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

Policy # 00296
Original Effective Date: 05/18/2011
Current Effective Date: 11/09/2020

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) ™‡ 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 $CHADS_2$ score ($\geq$ 2) or CHA_2DS_2-VASc score ($\geq$ 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 $\geq$ 3, see Policy Guidelines section for additional details).

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.***

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

Policy # 00296
Original Effective Date: 05/18/2011
Current Effective Date: 11/09/2020

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®‡, and Amplatzer®‡ 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.

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 atrial fibrillation 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).
HAS-BLED: Hypertension,Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR (international normalized ratio), Elderly, Drugs/alcohol concomitantly.

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).

Following patients may have an unacceptably high risk of bleeding with long-term oral anticoagulation:

- Thrombocytopenia or known coagulation defect associated with bleeding
- Recurrent bleeding, including gastrointestinal, genitourinary, respiratory
- Prior severe bleeding, including intracranial hemorrhage
- Combined use of dual antiplatelet and anticoagulant therapy
- Poor compliance or intolerance with anticoagulant therapy
- High risk of the patient falling or prior falls resulting in injury

Background/Overview

Atrial Fibrillation and Stroke

Atrial Fibrillation is the most common type of irregular heartbeat, affecting at least 2.7 million people in the U. S. 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 $CHADS_2$ score and the $CHADS_2$-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 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. 2018 American College of Chest Physicians guidelines (updated from 2012) recommend that CHA_2DS_2VASc be used to evaluate stroke risk, and patients initially identified as having a low stroke risk should not be given antithrombotic therapy. In addition, they recommend bleeding risk assessments be given to every patient at every patient contact and that "potentially modifiable bleeding risk factors" should be the initial focus.

Table 1. $CHA2DS_2$ and CHA_2DS_2-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 Lip et al (2018) 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 PLAATO system (ev3 Endovascular) was the first device to be approved by the FDA for LAA occlusion. The device was discontinued in 2007 for commercial reasons, and intellectual property was sold to manufacturers of the Watchman system. 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. Transesophageal

echocardiography and fluoroscopy are used to guide the procedure. Following 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 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 for the specific indication of LAAC but currently does not have FDA approval. The Amplatzer Amulet consists of a nitinol mesh disc to seal the ostium of the LAA and a nitinol mesh distal lobe, to be positioned within the LAA. The device is preloaded within a delivery sheath. The Percutaneous LAA Transcatheter Occlusion device (ev3) has also been evaluated in research studies but has not received the FDA approval. The Occlutech®‡ (Occlutech) Left Atrial Appendage Occluder has received a CE mark for coverage in Europe. The Cardioblate®‡ closure device (Medtronic) is currently being tested in clinical studies.

The Lariat Loop Applicator is a suture delivery device approved by the FDA, intended to close a variety of surgical wounds. It is not specifically approved for LAAC. While the Watchman and other devices are implanted in the endocardium, the Lariat is a non-implant epicardial device.

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 (RCT) 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 post implantation period, the device may be associated with increased thrombogenicity, 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 the 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 the FDA through the premarket approval process by the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients with Atrial Fibrillation 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 $CHADS_2$ or CHA_2DS_2-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.

Several other devices are being evaluated for LAA occlusion but are not approved in the U. S. for percutaneous LAAC. In 2006, the Lariat®‡ Loop Applicator device (SentreHEART), a suture delivery system, was cleared for marketing by the 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®‡ device (St. Jude Medical) and WaveCrest®‡ (Johnson & Johnson Biosense Webster) have CE approval in Europe for LAAC but are not currently approved in the U. S. for this indication.

Rationale/Source

Stroke prevention in patients with AF is an important goal of treatment. Treatment with anticoagulant medications is the most common approach to stroke prevention. Because most embolic strokes originate from the left atrial appendage, occlusion of the left atrial appendage may offer a nonpharmacologic alternative to anticoagulant medications to lower the risk of stroke. Multiple percutaneously deployed devices are being investigated for LAAC. One left atrial appendage device (the Watchman device) has approval from the U.S. FDA for stroke prevention in patients with AF.

For individuals who have AF who are at increased risk for embolic stroke who receive the Watchman percutaneous LAAC device, the evidence includes 2 randomized controlled trials (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. Among patients in which 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 Lariator Amplatzer), the evidence includes several nonrandomized comparator studies and uncontrolled case series. Relevant outcomes are overall survival, morbid events, and treatment-related morbidity. One nonrandomized study that compared outcomes among patients undergoing LAAC with the Lariat device with patients receiving anticoagulant or antiplatelet therapy reported fewer thromboembolic events in the group receiving the Lariat device. Two nonrandomized studies compared the Amplatzer cardiac plug with the Amplatzer amulet. While the amulet may be technically easier to implant, clinical outcomes were similar between the 2 groups. The remaining evidence consists of case series of these devices which report high procedural success but also numerous complications. In addition, these devices do not have U.S. Food and Drug Administration approval for LAAC. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 1 physician specialty society (2 responses) and 4 academic medical centers, 1 of which provided 4 responses, for a total of 8 responses, while this policy was under review in 2015. Input generally supported the use of a left atrial appendage closure device approved by the U.S. FDA for patients with an increased risk of stroke and systemic embolism, based on $CHADS_2$ or CHA_2DS_2-VASc score. Systemic anticoagulation therapy was recommended, but the long-term risks of systemic anticoagulation outweigh the risks of the device implantation.

Practice Guidelines and Position Statements

American Heart Association

In 2019, the American Heart Association, in collaboration with the American College of Cardiology and the Heart Rhythm Society, published an update of their guideline for the management of patients with atrial fibrillation. A new recommendation in the guideline states: "Percutaneous LAA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term anticoagulation." The class of recommendation is IIb and the level of evidence is B_NR (moderate quality of evidence, nonrandomized). No other LAA closure devices are mentioned in the guideline.

Guideline Comparison

In 2017, Andrade et al provided the following summary (see Table 2) comparing guidelines by American, Canadian, and European societies on left atrial appendage exclusion and closure for the management of atrial fibrillation.

Table 2. Comparison of American, Canadian, and European Guidelines on LAA Exclusion/Closure

Procedure	AHA/ACC/HRS	CCS	ESC
Surgical LAA closure (excision or obliteration of LAA)	May be considered in patients undergoing cardiac surgery (IIb)	Should be considered as part of surgical ablation of AF associated with mitral, aortic valve, or coronary artery bypass surgery	May be considered in patients undergoing cardiac surgery (IIb)More data needed to confirm safety and efficacy of thoracoscopic exclusion
Percutaneous LAA exclusion	No recommendation	Not be used, except in research or in systematically documented use protocols in patients at high risk of stroke (CHADS2 ≥2) and antithrombotic therapy precluded	May be considered in patients with contraindications for long term anticoagulant treatment (IIb)

Adapted from Andrade et al (2017).
ACC: American College of Cardiology; AF: atrial fibrillation; AHA: American Heart Association; CCS: Canadian Cardiovascular Society; $CHADS_2$: Congestive Heart Failure, Hypertension, Age, Diabetes, Stroke/Transient Ischemic Attack; ESC: European Society of Cardiology; HRS: Heart Rhythm Society; LAA: left atrial appendage.

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

Medicare National Coverage
Since 2016, the Centers for Medicare & Medicaid Services has a national coverage determination under coverage with evidence development for percutaneous left atrial appendage closure in atrial fibrillation, as follows:

> "LAAC devices are covered when the device has received U.S. 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 ≥2 (Congestive heart failure, Hypertension, Age > 75, Diabetes, Stroke/transient ischemia attack/thromboembolism) or CHA2DS2-VASc score ≥ 3

(Congestive heart failure, Hypertension, Age ≥ 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 ≥ 25 interventional cardiac procedures that involve transseptal puncture through an intact septum; and,
- Continues to perform ≥ 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.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this policy are listed in Table 3.

Table 3. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT02681042	Left Atrial Appendage Closure with SentreHeart Lariat Device	50	Mar 2019
NCT03276169	Left Atrial Function Changes after Left Atrial Appendage Closure in Patients with Persistent Atrial Fibrillation	105	Nov 2019
NCT02513797[a]	aMAZE Study: LAA Ligation with the LARIAT Suture Delivery System as Adjunctive to Pulmonary Vein Isolation for Persistent Atrial Fibrillation (aMAZE)	600	Dec 2021
NCT03204695[a]	A Prospective, Multicenter, Non-Randomized, Post-market Clinical Follow-up Study to Confirm Safety and Performance of the Coherex WaveCrest Left Atrial Appendage Occlusion System in Patients with Non-valvular Atrial Fibrillation	65	Mar 2021
NCT02426944	Left Atrial Appendage Closure vs Novel Anticoagulation Agents in Atrial Fibrillation	400	May 2020
NCT03463317	Left Atrial Appendage CLOSURE in Patients With Atrial Fibrillation at High Risk of Stroke and Bleeding Compared to Medical Therapy: a Prospective Randomized Clinical Trial	1512	Feb 2023
NCT02964208[a]	AMPLATZER LAA Occluder Post Approval Study (PAS)	1000	Oct 2023
NCT02879448	AMPLATZER™‡ Amulet™‡ Left Atrial Appendage Occluder Randomized Controlled Trial	1878	Dec 2023
NCT03399851	Comparison of Amplatzer Amulet vs. Watchman Device in Patients Undergoing Left Atrial	200	Dec 2025

NCT No.	Trial Name	Planned Enrollment	Completion Date
	Appendage Closure: the SWISS-APERO Randomized Clinical Trial		
NCT03302494[a]	WAveCrest Vs. Watchman TranssEptal LAA Closure to REduce AF-Mediated STroke 2 (WAVECREST2)	1250	Dec 2025
NCT03309332[a]	OSB Lead-AMPLATZER PFO Occluder New Enrollment PAS	1214	Dec 2027
Unpublished			
NCT01118299	AMPLATZER Cardiac Plug Clinical Trial	3000	Dec 2018 (updated 02/01/19)

NCT: national clinical trial.
[a] indicates industry-sponsored study.

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, 06:2020.
2. 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): 1093-100. PMID 20299623
3. 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 02 2014; 64(21): e1-76. PMID 24685669
4. Lip GYH, Banerjee A, Boriani G, et al. Antithrombotic Therapy for Atrial Fibrillation: CHEST Guideline and Expert Panel Report. Chest. Nov 2018; 154(5): 1121-1201. PMID 30144419
5. Lip GY, Frison L, Halperin JL, et al. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation: the HAS-BLED (Hypertension,

Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score. J Am Coll Cardiol. Jan 11 2011; 57(2): 173-80. PMID 21111555
6. Food and Drug Administration. Approval Letter: WATCHMAN LAA Closure Technology. 2015; http://www.accessdata.fda.gov/cdrh_docs/pdf13/p130013a.pdf.
7. 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
8. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Percutaneous left atrial appendage closure therapy for prevention of stroke. TEC Assessments 2014;Volume 29:Tab 5.
9. 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
10. 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): 1057-64. PMID 26226997
11. 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. Jun 23 2015; 65(24): 2614-2623. PMID 26088300
12. 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): 1203-14. PMID 26724488
13. Lip GY, Lane DA. Stroke prevention in atrial fibrillation: a systematic review. JAMA. May 19 2015; 313(19): 1950-62. PMID 25988464
14. 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
15. Noelck N, Papak J, Freeman M, et al. Effectiveness of Left Atrial Appendage Exclusion Procedures to Reduce the Risk of Stroke: A Systematic Review of the Evidence. Circ Cardiovasc Qual Outcomes. Jul 2016; 9(4): 395-405. PMID 27407055

16. 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
17. 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
18. 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
19. 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
20. 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 2018; 59(1): 128-139. PMID 28215062
21. Baman JR, Mansour M, Heist EK, et al. Percutaneous left atrial appendage occlusion in the prevention of stroke in atrial fibrillation: a systematic review. Heart Fail Rev. Mar 2018; 23(2): 191-208. PMID 29453694
22. 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): 534-42. PMID 19683639
23. 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): 720-9. PMID 23325525
24. 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): 1988-98. PMID 25399274
25. 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): 1790-8. PMID 23500276

26. 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. Jul 08 2014; 64(1): 1-12. PMID 24998121
27. 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): 1792-9. PMID 23973952
28. 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 01 2012; 79(5): 794-800. PMID 21542102
29. Montenegro MJ, Quintella EF, Damonte A, et al. Percutaneous occlusion of left atrial appendage with the Amplatzer Cardiac PlugTM in atrial fibrillation. Arq Bras Cardiol. Feb 2012; 98(2): 143-50. PMID 22286325
30. 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 01 2011; 77(5): 700-6. PMID 20824765
31. 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 01 2011; 123(4): 417-24. PMID 21242484
32. Swaans MJ, Post MC, Rensing BJ, et al. Percutaneous left atrial appendage closure for stroke prevention in atrial fibrillation. Neth Heart J. Apr 2012; 20(4): 161-6. PMID 22231152
33. 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. Jun 25 2013; 61(25): 2551-6. PMID 23583249
34. 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. Aug 2016; 37(31): 2465-74. PMID 26822918
35. Dukkipati SR, Kar S, Holmes DR, et al. Device-Related Thrombus After Left Atrial Appendage Closure: Incidence, Predictors, and Outcomes. Circulation. Aug 28 2018; 138(9): 874-885. PMID 29752398
36. Jazayeri MA, Vuddanda V, Turagam MK, et al. Safety profiles of percutaneous left atrial appendage closure devices: An analysis of the Food and Drug Administration Manufacturer and

User Facility Device Experience (MAUDE) database from 2009 to 2016. J Cardiovasc Electrophysiol. Jan 2018; 29(1): 5-13. PMID 28988455
37. 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): 1104-9. PMID 25938303
38. 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): 565-72. PMID 25104525
39. 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 09 2013; 62(2): 108-118. PMID 23062528
40. 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. Mar 15 2013; 111(6): 869-73. PMID 23312129
41. Miller MA, Gangireddy SR, Doshi SK, et al. Multicenter study on acute and long-term safety and efficacy of percutaneous left atrial appendage closure using an epicardial suture snaring device. Heart Rhythm. Nov 2014; 11(11): 1853-9. PMID 25068574
42. Gafoor S, Franke J, Bertog S, et al. Left atrial appendage occlusion in octogenarians: short-term and 1-year follow-up. Catheter Cardiovasc Interv. Apr 01 2014; 83(5): 805-10. PMID 24259397
43. 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
44. 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): 188-93. PMID 21050893
45. 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): 121-7. PMID 23765504
46. Fink T, Schluter M, Tilz RR, et al. Acute and long-term outcomes of epicardial left atrial appendage ligation with the second-generation LARIAT device: a high-volume electrophysiology center experience. Clin Res Cardiol. Dec 2018; 107(12): 1139-1147. PMID 29881879

47. Dar T, Afzal MR, Yarlagadda B, et al. Mechanical function of the left atrium is improved with epicardial ligation of the left atrial appendage: Insights from the LAFIT-LARIAT Registry. Heart Rhythm. Jul 2018; 15(7): 955-959. PMID 29477973
48. Litwinowicz R, Bartus M, Burysz M, et al. Long term outcomes after left atrial appendage closure with the LARIAT device-Stroke risk reduction over five years follow-up. PLoS ONE. 2018; 13(12): e0208710. PMID 30566961
49. Litwinowicz R, Bartus M, Malec-Litwinowicz M, et al. Left Atrial Appendage Occlusion for Secondary Stroke Prevention in Patients with Atrial Fibrillation: Long-Term Results. Cerebrovasc Dis. 2019; 47(3-4): 188-195. PMID 31121584
50. Litwinowicz R, Bartus M, Kapelak B, et al. Reduction in risk of stroke and bleeding after left atrial appendage closure with LARIAT device in patients with increased risk of stroke and bleeding: Long term results. Catheter Cardiovasc Interv. Nov 15 2019; 94(6): 837-842. PMID 30884101
51. Nietlispach F, Gloekler S, Krause R, et al. Amplatzer left atrial appendage occlusion: single center 10-year experience. Catheter Cardiovasc Interv. Aug 01 2013; 82(2): 283-9. PMID 23412815
52. 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): 551-8. PMID 24579432
53. 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): 528-36. PMID 22584492
54. 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): 347-53. PMID 23252940
55. 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
56. 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
57. Cruz-Gonzalez I, Gonzalez-Ferreiro R, Freixa X, et al. Left atrial appendage occlusion for stroke despite oral anticoagulation (resistant stroke). Results from the Amplatzer Cardiac Plug registry. Rev Esp Cardiol (Engl Ed). Jan 2020; 73(1): 28-34. PMID 31036510

58. Santoro G, Meucci F, Stolcova 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 2016; 11(10): 1188-94. PMID 25354761
59. Meerkin D, Butnaru A, Dratva D, et al. Early safety of the Amplatzer Cardiac Plug for left atrial appendage occlusion. Int J Cardiol. Oct 09 2013; 168(4): 3920-5. PMID 23890886
60. 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 01 2014; 83(5): 796-802. PMID 24327462
61. 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 09 2013; 62(2): 96-102. PMID 23665098
62. 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): 656-65. PMID 25736061
63. Landmesser U, Schmidt B, Nielsen-Kudsk JE, et al. Left atrial appendage occlusion with the AMPLATZER Amulet device: periprocedural and early clinical/echocardiographic data from a global prospective observational study. EuroIntervention. Sep 20 2017; 13(7): 867-876. PMID 28649053
64. Landmesser U, Tondo C, Camm J, et al. Left atrial appendage occlusion with the AMPLATZER Amulet device: one-year follow-up from the prospective global Amulet observational registry. EuroIntervention. Aug 03 2018; 14(5): e590-e597. PMID 29806820
65. Al-Kassou B, Omran H. Comparison of the Feasibility and Safety of First- versus Second-Generation AMPLATZER Occluders for Left Atrial Appendage Closure. Biomed Res Int. 2017; 2017: 1519362. PMID 29085833
66. January CT, Wann LS, Calkins H, et al. 2019 AHA/ACC/HRS focused update 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 Clinical Practice Guidelines and the Heart Rhythm Society. Heart Rhythm. Aug 2019; 16(8): e66-e93. PMID 30703530
67. 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

68. Center for Medicare & 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&ncdver=1&NCAId=281&bc=AAAAAAAACAAAAA%3d%3d&.

Policy History

Original Effective Date: 05/18/2011
Current Effective Date: 11/09/2020

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
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
10/03/2019	Medical Policy Committee review
10/09/2019	Medical Policy Implementation Committee approval. No change to coverage.

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

Policy # 00296
Original Effective Date: 05/18/2011
Current Effective Date: 11/09/2020

10/01/2020 Medical Policy Committee review
10/07/2020 Medical Policy Implementation Committee approval. Added to policy guideline section.
Next Scheduled Review Date: 10/2021

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 2019 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. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with 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: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

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