ABBREVIATED STATEMENT WATCHMAN™ Left Atrial Appendage Closure Device with Delivery System and WATCHMAN Access System

Indications for Use

The WATCHMAN Device is intended for the chronic, long-term management of patients with non-valvular atrial fibrillation (NVAF) who are at high risk for anticoagulation due to an increased risk of stroke or systemic embolism (SE) and who are either contraindicated for, or unwilling to take, long-term warfarin therapy. The WATCHMAN Device is intended for chronic closure of the left atrial appendage (LAA) in patients with NVAF. The WATCHMAN System is intended for use as a treatment option for patients who are not suitable candidates for warfarin due to an increased risk of stroke or systemic embolism (SE) and/or who are contraindicated for, or unwilling to take, long-term warfarin therapy. The WATCHMAN System is not intended for use as a sole treatment for the prevention of stroke or systemic embolism (SE) in patients with NVAF who are not at high risk for stroke or who are not candidates for the chronic, long-term management of NVAF. The WATCHMAN System is not intended for use as a sole treatment for patients with NVAF who are not at high risk for stroke or who are not candidates for the chronic, long-term management of NVAF.

The WATCHMAN Device is intended to be implanted as part of a comprehensive treatment strategy for the prevention of NVAF-related stroke or SE. The safety and effectiveness (and benefit-risk profile) of the WATCHMAN Device has not been established in patients for whom all available anticoagulation is determined to be contraindicated. The LAA is a thin-walled structure. Use caution when accessing the LAA and deploying the device. Do not release the WATCHMAN Device from the core wire if the device does not deploy properly. Do not use the WATCHMAN Device if: Intracardiac thrombus is visualized by echocardiographic imaging. An atrial septal defect (ASD) or atrial septal aneurysm is present. The LAA anatomy will not accommodate the device. See Table 46 in the DFU. Any of the customary contraindications for other percutaneous catheterization procedures (e.g., active infection, bleeding disorder, size too small to accommodate TEE probe or required catheters) or conditions (e.g., active infection, bleeding disorder, platelet dysfunction, active endocarditis) that may increase the risk of access-related complications or may require use of the WATCHMAN Access System in a non-standard configuration. Do not use the WATCHMAN Device if: Intracardiac thrombus is visualized by echocardiographic imaging. Atrial septal defect (ASD) or atrial septal aneurysm is present. The LAA anatomy will not accommodate the device. See Table 46 in the DFU. Any of the customary contraindications for other percutaneous catheterization procedures (e.g., active infection, bleeding disorder, size too small to accommodate TEE probe or required catheters) or conditions (e.g., active infection, bleeding disorder, platelet dysfunction, active endocarditis) that may increase the risk of access-related complications or may require use of the WATCHMAN Access System in a non-standard configuration.

WARNINGS

Do not use the WATCHMAN Device if: Intracardiac thrombus is visualized by echocardiographic imaging. Atrial septal defect (ASD) or atrial septal aneurysm is present. The LAA anatomy will not accommodate the device. See Table 46 in the DFU. Any of the customary contraindications for other percutaneous catheterization procedures (e.g., active infection, bleeding disorder, size too small to accommodate TEE probe or required catheters) or conditions (e.g., active infection, bleeding disorder, platelet dysfunction, active endocarditis) that may increase the risk of access-related complications or may require use of the WATCHMAN Access System in a non-standard configuration.

A device. See Table 5. Do not inject the WATCHMAN Device with a second device. The WATCHMAN Device was designed for use in the left atrial appendage. Site selection should be based on accurate LAA measurements obtained using fluoro and ultrasound guidance (TEE). Do not use the WATCHMAN Device if: Intracardiac thrombus is visualized by echocardiographic imaging. Atrial septal defect (ASD) or atrial septal aneurysm is present. The LAA anatomy will not accommodate the device. See Table 46 in the DFU. Any of the customary contraindications for other percutaneous catheterization procedures (e.g., active infection, bleeding disorder, size too small to accommodate TEE probe or required catheters) or conditions (e.g., active infection, bleeding disorder, platelet dysfunction, active endocarditis) that may increase the risk of access-related complications or may require use of the WATCHMAN Access System in a non-standard configuration.

Meta-Analysis Study Design

The efficacy and safety of WATCHMAN™ were assessed in both the PROTECT AF (N=351) and PREVAIL (N=407) trials. These trials included patients with NVAF and were evaluated using long-term follow-up in treatment arms that were blinded to the WATCHMAN Implant at WATCHMAN.com

Meta-Analysis of the WATCHMAN Implant

The efficacy and safety of WATCHMAN™ were assessed in both the PROTECT AF (N=351) and PREVAIL (N=407) trials. These trials included patients with NVAF and were evaluated using long-term follow-up in treatment arms that were blinded to the WATCHMAN Implant at WATCHMAN.com

Indications for use...

Introducing WATCHMAN™ LAAC Device


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Patients with AF have a 5x increased risk of stroke.1

AF-related strokes are more frequently fatal and disabling. 2,3 Approximately half of acute stroke victims will die or live with a significant disability, which may result in institutional care.

While warfarin is effective for many patients, long-term warfarin therapy is not well tolerated by some patients, highlighting the need for additional treatment options.
Need for Alternative Life Changing Stroke Risk Treatment Option

Atrial Fibrillation (AF) currently affects more than 5 million Americans. AF is projected to increase as population ages.

In non-valvular AF, approximately 90% of stroke-causing clots that come from the left atrium are formed in the left atrial appendage (LAA).

Patients with AF have a 5x greater risk of stroke. Strokes in patients with AF are the #1 cause of long term disability and the #3 leading cause of death.

Approximately 45% of patients with AF who are eligible for warfarin are NOT being treated (tolerance/adherence).

Lifestyle limitations when taking warfarin include high risk of bleeding, negative interactions with food and drugs, serious side effects that are often difficult to tolerate, and required frequent and ongoing monitoring.

Despite NOAC adoption and ability to switch NOACs, adherence remains a challenge. 50% of warfarin patients discontinue the therapy at 2 years, and 30% of NOAC patients stop taking any drug at 2 years.

Which Of Your NVAF Patients Are Right For WATCHMAN™?

The WATCHMAN implant may be an appropriate option for your non-valvular atrial fibrillation patients who meet these criteria. Patients must:

1. Have an increased risk for stroke and be recommended for anticoagulation (CHA2DS2-VASc ≥ 2)
2. Be suitable for warfarin
3. Have an appropriate reason to seek a non-pharmacologic alternative to warfarin

Consider WATCHMAN For NVAF Patients Who Have:

- A history of major bleeding while taking oral anticoagulants (OACs)
- A career or lifestyle that increases the risk of major bleeding (secondary to trauma)
- Prior experience of being inadequately controlled on OACs
  - Inability to maintain stable INR
  - Inability to comply with regular INR monitoring and unavailability of an approved alternative OAC

*Payer coverage policies may not be consistent with BSC device labeling

Life Changing Stroke Risk Treatment Option

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Lifestyle limitations when taking warfarin include high risk of bleeding, negative interactions with food and drugs, serious side effects that are often difficult to tolerate, and required frequent and ongoing monitoring.

Despite NOAC adoption and ability to switch NOACs, adherence remains a challenge. 50% of warfarin patients discontinue the therapy at 2 years, and 30% of NOAC patients stop taking any drug at 2 years.
WATCHMAN™ is delivered via a transfemoral approach and is designed to close the atrial appendage (LAA) to prevent migration of blood clots, thus reducing the risk of stroke and systemic embolism.

**Minimally Invasive, Local Solution**

21 mm 24 mm 27 mm 30 mm 33 mm

WATCHMAN is engineered to conform to the unique anatomy of the LAA to reduce embolization risk, as well as minimize the surface area facing the left atrium to reduce the risk of post-implant thrombus formation.

**Procedural Safety**

WATCHMAN has a 96% implant success rate in the hands of both new and experienced operators. Procedural complications were similar to other left-sided procedures (i.e., AF ablations). The EWOLUTION Registry is a European prospective registry which reflects CE Mark indications for use which differ from the FDA indications for use, but the procedure and device is similar around the world.

**WATCHMAN™ Reduces Ischemic Stroke Over No Therapy**

- Observed WATCHMAN Ischemic Stroke Rate
- Imputation based on published rate with adjustment for score (3.0)

**Procedure/Device Related Safety Events within 7 Days**

<table>
<thead>
<tr>
<th>Procedure/Device Related Safety Events (N=1019)</th>
<th>0%</th>
<th>2%</th>
<th>4%</th>
<th>6%</th>
<th>8%</th>
<th>10%</th>
<th>12%</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROTECT AF 1st Half N=232</td>
<td>9.9%</td>
<td>4.8%</td>
<td>4.1%</td>
<td>4.1%</td>
<td>3.8%</td>
<td>2.8%</td>
<td></td>
</tr>
<tr>
<td>PROTECT AF 2nd Half N=231</td>
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<tr>
<td>PREVAIL Only Baseline CHA2DS2-VASC = 3.5</td>
<td></td>
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<tr>
<td>CAP Baseline CHA2DS2-VASC = 3.5</td>
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<tr>
<td>PROVAIL Baseline CHA2DS2-VASC = 3.8</td>
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</tr>
</tbody>
</table>

**WATCHMAN: Proven Stroke Risk Reduction Alternative**

WATCHMAN has a 95% implant success rate in the hands of both new and experienced operators. Procedural complication rate similar to other left-sided procedures (i.e., AF ablation)

The EWOLUTION Registry is a European prospective registry which reflects CE Mark indications for use which differ from the FDA indications for use, but the procedure and device is similar around the world.
WATCHMAN™: Proven Stroke Risk Reduction Alternative

**WATCHMAN** is a safe alternative to long term warfarin therapy which offers comparable stroke risk and enables patients to stop taking warfarin.

**WATCHMAN** showed comparable efficacy to warfarin

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>HR</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stroke or SE</td>
<td>0.79</td>
<td>0.22</td>
</tr>
<tr>
<td>Ischemic stroke or SE</td>
<td>1.02</td>
<td>0.94</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>1.95</td>
<td>0.05</td>
</tr>
<tr>
<td>Ischemic stroke or SE &gt; 7 days</td>
<td>0.22</td>
<td>0.004</td>
</tr>
<tr>
<td>CV/unexplained death</td>
<td>1.56</td>
<td>0.21</td>
</tr>
<tr>
<td>All-cause death</td>
<td>0.73</td>
<td>0.07</td>
</tr>
<tr>
<td>Major bleed, all</td>
<td>1.00</td>
<td>0.98</td>
</tr>
<tr>
<td>Major bleeding, non-procedure-related</td>
<td>0.51</td>
<td>0.002</td>
</tr>
</tbody>
</table>

**EPIDEMIOLOGY**

**Reduction**: Cardiovascular/Unexplained Death

- **52%** (p=0.002)

**Reduction**: Major Bleeding >6 months post-procedure

- **72%** (p=0.001)

**Reduction**: Hemorrhagic Stroke

- **78%** (p=0.004)

**Intra-LAA Design**

Unique intra-LAA design to avoid contact with the left atrial wall

**160 Micron Membrane**

Polyethylene terephthalate (PET) cap designed to block emboli and promote healing

**Proximal Face**

Minimizes surface area facing the left atrium to reduce post-implant thrombus formation

**Nitinol Frame**

Conforms to the unique anatomy of the LAA to reduce embolization risk

**10 Active Fixation Anchors**

Designed to engage tissue for stability

**WATCHMAN** showed comparable efficacy to warfarin

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**WATCHMAN** is a proven stroke risk reduction alternative with statistical reductions in:

- Cardiovascular/Unexplained Death: 52% (p=0.002)
- Major Bleeding > 6 months post-procedure: 72% (p=0.001)
- Hemorrhagic Stroke: 78% (p=0.004)

**Intra-LAA Design**

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**WATCHMAN™**

Proven Stroke Risk Reduction Alternative

52% reduction in Cardiovascular/Unexplained Death

72% reduction in Major Bleeding > 6 months post-procedure

78% reduction in Hemorrhagic Stroke

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Pre-loaded Delivery System

**Dual Catheter Delivery: One Access Sheath Fits All Device Sizes**

**WATCHMAN™ Delivery Catheter**
- Deployment Knob
- Y-Adapter
- Hemostasis Valve
- Pre-loaded Delivery System
  - Reduces procedure prep time
- Flexible Core Wire
  - Provides for natural position post deployment
- Visualization Aid
  - Radiopaque marker band guides placement
- Tri-Cut Tip
  - Facilitates recapture and maintains sheath integrity

**WATCHMAN Access Sheath**
- Hemostasis Valve
- Sideport

**Reduces procedure prep time**
- **Flexible Core Wire** provides for natural position post deployment.
- **Visualization Aid** uses a radiopaque marker band to guide placement.
- **Tri-Cut Tip** facilitates recapture and maintains sheath integrity.

**2008 CAP Registry**
- Endpoints: Collect additional safety and efficacy data to be pooled with PROTECT Af
- n = 146, mean CHA2DS2-VASc = 3.9, mean age = 76

**2009 ASAP* Endpoints**
- Efficacy Comparison: CHADS2 score expected stroke rate
- n = 150, mean CHA2DS2-VASc = 4.4, mean age = 72.5

**2010 PREVAIL Endpoints**
- Safety and Efficacy Comparison: Warfarin
- n = 407 pts, mean CHA2DS2-VASc = 4.0, mean age = 76

**2012 CAP2 Registry Endpoints**
- Collect additional safety and efficacy data
- n = 579, mean CHA2DS2-VASc = 4.4, mean age = 75

**2013 Real World Registries in Europe and Asia* Endpoints**
- Additional information in a real-world setting

**2016 ASAP-TOO Endpoints**
- Safety and Efficacy Comparison: Single Antiplatelet or No Therapy
- Ongoing study in subjects with NVAF deemed not suitable for OAC Therapy

- **92%** of patients successfully implanted with WATCHMAN discontinued warfarin at 45 days
- **99%** of patients successfully implanted with WATCHMAN were off warfarin at 1 year

**WATCHMAN: The Leader in Left Atrial Appendage Closure**
**History of Clinical Leadership**

**WATCHMAN™** is the most studied LAAC device, and the only one proven with long-term data from randomized trials.

<table>
<thead>
<tr>
<th>Year</th>
<th>Study</th>
<th>Endpoints</th>
<th>Comparison</th>
<th>n</th>
<th>Mean CHADS2</th>
<th>Mean Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>PILOT</td>
<td>Feasibility and Safety</td>
<td>Non-randomized</td>
<td>66</td>
<td>1.8</td>
<td>68.5</td>
</tr>
<tr>
<td>2005</td>
<td>PROTECT AF</td>
<td>Safety and Efficacy</td>
<td>Warfarin</td>
<td>707</td>
<td>3.5</td>
<td>72</td>
</tr>
</tbody>
</table>

*The ASAP, ESC expanded guidelines and indications and Real World Registries in Europe and Asia studied the patient population not in the scope of the FDA approved indications for use.

**Sheath Options Facilitate Access to the LAA**

- **Single Curve**
- **Double Curve**
- **Anterior Curve**

12F inner, 14F outer diameter; 75 cm working length

- **Radiopaque Marker Bands**
  - Help guide precise sheath placement

- **Side Holes**
  - Allows multi-directional contrast for LAA visualization

**One-Step Deployment: Recapturable and Repositionable**

**Distal Tip**
- **Pre-Deployment**
- **Full Deployment**

- Designed to be repositioned if necessary

**Sheath Options**

- 33 mm
- 27 mm
- 21 mm

**Patients Studied**

- >2,400 patients
- ~6,000 patient-years
- >20,000 patients implanted worldwide

**WATCHMAN Delivery System**
**WATCHMAN™** is a one-time procedure and the only implant of its kind approved by the FDA.

### The Implant Procedure

**1**
Using a standard percutaneous technique, a guidewire and vessel dilator are inserted into the femoral vein.

**2**
The implant procedure is performed with fluoroscopy and transesophageal echocardiography (TEE). The interatrial septum is crossed using a standard transseptal access system.

**3**
The access sheath is advanced over the guidewire into the left atrium and then navigated into the distal portion of the LAA over a pigtail catheter.

**4**
WATCHMAN is then deployed and released in the LAA.

**5**
Heart tissue grows over the WATCHMAN Implant and the LAA is permanently sealed. Patients remain on warfarin for at least 45 days post-procedure. TEE is used to confirm seal.

### Post Procedure

Following the procedure, patients take warfarin and aspirin for 45 (±15 days) or until there is adequate seal. After discontinuing warfarin, patients take clopidogrel and an increased dose of aspirin, followed by ongoing aspirin therapy.

### Implant

<table>
<thead>
<tr>
<th>45 Days</th>
<th>6 Months</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin + Aspirin</td>
<td><strong>TEE</strong></td>
<td><strong>Plavix + Aspirin</strong></td>
</tr>
<tr>
<td><strong>TEE</strong>*</td>
<td>Aspirin daily</td>
<td><strong>TEE</strong></td>
</tr>
<tr>
<td>Aspirin daily</td>
<td><strong>TEE</strong></td>
<td>Aspirin daily</td>
</tr>
</tbody>
</table>

* If adequate seal is not demonstrated (leak >5mm) at 45 day follow-up, assess seal with TEE at 6 months.