneous Left-Atrial Appendage Closure Devices for Stroke Prevention in Atrial Fibrillation

Policy # 00296  
 Original Effective Date: 05/18/2011  
 Current Effective Date: 10/17/2018

04/20/2016 Medical Policy Implementation Committee approval. An FDA-approved left atrial appendage closure device is considered medically necessary with conditions.  
 01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes and CPT Coding Update  
 04/06/2017 Medical Policy Committee review  
 04/19/2017 Medical Policy Implementation Committee approval. No change to coverage.  
 06/07/2018 Medical Policy Committee review  
 06/20/2018 Medical Policy Implementation Committee approval. No change to coverage.  
 10/04/2018 Medical Policy Committee review  
 10/17/2018 Medical Policy Implementation Committee approval. Added policy guidelines  
 Next Scheduled Review Date: 10/2019

### Coding

*The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)†, copyright 2017 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 Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana 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 Blue Cross Blue Shield of Louisiana 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 Blue Cross Blue Shield of Louisiana 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	33340
HCPCS	No codes
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. 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

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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 the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated 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:** 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.

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