Intracardiac Ischemia Monitoring

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This Medical Policy document describes the status of medical technology at the time the document was developed. Since that time, new technology may have emerged, or new medical literature may have been published. This Medical Policy will be reviewed regularly and updated as scientific and medical literature becomes available; therefore, policies are subject to change without notice.

DESCRIPTION

According to the American Heart Association (AHA), At-a-Glance document is based on the association's 2022 Heart Disease and Stroke Statistics Update, which is compiled annually by the AHA, the National Institutes of Health, and other collaborators. The estimated annual incidence of heart attack in the United States was 605,000 new attacks and 200,000 recurrent attacks. Average age at the first heart attack is 65.6 years for males and 72.0 years for females. CVD accounted for approximately 19.05 million global deaths in 2020.

Early identification of acute myocardial infarction (AMI) and prompt treatment has been shown to significantly improve clinical outcomes. Clinical studies have shown that most of the irreversible damage to the myocardium occurs during the first 2 hours after coronary occlusion.

The mean time from AMI symptom onset to arrival at a hospital for treatment has been estimated to be 2.5-3.0 hours. Restoration of coronary blood flow, regardless of the

method used, can abort infarction within the first 30 minutes after coronary occlusion. Investigators have noted the benefit of fibrinolytic therapy, compared with placebo, as considerably higher in individuals treated within 2 hours after symptom onset compared to those treated later. Evidence exists that expeditious restoration of blood flow in the obstructed artery after the onset of symptoms in individuals with the most severe type of AMI, the ST elevation MI (STEMI), is a key determinant of short- and long-term outcomes.

This policy will address intracardiac ischemia monitoring which utilizes an implantable electrogram device that records cardiac data and detects ischemic events using a standard pacemaker intracardiac lead positioned in the right ventricular apex. This implantable warning system emits a vibrational alarm when impending acute ischemic events are detected prior to symptom onset. The device is currently intended only for use in individuals considered high risk for ischemic cardiac events, such as those with previous acute coronary events, diabetes, or renal insufficiency. The proposed purpose of the device is to reduce the time from ischemic event onset to presentation in an emergency room with proposed potential clinical benefits related to faster emergent care.

The AngelMed® Guardian System (Angel Medical Systems, Inc., Shrewsbury, NJ) is an intracardiac ST-segment electrogram device currently being manufactured as an implantable ischemia monitor. The Guardian detects acute ischemic events by analyzing ST-segment shifts which are typically identified by electrocardiography (ECG) in the emergency room setting after the onset of symptoms, such as chest pain, shortness of breath, nausea, diaphoresis (sweating), etc. The ST-segment shifts are calculated by the device as the difference between the ST deviation of a current 10-second electrogram window and a baseline ST deviation value. If the ST-segment shift is greater than a heart rate-dependent programmable threshold, then the device generates an emergency alert signal. Device components include a programmable implantable monitoring device (IMD), right ventricle lead, lead adapter, external alarm device (EXD) and a programmer.

The ALERTS (AngelMed for Early Recognition and Treatment of STEMI) is a manufacturer-sponsored, Phase II, prospective clinical trial intended to assess the safety and potential to reduce time to treatment, heart muscle damage and survival benefit in a large group of high-risk cardiac subjects, due to acute coronary syndrome (ACS) or prior bypass surgery, at multiple centers in the U.S. In 2014, Gibson and colleagues published an article which describes the ALERTS trial as follows:

The goal of the randomized, prospective ALERTS Trial is to evaluate the efficacy of an implantable monitoring device (IMD) in reducing the composite of either cardiac or unexplained death, new Q-wave myocardial infarction, or symptom-to-door time of > 2 hours for confirmed thrombotic events. The IMD alerts the patient in real time when ST-segment deviation from a personalized baseline exceeds the trigger threshold. The trial is designed to enroll high-risk post-acute coronary syndrome patients or patients with previous multi-vessel coronary artery bypass surgery. All patients have the IMD

implanted, with 1:1 unblinded randomization to the alerting feature being either turned on versus turned off for the first 6 months. Randomization occurs at the first follow-up visit, 7 to 14 days after the implantation of the IMD. Subjects then return for follow-up visits at months 1, 3, and 6 and thereafter every 6 months until closure of the investigational device exemption. Subjects who cannot be implanted successfully or who have the device explanted are removed from the study and followed up for a minimum of 30 days post-procedure. If a subject experiences a device-related complication and/or adverse experience, the subject is followed up until resolution or until the condition becomes stable and no further change is anticipated.

On March 16, 2016, the FDA Circulatory System Devices Panel issued a Premarket Approval (PMA) final report with 6-month results of the ALERTS trial as follows:

At the end of the randomized period of the study, there were 52 confirmed occlusive events (34 events in 27 subjects in the treatment group, and 18 events in 17 subjects in the control group) that had positive tests by cardiac enzymes, ECG, angiography, stress test, or multiple tests. Each of these events had prior associated Guardian ST detection captures (in the control group) or emergency alarms (in the treatment group). Of note, 94% of events in both groups were confirmed either by cardiac enzymes, ECG, angiography, or multiple tests. Six percent of events (2 treatment, 1 control) were confirmed by a positive stress test alone; the 2 stress tests in the treatment group were nuclear stress tests. Confirmed occlusive events were used in the calculation of the following efficacy endpoints:

- Primary efficacy endpoint: confirmed occlusive events for which the time from occlusion-to-door was greater than 2 hours were counted as “late arrival” events as a component of the composite endpoint.
- Secondary efficacy endpoint (late arrival): this “late arrival” component of the composite primary efficacy endpoint was analyzed separately.
- Secondary efficacy endpoint (time-to-door): all confirmed occlusive events were analyzed to compare the occlusion-to-door times between groups.

The PMA report concluded:

- The results of the ALERTS study demonstrated the Guardian’s ability to reduce the time from onset of a coronary occlusion to presentation at a medical facility for treatment.

According to the FDA, the PMA final report was reviewed and discussed by the Division of Cardiovascular Devices (DCD) within the Center for Devices and Radiological Health (CDRH) at a panel hearing in 2016 where the request for FDA clearance was rejected, based on multiple study limitations that were identified, including the quality of the ECG data and the inconsistency of the Q-wave results which caused the sponsor to terminate the study earlier than the protocol required (FDA, 2016; Rogers, 2016).

However, an amended protocol of trial data analysis from the ALERTS trial was resubmitted to the FDA and was the basis for FDA clearance of the AngelMed Guardian System on April 9, 2018. According to the FDA, this approval was based, in part, on this

additional retrospective post-hoc analysis. The AngelMed Guardian System is indicated for:

- Use in patients who have had prior acute coronary syndrome (ACS) events and who remain at high risk for recurrent ACS events. The Guardian System is indicated as an adjunct to patient recognized symptoms (FDA, 2018).

According to the FDA Summary of Safety and Effectiveness Data (SSED), "In the absence of symptoms, the Guardian System may identify asymptomatic ACS events and prompt the patient to seek medical attention."

Contraindications to use of the AngelMed Guardian System were also provided in the SSED. The AngelMed Guardian System should not be implanted in:

1. Patients with cognitive impairment that would prevent recognition of alarms; and
2. Patients who cannot feel the vibration from the IMD; and
3. Patients with implanted pacemaker, implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy (CRT) devices; and
4. Patients where a pacemaker lead cannot be placed safely (FDA, 2018).

In 2019 final results of the ALERTS trial were published which noted the following:

- The implantable cardiac system detects early ST-segment deviation and alerts patients of a potential occlusive event. Although the trial did not meet its pre-specified primary efficacy endpoint, results suggest that the device may be beneficial among high-risk subjects in potentially identifying asymptomatic events (Gibson, 2019; Holmes, 2019).

Prior to the results of the ALERTS study, the only published evidence regarding the Guardian System in the U.S. came from one study of 37 human subjects considered to be at high risk for cardiac events due to prior ACS. The implanted monitor continuously evaluated the subjects' ST segments sensed from a conventional pacemaker right ventricle apical lead and issued a device-generated alert when ischemic events were detected. During the median follow-up time of 1.52 years, the median alarm-to-emergency room door time was 19.5 minutes (6, 18, 21, and 60 minutes, respectively). Device-generated alerts for demand-related ischemia at elevated heart rates, reflective of flow-limiting coronary obstructions, occurred in 4 subjects, and there were two false-positive ischemia alarms related to arrhythmias, and one alarm due to a programming error.

Summary of Evidence

Based on the review of the peer reviewed literature there is there is insufficient scientific evidence to demonstrate the safety and efficacy of the AngelMed Guardian System for intracardiac ischemia monitoring. Further studies are needed to evaluate the effects of this technology on patient outcomes regarding this programmable implantable monitoring (IMD) device in the setting of silent ischemic attacks and acute coronary syndrome

(ACS). The evidence is insufficient to determine the effects of this technology on net health outcomes.

Practice Guidelines and Position Statements

American College of Cardiology/American Heart Association/Heart Failure Society of America
In 2017, the American College of Cardiology/American Heart Association/Heart Failure Society of America Focused update of the 2013 American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) Guideline for the Management of Heart Failure does not address the use of non-invasive wireless technology to monitor pulmonary fluid levels as an early indicator for heart failure decompensation or arrhythmia detection.

Regulatory Status
In 2018, the United States FDA approved the AngelMed Guardian System. The AngelMed Guardian System is an implantable cardiac monitor with patient alerting capability and an additional external alarm device. The Guardian System is indicated for use in patients who have had prior acute coronary syndrome (ACS) events and who remain at high risk for recurrent ACS events.

The Guardian System is indicated as an adjunct to patient recognized symptoms. The Guardian System detects potential ongoing ACS events, characterized by sustained ST segment changes, and alerts the patient to seek medical attention for those potential ACS events.

A Guardian System alert is a more accurate predictor of ACS events when compared to patient recognized symptoms alone and demonstrates a reduced rate over time of patient presentations without ACS events (false positives) when compared to patient recognized symptoms alone.

In the absence of symptoms, the Guardian System may identify asymptomatic ACS events and prompt the patient to seek medical attention.

Contraindications
The AngelMed Guardian System should not be implanted in:
1. Patients with cognitive impairment that would prevent recognition of alarms
2. Patients who cannot feel the vibration from the IMD
3. Patients with implanted pacemaker, implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy (CRT) devices
4. Patients where a pacemaker lead cannot be placed safely

PRIOR APPROVAL

Not Required.

POLICY

See Related Medical Policies

- 02.02.22 Non-invasive Heart Failure and Arrhythmia Management and Monitoring System
- 02.02.23 Percutaneous Left-Atrial Appendage Closure Devices for Stroke Prevention in Atrial Fibrillation

Intracardiac ischemia monitoring (AngelMed® Guardian System) is considered **investigational** for all indications including but not limited to the detection of acute myocardial ischemic events, because the evidence is insufficient to determine the effects of this technology on net health outcomes.

Policy Guidelines

Ischemia: A decrease in the blood supply to a bodily organ, tissue, or part caused by constriction or obstruction of the blood vessels.

ST Elevation MI (STEMI): Refers to the characteristic changes read on an EKG where a segment of the EKG tracing is elevated (ST segment) which corresponds with ventricular systolic depolarization. A STEMI indicates the location of damage to the myocardium which, in the case of myocardial infarction (MI), indicates that an evolving MI is either occurring or has already occurred.

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- 0525T Insertion or replacement of intracardiac ischemia monitoring system, including testing of the lead and monitor, initial system programming, and imaging supervision and interpretation; complete system (electrode and implantable monitor)
- 0526T Insertion or replacement of intracardiac ischemia monitoring system, including testing of the lead and monitor, initial system programming, and imaging supervision and interpretation; electrode only
- 0527T Insertion or replacement of intracardiac ischemia monitoring system, including testing of the lead and monitor, initial system programming, and imaging supervision and interpretation; implantable monitor only
- 0528T Programming device evaluation (in person) of intracardiac ischemia monitoring system with iterative adjustment of programmed values, with analysis, review, and report
- 0529T Interrogation device evaluation (in person) of intracardiac ischemia monitoring system with analysis, review, and report

- 0530T Removal of intracardiac ischemia monitoring system, including all imaging supervision and interpretation; complete system (electrode and implantable monitor)
- 0531T Removal of intracardiac ischemia monitoring system, including all imaging supervision and interpretation; electrode only
- 0532T Removal of intracardiac ischemia monitoring system, including all imaging supervision and interpretation; implantable monitor only

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POLICY HISTORY		
Date	**Reason**	**Action**
January 2022	Annual Review	Policy Revised, New Medical Policy Created

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

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