Fact Sheet: The WATCHMAN™ Left Atrial Appendage (LAA) Closure Device

About WATCHMAN™

- Atrial Fibrillation (AF) is not a life-threatening condition itself, but the most common sustained arrhythmia and a major risk factor for stroke, making a person five times more likely to suffer a stroke. AF is marked by an irregular and often rapid heart rate that commonly causes poor blood flow to the body. Across Europe, about six million people have AF, with approximately one to two percent of the general population being affected. AF affects around 800,000 people a year in the UK.
- Over 90 percent of strokes in patients with AF are caused by emboli (blood clots) forming in the Left Atrial Appendage (LAA) and migrating from there and blocking circulation to the brain.
- The WATCHMAN™ Left Atrial Appendage (LAA) Closure Device is a proven device alternative to warfarin for reducing the risk of stroke in patients with AF. This has been shown in two landmark studies – PROTECT AF and ASA Plavix (ASAP). Data from the latter showed a 77 percent reduction of ischemic stroke risk in patients with AF, who have been implanted with the device and are contraindicated to warfarin.
- It is designed to be permanently implanted at or slightly distal to the ostium (opening) of the LAA to trap potential emboli before they exit the LAA and dislodge into circulation, potentially causing a stroke.

The WATCHMAN™ device implant procedure

- The WATCHMAN™ (LAA) Closure Device consists of the implantable device and the tools for implantation.
- The implantable device consists of a self-expanding nickel titanium (nitinol) frame structure with fixation anchors and a PET fabric that covers the atrial facing surface of the device, which is designed to prevent clots from exiting the LAA.
- The device is preloaded within a delivery catheter and is available in five different sizes (21, 24, 27, 30 and 33 mm) to accommodate the unique anatomy of each patient's LAA and allow appropriate sizing within the ostium.
- The WATCHMAN™ implant procedure is performed under general anaesthesia in a catheterisation laboratory setting. The device is implanted via a trans-septal approach by using the catheter-based delivery system, which is capable of recapturing the device, if necessary.
To gain access into the LAA, the WATCHMAN™ Access Sheath is utilised and serves as a conduit for the delivery catheter. It is available in both a single curve (90 degree angle) and double curve distal tip configuration.

To measure the LAA and determine which size of the WATCHMAN™ device needs to be implanted, a transesophageal echocardiogram (TEE) is performed upfront to better visualise the structure of the heart.

After the inter-atrial septum is crossed using a standard trans-septal access system, the WATCHMAN™ Access Sheath and Dilator are advanced over a guide wire into the left atrium. The access sheath is then carefully advanced into the distal portion of the LAA over a pigtail catheter. The WATCHMAN™ Delivery System is prepped, inserted into the access sheath, and slowly advanced under fluoroscopic guidance. The WATCHMAN™ device is then deployed into the LAA.

The device release criteria are confirmed via fluoroscopy and a TEE prior to releasing the device. The entire procedure usually lasts about an hour and the patient typically needs to stay in the hospital for 24 hours afterwards.

The procedure is conducted by a team of physicians, which includes structural heart interventional cardiologists/electrophysiologists and physicians with special expertise in echocardiographic imaging.

After the procedure, warfarin therapy for a minimum of 45 days (International Normalised Ratio/INR 2.0 to 3.0) is required in all patients receiving a WATCHMAN™ device who are eligible for warfarin therapy or other equivalent oral anticoagulant. At 45 days after the implantation, a TEE is performed for further assessment of the device. Physicians may then decide to discontinue warfarin therapy for individual patients. In the PROTECT AF study 86 percent of the patients implanted with a WATCHMAN™ device were able to stop taking warfarin after 45 days. Patients contraindicated to anticoagulation therapy and patients who are no longer taking warfarin should begin treatment with 75mg clopidogrel and an adult aspirin dose daily for up to six months and should remain on one adult aspirin indefinitely.

Closing off the LAA requires extensive training and a Certification to Implant, which can be obtained after successfully completing the comprehensive, three-step physician training programme developed by Boston Scientific. To educate future implanters on the optimal procedure for WATCHMAN™, Boston Scientific is strongly committed to a unique training programme, which consists of online courses, hands-on training with Virtual Reality technology at the Institute for Therapy Advancement and patient cases at one of the 15 existing Professional Training Centres (PTCs).

\(^1\) Also referred to as TOE.
Patient eligibility
In August 2012, the WATCHMAN™ LAA Closure Device received approval for expanded use in Europe based on results from the ASA Plavix (ASAP) study. This indication expansion offers a treatment alternative to patients with AF, both indicated and contraindicated to anticoagulation therapy, thus extending the benefits of the therapy to a wider population and especially to those at higher risk than others. The LAA closure procedure aims at reducing the risk of ischemic stroke and systemic thromboembolism by closing off the LAA permanently and thereby avoiding the migration of emboli to the brain.

Current treatment guidelines
Management of AF patients is aimed at reducing symptoms and risk of severe complications associated with AF such as stroke. These therapeutic goals need to be pursued in parallel, especially upon the initial presentation of newly detected AF. There are a number of ways that AF can be managed ranging from opportunistic screening, ECGs, cardioversion (either electrical or pharmacological cardioversion using antiarrhythmic medicines) to return the heart to normal rhythm and anticoagulation with aspirin, warfarin and heparin, which reduce the risk of blood clots potentially causing stroke. Management differs according to the type of AF and according to specific patients’ characteristics such as the presence of comorbidities or risk factors.

Recommendations for antithrombotic therapy should always be based on the presence (or absence) of risk factors for stroke and thromboembolism. The current ESC guidelines use the CHADS2 stroke risk stratification scheme as a simple, initial (and easily remembered) means of assessing stroke risk in patients with AF. In patients with a CHADS2 score of ≥2, long-term OAC therapy, e.g. with vitamin K antagonists (VKA), is recommended in a dose adjusted to achieve an INR value in the range of 2.0–3.0, unless contraindicated. The gold standard here is warfarin. In patients with a CHADS2 score of 0–1, or where a more detailed stroke risk assessment is indicated, it is recommended to use a more comprehensive risk factor-based approach, incorporating other risk factors for thromboembolism as well, for example by using the CHA2DS2-VASc score.

In addition, surgical approaches to thrombo-prophylaxis such as permanently closing off the LAA can offer treatment alternatives to patients who do not tolerate or are contraindicated to long-term therapy with OACs. This has already been reflected by recent revisions of common treatment guidelines:

- In August 2012, the European Society of Cardiology (ESC) announced the inclusion of LAA closure devices like WATCHMAN™ in the revised “Guidelines for Management of Patients with Atrial Fibrillation”. The new Guidelines recommend LAA closure as a class IIb, level of evidence b, for patients with a high stroke risk and contraindications for long-term oral anticoagulation, based on existing clinical evidence such as the
PROTECT AF trial. Previous versions of the guidelines had already suggested that occlusion of the LAA may reduce stroke in AF patients.\textsuperscript{15} 

- Guidelines of the American Heart Association recommend the removal of the LAA during cardiac procedures such as coronary bypass or valve repair surgery for patients at risk of developing post-operative AF.\textsuperscript{16} This is mainly due to the fact that surgical approaches to LAA ligation using sutures or staples have failed to demonstrate consistent closure.
- According to the guidelines of the National Institute for Health and Clinical Excellence (NICE), the percutaneous occlusion of the LAA is efficacious in reducing the risk of thromboembolic complications associated with non-valvular AF. NICE also recommends that the procedure should be carried out by clinicians with specific training and appropriate experience in the procedure.\textsuperscript{17}

**Existing clinical evidence**

WATCHMAN™ is the most studied LAA closure device with over 2,000 patients enrolled in prospective studies and over 4,000 patient years of follow-up. In addition, it is the only LAA closure device whose efficacy that has been demonstrated under a large multi-centre, prospective, randomised clinical trial.

- **The PROTECT AF Trial**
  The WATCHMAN™ LAA Closure Device for Embolic PROTECTion in Patients with Atrial Fibrillation (PROTECT AF) trial was designed to demonstrate the safety and effectiveness of the device in patients with non-valvular AF who are eligible for warfarin therapy and have a CHADS\(_2\) stroke risk score of 1 or higher. 707 patients were randomised 2:1 to the WATCHMAN™ device or warfarin in this non-inferiority trial. WATCHMAN™ achieved its primary endpoint with a 38 percent relative risk reduction for stroke, cardiovascular death and systemic embolism compared to long-term warfarin therapy.\textsuperscript{18} In addition, the study also showed a 29 percent relative risk reduction in all stroke.

- **The ASAP Study**
  The ASAP (Aspirin And Plavix\textsuperscript{®}) registry was a non-randomised feasibility study designed to determine if the WATCHMAN™ device is a safe and effective treatment for patients with atrial fibrillation who are contraindicated to long-term oral anticoagulation therapy. The prospective, multi-centre study evaluated 150 patients with AF not eligible for warfarin therapy, who were implanted and treated with dual antiplatelet therapy for six months post-procedure. Subjects were followed for a mean average of 14.4 months. Data showed a 77 percent reduction of ischemic stroke risk in high risk patients with AF who are contraindicated to warfarin.
The PREVAIL Trial
In follow-up to PROTECT AF, the WATCHMAN™ device is currently being evaluated in a second clinical study. The Prospective Randomised EVALuation of the WATCHMAN™ LAA Closure Device In Patients with Atrial Fibrillation Versus Long Term warfarin Therapy (PREVAIL) trial enrolled 407 patients at 42 sites and is comparing the WATCHMAN™ device to warfarin in high-risk patients with AF, who are eligible for long-term warfarin therapy. First primary endpoints are the same as in PROTECT AF (ischemic and haemorrhagic stroke, systemic embolism and cardiovascular death).

Market availability
In March 2011, Boston Scientific announced the completed acquisition of Atritech Inc., the company which originally developed WATCHMAN™. The device received the CE Mark in 2005 and was commercialised outside the United States in 2009. In the US, the WATCHMAN™ device is an investigational device, limited by applicable law to investigational use only and not available for sale. Today, WATCHMAN™ is available in 30 countries worldwide, including most European countries. Boston Scientific is dedicated to actively training physicians in even more countries on the safe and effective use of the device to make this therapy option available to a larger patient base in the future.

About Boston Scientific
Boston Scientific is a worldwide developer, manufacturer and marketer of medical devices whose products are used in a broad range of interventional medical specialties. For more information, please visit: www.bostonscientific.com/watchman-eu/

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