**WATCHMAN™ LEFT ATRIAL APPENDAGE CLOSURE**

**Approval/Coverage Status & Clinical Evidence Summary**

**FDA Approved on March 13, 2015**

The WATCHMAN Left Atrial Appendage Closure (LAAC) implant procedure received FDA approval on March 13, 2015, and has been established as safe and effective for treating patients within its approved indication. The device is indicated to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who:

* Are at increased risk for stroke and systemic embolism based on CHADS2 or CHA2DS2-VASc January CT, et al 2014 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 non-pharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared to warfarin.

**CMS National Coverage Determination established February 8, 2016**

CMS finalized a National Coverage Determination for percutaneous LAAC (20.34) on February 8, 2016. The NCD establishes uniform coverage and access to the WATCHMAN Device for Medicare beneficiaries who meet specific patient criteria, including:

* A CHADS2 score ≥ 2 or CHA2DS2-VASc score ≥ 3
* A suitability for short-term warfarin but deemed unable to take long term oral anticoagulation
* Documented evidence of a formal shared decision making interaction between the patient and an independent non-interventional physician using an evidence-based decision tool on oral anticoagulation.

To access the NCD for percutaneous LAAC therapy in its entirety, visit the CMS website at <https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=281>

**Clinical Condition and Treatment Options**

Atrial fibrillation (AF) is the most common cardiac arrhythmia, currently affecting more than 5 million Americans Go AS, et al 2013. In AF, the left atrium does not beat - instead it fibrillates meaning that it barely moves. Because of this, AF patients have a five-fold increased risk of stroke due to blood pooling in the left atrium and left atrial appendage (LAA). The pooled blood can form blood clots (i.e., thrombus formation), which can break off and go into the systemic circulation and lodge somewhere else in the body. Most commonly, these clots will lodge in the brain causing a stroke. Ninety-one percent of left atrial thrombi in non-valvular atrial fibrillation have been shown to be isolated to, or originate in, the LAA Blackshear JL, et al 1996. The most common treatment for reducing the risk of these strokes from forming is using oral anticoagulants. Warfarin has been used for many years and works by interfering with the body’s clot forming mechanisms. Despite its proven efficacy, long-term warfarin therapy is not well-tolerated by some patients, has a very narrow therapeutic range, and carries a high risk for bleeding complications.

**WATCHMAN Left Atrial Appendage Closure**

The WATCHMAN Left Atrial Appendage Closure Device is a first-of-its-kind, proven alternative to long-term warfarin for stroke risk reduction in patients with non-valvular atrial fibrillation. WATCHMANis the most studied LAAC device in the world and is the only one with long-term data from randomized trials and prospective, multi-center registries.

The WATCHMAN Device is indicated to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who:

* Are at increased risk for stroke and systemic embolism based on CHADS2 or CHA2DS2-VASc January CT, et al 2014 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 non-pharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared to warfarin.

The WATCHMANLeft Atrial Appendage is an implant that acts as a physical barrier, sealing the LAA to prevent thromboemboli from entering into the arterial circulation from the LAA, thereby reducing the risk of stroke and potentially eliminating the need for warfarin therapy in those patients with non-valvular AF who are eligible for warfarin. Implant of the WATCHMANDevice is performed under general anesthesia in a cardiac catheterization laboratory. The WATCHMANDevice is implanted percutaneously via a transcatheter approach, using a standard transseptal technique.

**Clinical Evidence**

The WATCHMANclinical program consists of five prospective investigational studies (PILOT, PROTECT AF, CAP,PREVAIL, and CAP2) which include more than 2,400 patients implanted and >8,000 patient-years of follow-up regarding WATCHMAN TM Device performance. Final, five-year results from the PROTECT AF, CAP and PREVAIL studies have been published and/or presented. These long-term data continue to demonstrate the WATCHMANDevice is a safe alternative to long-term warfarin therapy which offers comparable stroke risk reduction and enables patients to stop taking warfarin.

The PILOT study Sick PB, et al 2007 enrolled the first clinical study patient in 2002, and proved the safety and feasibility of WATCHMAN™ implant. The prospective randomized study, PROTECT AF Holmes D, et al 2009 enrolled the first clinical study patient in 2005 and was published in the *Lancet* in August 2009 with a mean follow-up of 18 months. The efficacy results were very compelling in that 87% of patients were successfully implanted with the device and able to discontinue warfarin therapy 45 days post-implant. Patients in the device group also had a 38% lower risk of stroke, systemic embolism, and cardiovascular or unexplained death when compared to patients treated with warfarin alone. Several subsequent analyses have been performed over the course of follow-up, and continue to demonstrate a durable benefit in primary efficacy event reduction. Reddy V, et al 2013, Reddy V, et al 2014, Holmes DR, et al 2014

Next, the prospective, multi-center **C**ontinued **A**ccess to **P**ROTECT AF (CAP) Registry enrolled the first trial patient in 2009 and enrolled a total of 566 patients using the same inclusion and exclusion criterial as the PROTECT AF study. These patients have completed all study follow-up (mean 4.2 years) with final results presented at the Transcatheter Cardiovascular Therapeutics conference in 2017 and published in *JACC* Kar S, et al 2017. Ninety-four percent (94%) of patients in the study were successfully implanted and procedure complications were significant reduced when compared to the PROTECT AF experience Reddy V, et al 2011. In addition, 96% of patients discontinued warfarin after 45 days post-implant. While there was not a warfarin control arm as a comparator in the study, the rate of ischemic strokes in CAP was similar to the rate seen in the PROTECT AF device arm (1.2 vs 1.4 per 100 patient years, respectively).

The cadence and growing body of clinical evidence continues to support the medical value and safety of the WATCHMAN™ implant therapy. The PREVAIL randomized control study enrolled it’s first patient in 2012, all patients have completed the required follow-up (mean 4.0 years). First results were published in 2014 in *JACC* and support that WATCHMAN™ was successfully implanted with low complication rates and no differences in procedure-related events between new and experienced operators Holmes DR, et al 2014. Since the device was approved by the FDA in March of 2015, procedural safety data for both new and experience operators continues to show consistent results between 1.5% and 2% for major serious adverse events. Varosy P, et al 2017 and Reddy, et al 2017 Furthermore, PREVAIL also showed that 92% of patients were able to discontinue warfarin therapy 45 days post implant, and >99% were able to discontinue warfarin therapy after 12 months.

Because the efficacy endpoint of the trial used a Bayesian statistical model that incorporated a portion of the PROTECT AF results, efficacy results for PREVAIL are presented in conjunction with PROTECT AF in order to fully describe the effect of LAAC therapy compared to warfarin. As a result, a patient-level meta-analysis using the final results of both randomized trials and were published in 2017 in *JACC* Reddy V, et al 2017. The 5-Year Patient-Level Meta-Analysis of PROTECT AF and PREVAIL (2:1 Randomization) provided the totality of the evidence from both randomized trials for the WATCHMAN™ therapy after study required follow-up was completed for both randomized trials. This analysis demonstrated that LAAC with WATCHMAN provided stroke reduction in non-valvular atrial fibrillation patients that was comparable to warfarin with additional, statistically significant reductions in disabling or fatal stroke, hemorrhagic stroke, cardiovascular and all-cause mortality, as well as major non-procedure related bleeding.

The totality of the clinical evidence of WATCHMAN™ reinforces the following clinical outcomes Reddy VY, et al 2017

* A reduction of 18% (p=0.27) in all-cause stroke, systemic embolism and cardiovascular/unexplained mortality
* Comparable to warfarin for stroke, with statistically significant reductions by 55% in disabling/fatal stroke (p=0.03) and an 80% reduction in hemorrhagic strokes (p=0.002)
* Statistically significant reductions in all-cause and CV/unexplained mortality respectively 27% (P=0.04) and 41% (p=0.03)
* 72% reduction in major bleeding >6 months post-procedure vs warfarin Price MJ, et al 2015

The WATCHMAN™ Device is the only FDA approved device for percutaneous left atrial appendage closure and is the most studied LAAC device in the world. WATCHMAN is the only LAAC device with long-term clinical data from both randomized clinical trial and prospective, multi-center registries, with five year follow-up data on the majority of patients. These long-term data demonstrate that the WATCHMAN TM Device is a safe alternative to long-term warfarin therapy which offers comparable stroke risk reduction and enables patients to stop taking warfarin.

**References**

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