AFTER CRYPTOGENIC STROKE, MAKE PREVENTION THE PRIORITY
FIGHTING THE FEAR OF THE UNKNOWN

1/3 OF ISCHEMIC STROKES
• Approximately one-third of ischemic strokes are cryptogenic1.
• Each year, there are approximately 200,000 and 300,000 strokes in the US and the EU, respectively1,2.

MULTIPLE POTENTIAL MECHANISMS
• Several mechanisms are implicated in patients with cryptogenic stroke, including but not limited to:
  – Occult paroxysmal AF2
  – Paradoxical embolism through a PFO2
  – Substenotic atherosclerosis2

HIGHER PREVALENCE OF PFO
• Prevalence of PFO in the general population is reported between 17%-35%3.
• In patients with cryptogenic stroke, PFO was found in up to 45% of cases3.

POTENTIAL FOR RECURRENCE
• Rate of stroke recurrence in patients with PFO has been estimated to be 20.4% at 2 years3 and 25% 4 years4,5.
• Patients with PFO and prior cryptogenic stroke have a higher risk for further cerebrovascular events6.

MULTIPLE CONSIDERATIONS DURING TREATMENT PLANNING

CRYPTOGENIC STROKE
• Anticoagulation vs Antiplatelets?
• Patient compliance?
• Implications for younger, more active patients?

CONSIDER ALTERNATIVE THERAPIES
• Age of patient?
• Paradoxical embolism?

RETURN TO PRIMARY CARE PHYSICIAN (PCP)
• Limited exposure to cryptogenic stroke patients
• Limited knowledge of current clinical data

INTERVENTIONAL CARDIOLOGY (IC) REFERRAL
• Confirm PFO
• Consider closure

COMMON CHALLENGES IN TREATING CRYPTOGENIC STROKE*

UNKNOWN ETIOLOGY
AN EVERYDAY OCCURRENCE
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TERRIFIED OF HAVING ANOTHER STROKE
“Having no control is so scary. Walking around in fear of having another stroke, or being on major blood thinners forever. I just wanted to live a normal life without constant worry.”
– Heidi Easley, cryptogenic stroke patient at 37

*Based on a survey conducted by Abbott December, 2017 of physicians treating cryptogenic stroke.
See important safety information referenced within.
THE EVIDENCE IS IN
Three large clinical studies confirm the superiority of PFO closure to medical management in reducing risk of stroke recurrence.

<table>
<thead>
<tr>
<th>Devices Used</th>
<th>RESPECT10</th>
<th>REDUCE11</th>
<th>CLOSE12</th>
</tr>
</thead>
<tbody>
<tr>
<td>100% AMPLATZER™ PFO Occluder</td>
<td>39% GORE HELEX, 61% GORE Cardioform</td>
<td>51% AMPLATZER™ PFO Occluder; 49% multiple approved PFO Occluder devices</td>
<td></td>
</tr>
<tr>
<td>Patients</td>
<td>980</td>
<td>664</td>
<td>473</td>
</tr>
<tr>
<td>Follow-Up-Patient Years</td>
<td>5,810 (mean 5.9 yrs)</td>
<td>2,232 (median 3.2 yrs)</td>
<td>NR* (mean 5.4 yrs)</td>
</tr>
<tr>
<td>Anticoagulant Allowed in Control Group?</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Relative Risk Reduction</td>
<td>62% (Recurrent ischemic stroke of unknown mechanism)</td>
<td>77% (Recurrent ischemic stroke)</td>
<td>97% (Recurrent ischemic stroke)</td>
</tr>
<tr>
<td>Effective Closure</td>
<td>94.2% Freedom from &gt;9 bubbles (Evaluated after 6 months)</td>
<td>94.5% Freedom from &gt;25 bubbles (Evaluated after 12 months)</td>
<td>NR*</td>
</tr>
</tbody>
</table>

*Not Reported
See important safety information referenced within.

INDICATIONS AND USAGE
The AMPLATZER™ PFO Occluder is indicated for percutaneous transcatheter closure of a patent foramen ovale (PFO) to reduce the risk of recurrent ischemic stroke in patients predominantly between the ages of 18 and 60 years, who have had a cryptogenic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude known causes of ischemic stroke.

LOW RISK OF DEVICE-RELATED EVENTS10-15
DEMONSTRATED ACROSS SIX TRIALS, 990 PATIENTS*

LOW RISK OF ATRIAL FIBRILLATION (AF)10
No statistical difference between closure and medical therapy groups (0.48 vs. 0.34 per 100 patient-years, P = 0.36).

*Patients in device group of each trial implanted with AMPLATZER PFO occluder devices.

**0% DEVICE EMBOLIZATION, AORTIC EROSION/DISSECTION DEVICE THROMBUS

**No statistical difference between closure and medical therapy groups (0.48 vs. 0.34 per 100 patient-years, P = 0.36).
MAKE PREVENTION THE PRIORITY
BY REFERRING TO AN INTERVENTIONAL CARDIOLOGIST, YOU CAN HELP REDUCE RISK FOR A WIDE RANGE OF PATIENTS

NEUROLOGIST CONSIDERS
• Is stroke cryptogenic? (Rule out known causes)
• Eligible for alternative therapy? (Consider age and medical history)
• Possibility of PFO? (Determine likelihood of paradoxical embolism)

CARDIOLOGIST DETERMINES
• Presence of PFO?

PFO CLOSURE

ONLY YOU CAN PREVENT STROKE RECURRENCE WITH A PFO CLOSURE REFERRAL

See important safety information referenced within.
THE TURNING POINT FOR CRYPTOGENIC STROKE TREATMENT

Which of your patients can benefit from:

• Reduced risk of recurrence?
• Excellent safety profile?

LEARN MORE AT CRYPTOGENICSTROKE.COM

INDICATIONS AND IMPORTANT SAFETY INFORMATION

The AMPLATZER™ PFO Occluder is indicated for percutaneous transcatheter closure of a patent foramen ovale (PFO) to reduce the risk of recurrent ischemic stroke in patients, predominantly between the ages of 18 and 60 years, who have had a cryptogenic stroke due to a presumed paradoxical embolism, as determined by a neurologist and cardiologist following an evaluation to exclude known causes of ischemic stroke. CONTRAINDICATIONS Patients with intra-cardiac mass, valve, or tumor or thrombus at the intended site of implant, or documented evidence of venous thrombus in the vessels through which access to the PFO is gained. • Patients whose vasculature, through which access to the PFO is gained, is inadequate to accommodate the appropriate sheath size. • Patients with anatomy in which the AMPLATZER™ PFO device size required would interfere with other intracardiac or intravascular structures, such as valves or pulmonary veins. • Patients with other source of right-to-left shunts, including an atrial septal defect and/or fenestrated septum. • Patients with active endocarditis or other untreated infections. WARNINGS Patients who are at increased risk for venous thromboembolic events should be managed with thromboembolic risk reduction regimen after the PFO Closure following standard of care. • Do not use this device if the sterile package is open or damaged. • Prepare for situations that require percutaneous or surgical removal of the device.

This includes available of a surgeon. • Embolized devices must be removed as they may disrupt critical cardiac functions. Do not remove an embolized occluder through intracardiac structures unless the occluder is fully recaptured inside a catheter or sheath. • Patients who are allergic to nickel can have an allergic reaction to this device. • This device should be used only by physicians who are trained in standard transcatheter techniques. • Transient hemodynamic compromise may be encountered during device placement, which may require fluid replacement or other medications as determined by the physician. • Do not release the device from the delivery catheter if the device does not conform to its original configuration, or if the device position is unstable or if the device interferes with any adjacent cardiac structure (such as Superior Vena Cava (SVC), Pulmonary Vein (PV), Mitral Valve (MV), Coronary Sinus (CS), aorta (AO)). If the device interferes with an adjacent cardiac structure, recapture the device and redeploy. If still unsatisfactory, recapture the device and either replace with a new device or refer the patient for alternative treatment. • Ensure there is sufficient distance from the PFO to the aortic root or SVC (typically defined as 9 mm or greater as measured.

PRECAUTIONS
The safety and effectiveness of the AMPLATZER™ PFO Occluder has not been established in patients (with): • Age less than 18 years or greater than 60 years because enrollment in the pivotal study (the RESPECT trial) was limited to patients 18 to 60 years old. • A hypercoagulable state including those with a positive test for a anticardiolipin antibody (IgG or IgM), Lupus anticoagulant, beta-2 glycoprotein-1 antibodies, or persistently elevated fasting plasma homocysteine despite medical therapy. • Unable to take antplatelet therapy. • Atherosclerosis or other arteriopathy of the intracranial and extracranial vessels associated with a ≥80% luminal stenosis. • Acute or recent (within 6 months) myocardial infarction or unstable angina. • Left ventricular aneurysm or akinesis. • Mitral valve stenosis or severe mitral regurgitation irrespective of etiology. • Aortic valve stenosis (mean gradient greater than 40 mmHg) or severe aortic valve regurgitation. • Mitral or aortic valve vegetation or prosthesis. • Aortic arch plaques protruding greater than 4 mm into the aortic lumen. • Left ventricular dilated cardiomyopathy with left ventricular ejection fraction (LVEF) less than 35%. • Chronic, persistent, or paroxysmal atrial fibrillation or atrial flutter. • Uncontrolled hypertension or uncontrolled diabetes mellitus. • Diagnosis of lacunar infarct probably due to intrinsic small vessel as qualifying stroke event. • Arterial dissection as cause of stroke n Index stroke of poor outcome (modified Rankin score greater than 3) n Pregnancy at the time of implant. • Multi-organ failure. • Use on or before the last day of the expiration month that is printed on the product packaging label. • This device was sterilized with ethylene oxide and is for single use only. Do not reuse or re-sterilize this device. Attempts to re-sterilize this device can cause a malfunction, insufficient sterilization, or harm to the patient. • The AMPLATZER™ PFO Occluder device consists of a nickel–titanium alloy, which is generally considered safe. However, in vitro testing has demonstrated that nickel is released from this device for a minimum of 60 days. Patients who are allergic to nickel may have an allergic reaction to this device, especially those with a history of metal allergies. Certain allergic reactions can be serious; patients should be instructed to notify their physicians immediately if they suspect they are experiencing an allergic reaction such as difficulty breathing or inflammation of the face or throat. Some patients may also develop an allergy to nickel if this device is implanted. • Store in a dry place. • Pregnancy – Minimize radiation exposure to the fetus and the mother. • Nursing mothers – There has been no quantitative assessment for the presence of leachables in breast milk. • ADVERSE EVENTS Potential adverse events that may occur during or after a procedure using this device may include, but are not limited to: Air embolus; Allergic drug reaction; Allergic dye reaction; Allergic metal reaction: Nitinol (nickel, titanium), platinum/iridium, stainless steel (chromium, iron, manganese, molybdenum, nickel); Anesthesia reactions; Anemia; Arrhythmia; Bacterial endocarditis; Bleeding; Brachial plexus injury; Cardiac perforation; Cardiac tamponade; Cardiac thrombus; Chest pain; Device embolization; Device erosion; Deep vein thrombosis; Death; Endocarditis; Esophagus injury; Fever; Headache/migraine; Hypertension/hypotension; Myocardial infarction; Pacemaker placement secondary to PFO device closure; Palpitations; Percardial effusion; Pericardial tamponade; Pericarditis, Peripheral embolism; Pleural effusion; Pulmonary embolism; Reintervention for residual shunt/ device removal; Seizure; Stroke; Transient ischemic attack; Thrombus; Valvular regurgitation; Vascular access site injury; Vessel perforation.

REFERENCES