MEDICAL POLICY

POLICY TITLE	**LEFT-ATRIAL APPENDAGE CLOSURE DEVICES FOR STROKE PREVENTION IN ATRIAL FIBRILLATION**
POLICY NUMBER	**MP 1.127**

Effective Date:	**9/1/2023**

I. POLICY

The use of a device with U.S. Food and Drug Administration (FDA) approval for percutaneous left atrial appendage closure (e.g., the Watchman or Amplatzer Amulet) may be considered **medically necessary** for the prevention of stroke in individuals with atrial fibrillation when the following criteria are met:

- There is an increased risk of stroke and systemic embolism based on $CHADS_2$ or CHA_2DS_2-VASc score and systemic anticoagulation therapy is recommended; **AND**

- The long term risks of systemic anticoagulation clearly outweigh the risks of the device implantation (see Policy Guidelines).

The use of a device with FDA approval for percutaneous left atrial appendage closure (e.g., the Watchman) for stroke prevention in individuals who do not meet the above criteria is considered **investigational.** There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with the above procedure.

The use of other percutaneous left atrial appendage closure devices, including but not limited to the Lariat, and Amplatzer Cardiac Plug devices, for stroke prevention in individuals with atrial fibrillation is considered **investigational**. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with the above procedure.

Surgical closure of the left atrial appendage, including use of a clip, may be considered **medically necessary** for the prevention of stroke when **ALL** of the following criteria are met:

- Individual has a documented diagnosis of paroxysmal or persistent atrial fibrillation
- Individual has an increased risk of stroke and systemic embolism based on $CHADS_2$* ≥ 2 or CHA_2DS_2-VASc** score ≥ 3
- Systemic anticoagulation therapy is recommended
- Closure is performed only:
    - in conjunction with open cardiac surgical procedures for another indication; **AND**
    - using a U.S. Food and Drug Administration (FDA) approved device.

The use of a device with FDA approval for surgical closure of left atrial appendage for stroke prevention in patients who do not meet the above criteria is considered **investigational.** There

is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with the above procedure.

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 individuals treated with systemic anticoagulation. An example is the HAS-BLED score, which is validated to assess the annual risk of significant bleeding in individuals with atrial fibrillation treated with warfarin. The score ranges 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 (Pisters et al, 2010)

Letter	Clinical Characteristic	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)	1
D	Drugs or alcohol (1 point each)	1 or 2

Adapted from Pisters et al (2010).

Risk of major bleeding in individuals 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 individuals for adverse risks, closer monitoring of international normalized ratio, or differential dose selections of oral anticoagulants or aspirin..

Cross-references:

MP 1.039 Closure Devices for Patent Foramen Ovale and Atrial Septal Defects (ASD**)**
MP 2.083 Open and Thoracic Approaches to Treat Atrial Fibrillation and Atrial Flutter (Maze and Related Procedures)

II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. Please see additional information below.

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FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at: https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies

III. DESCRIPTION/BACKGROUND

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Atrial Fibrillation and Stroke

Atrial Fibrillation (AF) 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 non-treated 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 CHA_2DS_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. Food and Drug Administration (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. Newer agents do not require the frequent monitoring seen with warfarin therapy; however, specific reversal agents do not exist for all of these agents. The 2018 American College of Chest Physicians (updated from 2012) recommend that CHA_2DS_2-VASc 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. $CHADS_2$ 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	1 ($CHADS_2$) 2 (CHA_2DS_2-VASc)
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 one to two months. After this period, patients are maintained on antiplatelet agents (i.e., aspirin and/or clopidogrel) indefinitely. The Watchman FLX device is a next-generation Watchman device that is also FDA-approved for LAAC. This device is based on the design of the Watchman device, is fully recapturable and repositionable, and was made to occlude a wider size range of LAA than the original Watchman device.8, The Amplatzer cardiac plug (St. Jude Medical), is FDA-approved for closure of atrial septal defects but not for LAAC. A second-generation device developed for the specific indication of LAAC, the Amplatzer Amulet (Abbott), received FDA approval in August 2021.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.

In September 2021, the FDA sent a letter to healthcare providers indicating that women undergoing percutaneous LAA closure may be at higher risk of adverse procedural outcomes than men. This was based on an analysis of registry data from 49,357 patients who underwent LAA closure with the Watchman device. When adjusted for multiple confounding factors, the study found women were more likely than men to experience any adverse event, major adverse events, and major bleeding. Women also had a significantly higher risk of death (adjusted odds ratio [OR], 2.01; 95% confidence interval [CI] 1.31 to 3.09) but absolute risk was low for both women and men (0.3% vs. 0.1%). In their letter, the FDA stated that they believe the benefits continue to outweigh the risks for approved LAA closure devices when used in accordance with their instructions for use.

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.

Ideally, percutaneous LAAC devices would represent an alternative to oral anticoagulation for the prevention of stroke in patients with AF, However, during the post implantation period the LAAC device may be associated with increased thrombogenicity, therefore, anticoagulation is used during the periprocedural period. Most studies evaluating percutaneous LAAC devices have included patients who are eligible for anticoagulation.

REGULATORY STATUS

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 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. In 2020, the Watchman FLX device (Boston Scientific) was approved by the FDA based on the single-arm, nonrandomized PINNACLE FLX study.8, The Amplatzer™ Amulet™ Left Atrial Appendage Occluder (Abbott) received FDA approval in 2021 through the premarket approval process based on results from the Amplatzer Amulet Left Atrial Appendage Occluder Randomized Controlled Trial (Amulet IDE Trial).9, The Watchman and Amplatzer Amulet devices are 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 United States for percutaneous LAAC. In 2006, the Lariat™ 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 Cardiac Plug device (St. Jude Medical) and WaveCrest™ (Johnson & Johnson Biosense Webster) have CE approval in Europe for LAAC but are not currently approved in the United States for this indication.

IV. RATIONALE

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SUMMARY OF EVIDENCE

For individuals who have atrial fibrillation (AF) who are at increased risk for embolic stroke who receive an FDE-approved percutaneous left atrial appendage closure (LAAC) device (e.g., the Watchman or Amulet device), the evidence includes randomized controlled trials (RCTs) and observational studies. 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 Watchman 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. Evidence for the Amplatzer Amulet device comes from 2 RCTs comparing the Amulet and Watchman devices, one of which was a short-term trial that assessed periprocedural outcomes at 45 days. The second trial comparing the Amulet and Watchman devices found the Amulet device to be noninferior to the Watchman device after 18 months of follow-up for a composite efficacy outcome that included ischemic stroke or systemic embolism and for a composite safety outcome that included all-cause mortality, major bleeding or procedure-related complications. One additional RCT evaluated the use of either the Amplatzer Amulet or Watchman device versus anticoagulants; subgroup analyses according to device were not performed. After up to 4 years of follow-up, the study found LAAC LAA closure with either the Watchman or Amulet was noninferior to anticoagulants for a composite outcome that included stroke, transient ischemic attack (TIA) TIA, systemic embolism, clinically significant bleeding, significant periprocedural or device-related complications, or cardiovascular mortality. 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 or Amplatzer Amulet device (e.g., the Lariat or Amplatzer Cardiac Plug), the evidence includes several nonrandomized comparator studies and uncontrolled observational studies. 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. Evidence from other observational studies of these devices which report high procedural success but also numerous complications. In addition, these devices do not have U.S. FDA approval for LAAC. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

V. DEFINITIONS

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ATRIAL FIBRILLATION is a condition where there is disorganized electrical conduction in the atria, resulting in ineffective pumping of blood into the ventricle.

ISCHEMIA is a temporary deficiency of blood flow to an organ or tissue.

STROKE is a condition due to the lack of oxygen to the brain which may lead to reversible or irreversible paralysis. The damage to a group of nerve cells in the brain is often due to interrupted blood flow, caused by a blood clot or blood vessel bursting. Depending on the area of the brain that is damaged, a stroke can cause coma, paralysis, speech problems, and dementia.

THROMBOEMBOLISM is a condition in which a blood vessel is blocked by an embolus carried in the bloodstream from the site of formation of the clot.

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VII. DISCLAIMER

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Capital Blue Cross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice, and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Covered when medically necessary:

Procedure Codes							
33340	33268						

Investigational; therefore, not covered:

Procedure Codes							
33267	33269						

ICD-10-CM Diagnosis Codes	Description
I48.0	Paroxysmal atrial fibrillation
I48.11	Longstanding persistent atrial fibrillation
I48.19	Other persistent atrial fibrillation
I48.20	Chronic atrial fibrillation, unspecified
I48.21	Permanent atrial fibrillation
I48.91	Unspecified atrial fibrillation

IX. REFERENCES

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POLICY TITLE	LEFT-ATRIAL APPENDAGE CLOSURE DEVICES FOR STROKE PREVENTION IN ATRIAL FIBRILLATION
POLICY NUMBER	MP 1.127

X. POLICY HISTORY

TOP

MP 1.127	**02/26/2020 Consensus review**. Policy statement unchanged. Background and references updated. Coding reviewed.
	01/19/2021 Consensus review. No change in policy statement. Description/Background, Rationale, and References updated.
	12/03/2021 Administrative update. New codes 33267, 33268, and 33269 added to policy.
	02/15/2022 Minor review. Added surgical closure of the left atrial appendage to policy with criteria. "Percutaneous" removed from policy name. Description/Background updated. References added. Codes 33267 and 33269 moved to INV.
	5/9/2023 Minor review. Updated policy statement to include FDA approved Amplatzer Amulet. Updated background, regulatory status, rationale, and references. Table 1 updated. Coding reviewed.

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