Anthem

Medical Policy

Subject: Intracardiac Ischemia Monitoring
Document #: MED.00111
Status: Reviewed

Publish Date: 04/10/2024
Last Review Date: 02/15/2024

Description/Scope

This document addresses 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.

Position Statement

Investigational and Not Medically Necessary:

Intracardiac ischemia monitoring is considered **investigational and not medically necessary** for all indications including, but not limited to, detection of acute myocardial ischemic events.

Rationale

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 (Gibson, 2014).

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 primary safety objective of the ALERTS study was to demonstrate that the rate of freedom from system-related complications among subjects implanted with a Guardian System was greater than 90% at 6 months. The trial met its primary safety objective with a 96.7% freedom from system-related complications (posterior probability > 0.9999) …System-related complications occurred with an incidence similar to those observed historically in studies of single-chamber pacemakers…The primary efficacy objective of the ALERTS study was to demonstrate that the rate of a composite primary endpoint was lower in the treatment group in the first 6-months after device implant and randomization. The trial did not meet its primary efficacy endpoint. As a first-in-class device, several limitations of the study design, that were not anticipated at the time the trial was initiated, negatively impacted the primary efficacy endpoint. The study met two of its secondary endpoints reflecting its designed purpose of prompting individuals to seek medical attention quickly after confirmed occlusive events:

- Treatment group subjects achieved significantly shorter occlusion-to-door times than control group participants. The median time from the first Guardian detection of an occlusion to arrival at a medical facility was 51 minutes for the treatment group compared to 22 days in the control group.
- The rate of late arrival (>2 hours) after the onset of a coronary occlusion was lower in the treatment than the control group. In terms of the clinical goal of early arrival (≤2 hours), 85% of confirmed occlusive events in the treatment group had an arrival time to a medical facility within 2 hours, compared to just 6% of confirmed occlusive events in the control group.

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 participants' 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 participants, and there were two false-positive ischemia alarms related to arrhythmias, and one alarm due to a programming error (Fischell, 2010).

At the present time, there is insufficient scientific evidence to permit reasonable conclusions concerning the effect of the Guardian System for intracardiac ischemia monitoring on health outcomes. Future study is needed to inform the utility of this IMD in the setting of silent ischemic attacks and ACS.

Background/Overview

According to the American Heart Association (AHA), there are over one million acute myocardial infarction (AMI) events each year in the United States with more than 400,000 of these resulting in death (approx. 37-38%). Early identification of AMI and prompt treatment has been shown to significantly improve clinical outcomes. Experimental and clinical studies have shown that most of the irreversible damage to the myocardium occurs during the first 2 hours after coronary occlusion (Milavetz, 1998).

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 (Boersma, 2006).

Definitions

Investigational Device Exemption (IDE): Allows for an investigational device to be used in a clinical study, in order to collect safety and effectiveness data required to support a Premarket Approval (PMA) application or a Premarket Notification (510[k]) submission to FDA.

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.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-

coverage of these services as it applies to an individual member.

When services are Investigational and Not Medically Necessary:
When the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT

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

HCPCS

C1833	Monitor, cardiac, including intracardiac lead and all system components (implantable)

ICD-10 Diagnosis

	All diagnoses

References

Peer Reviewed Publications:

1. Boersma E.; Primary Coronary Angioplasty vs. Thrombolysis Group. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. Eur Heart J. 2006; 27(7):779-788.
2. Ellestad MH, Messenger J, Montgomery B, et al. Intracardiac electrogram and ischemia alert. J Am Coll Cardiol. 2012; 59(6):631-633.
3. Fischell TA, Fischell DR, Avezum A, et al. Initial clinical results using intracardiac electrogram monitoring to detect and alert patients during coronary plaque rupture and ischemia. J Am Coll Cardiol. 2010; 56(14):1089-1098.
4. Forleo GB, Tesauro M, Panattoni G, et al. Impact of continuous intracardiac ST-segment monitoring on mid-term outcomes of ICD-implanted patients with coronary artery disease. Early results of a prospective comparison with conventional ICD outcomes. Heart. 2012; 98(5):402-407.
5. Gibson MC, Krucoff M, Fischell D, et al. Rationale and design of the AngeLmed for Early Recognition and Treatment of STEMI trial: a randomized, prospective clinical investigation. Am Heart J. 2014; 168(2):168-174.
6. Hopenfeld B, John MS, Fischell DR, et al. The Guardian: an implantable system for chronic ambulatory monitoring of acute myocardial infarction. J Electrocard. 2009; 42(6):481-486.
7. Kent DM, Ruthazer R, Griffith JL, et al. Comparison of mortality benefit of immediate thrombolytic therapy versus delayed primary angioplasty for acute myocardial infarction. Am J Cardiol. 2007; 99(10):1384-1388.
8. Krucoff MW. From ST-elevation myocardial infarction to ST elevation with no myocardial infarction--review and overview of a new horizon of computerized electrocardiographic ischemia detection using high-fidelity implantable devices. J Electrocardiol. 2009; 42(6):487-493.
9. Mendenhall GS, Saba S. 12-lead surface electrocardiogram reconstruction from implanted device electrograms. Europace. 2010; 12(7):991-998.
10. Milavetz JJ, Giebel DW, Christian TF, et al. Time to therapy and salvage in myocardial infarction. J Am Coll Cardiol. 1998; 31(6):1246-1251.
11. Papavasileiou LP, Forleo GB, Romeo F. Early detection of chronic myocardial ischemia in a patient implanted with an ICD capable of intracardiac electrogram monitoring. J Invasive Cardiol. 2011; 23(12):532-533.

Government Agency, Medical Society, and Other Authoritative Publications:

1. Gibson CM, Holmes D, Mikdadi G3 et al. Implantable Cardiac Alert System for Early Recognition of ST-Segment Elevation Myocardial Infarction. J Am Coll Cardiol. 2019; 73(15):1919-1927.
2. Holmes DR Jr, Krucoff MW, Mullin C, et al. Implanted Monitor Alerting to Reduce Treatment Delay in Patients With Acute Coronary Syndrome Events. J Am Coll Cardiol. 2019; 74(16):2047-2055.
3. Rogers T, Steinvil A, Torguson R, Waksman R. Overview of the 2016 US Food and Drug Administration Circulatory System Devices Panel Meeting on the AngelMed Guardian System. Circulation. 2016; 134(3):262-264.
4. U.S. Food and Drug Administration (FDA). Circulatory System Devices Panel. AngelMed Guardian® System for the Alerting of Patients to ST Segment Changes Indicative of Coronary Artery Occlusion. PMA P150009S. Meeting date: March 16, 2016. Available at: http://www.fda.gov/downloads/advisorycommittees/committeesmeetingmaterials/medicaldevices/medicaldevicesadvisorycommittee/circulatorysystemdevicespanel/ucm490461.pdf. Accessed on December 11, 2023.
5. U.S. Food and Drug Administration (FDA). Center for Devices and Radiologic Health (CDRH). Premarket approval application (PMA) for the AngelMed Guardian System. PMA P150009. Summary of Safety and Effectiveness Data (SSED). April 9, 2018. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150009B.pdf. Accessed on December 11, 2023.

Websites for Additional Information

1. Society for Cardiovascular Angiography and Interventions (SCAI). Website for information about cardiac topics. Available at:

http://www.scai.org/Default.aspx. Accessed on December 11, 2023.

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AngelMed Guardian System
Intracardiac Ischemia Monitoring
Intracardiac ST-segment Electrogram
ST-segment Monitoring

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Reviewed	02/15/2024	Medical Policy & Technology Assessment Committee (MPTAC) review. Revised Definitions and References sections. Updated Rationale section.
Reviewed	02/16/2023	MPTAC review. The References section was updated.
Reviewed	02/17/2022	MPTAC review. The References section was updated.
	12/29/2021	Updated Coding section with 01/01/2022 HCPCS changes; added C1833 effective 01/01/2022.
Reviewed	02/11/2021	MPTAC review. References section was updated.
Reviewed	02/20/2020	MPTAC review. The Rationale and References sections were updated.
Reviewed	03/21/2019	MPTAC review. The Rationale and References sections were updated.
	12/27/2018	Updated Coding section with 01/01/2019 CPT and HCPCS changes; added 0525T-0532T; removed C9750 deleted 12/31/2018.
	09/20/2018	Updated Coding section with 10/01/2018 HCPCS changes; added C9750.
Reviewed	05/03/2018	MPTAC review. The References section was updated.
	12/27/2017	The document header wording updated from “Current Effective Date” to “Publish Date.” Updated Coding section with 01/01/2018 CPT changes; added code 93799, removed codes 0302T-0307T deleted 12/31/2017.
Reviewed	05/04/2017	MPTAC review. The References section was updated.
Reviewed	05/05/2016	MPTAC review. The Rationale and References sections were updated. Removed ICD-9 codes from Coding section.
Reviewed	05/07/2015	MPTAC review. The Rationale and References were updated.
Reviewed	05/15/2014	MPTAC review. The Rationale and References were updated
Reviewed	05/09/2013	MPTAC review. References were updated. Definitions were added.
New	05/10/2012	MPTAC review. Initial document development.
