Cigna Medical Coverage Policy

Subject **Computerized Electrocardiograph (ECG) Analysis**

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Implantable Cardioverter Defibrillator (ICD)
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Coverage Policy

Cigna does not cover signal-averaged electrocardiography (SAECG) (CPT® code 93278) for any indication because it is considered experimental, investigational or unproven.

Cigna does not cover remote algorithmic analysis of electrocardiographic-derived data (CPT code 0206T) for any indication because it is considered experimental, investigational or unproven.

Cigna does not cover electrocardiographic body surface mapping (CPT codes 0178T-0180T) for any indication because it is considered experimental, investigational or unproven.

General Background

Significant effort has been directed to the identification of patients at high risk for ventricular arrhythmias and in the diagnosis of patients with known or suspected coronary artery disease (CAD). Various non-invasive methods may be used for risk stratification in patients recovering from acute myocardial infarction (MI), and in patients with heart failure and diminished left ventricular ejection fraction. Standard 12-lead electrocardiography (ECG), Holter monitoring, microvolt T-wave alternans, and exercise stress testing may be used to determine the need for interventions such as drugs or automatic implantable cardioverter defibrillators (ICDs). Non-invasive methods used to determine the presence or evaluate the risk of CAD include 12-lead ECG, stress testing, with or without nuclear imaging, pharmacologic stress testing, and echocardiography, in combination with evaluation of medical and family history. Advanced imaging techniques, including computed tomography angiography (CTA) and cardiovascular magnetic resonance (CMR) are also being explored for the evaluation of CAD. No single non-invasive test has been demonstrated to identify patients with CAD with high sensitivity and specificity. Coronary angiography (CA) remains the best reference standard in the diagnosis of CAD. In low risk patients

who are not generally referred for CA, noninvasive diagnostic testing is considered an acceptable reference standard. Stress testing in particular, with or without imaging, provides incremental risk prediction as the basis for management and treatment decisions (American Heart Association, 2010; Topol, 2007; Coeytaux et al., 2010)

SAECG has been proposed as an additional method of risk stratification. SAECG is a noninvasive technique in which segments of a standard electrocardiogram (ECG) are computer-analyzed to detect small electrical impulses, called ventricular late potentials that follow the QRS segment. These impulses are imbedded in the ECG and are normally obscured by skeletal muscle activity and other extraneous causes of "noise" encountered in recording a typical ECG. With SAECG, signals are amplified, filtered, and then averaged using computer software. Ventricular late potentials are associated with elevated risk of ventricular tachyarrhythmias and sudden cardiac death, particularly in patients who have had recent myocardial infarction (MI) or who have cardiac abnormalities, such as coronary artery disease. An electrophysiologic (EP) study, an invasive procedure, is also commonly used to evaluate risk of sudden cardiac death. Although ventricular arrhythmias induced during EP studies are a strong predictor of risk, non-inducibility does not necessary indicate a positive prognosis. There is no single test capable of accurately predicting SCD risk in various clinical settings and patient populations. The relative ability of each test to identify risk varies, and the optimal way to combine these tests is unclear. The sensitivity of an abnormal SAECG is reported to vary between 30–76%, and specificity between 63–96%. SAECG has a low positive predictive value for SCD (7–40%). The negative predictive value is high (>95%), but this is related to the low event rate of SCD ((Goldberger et al., 2009, Kusmirek and Gold, 2007; Zipes et al., 2006)

Several devices In addition to SAECG have been developed in an effort to enhance ECG capabilities, including devices that use algorithmic analysis of ECG data or body surface mapping to evaluate patients with suspected coronary artery disease (CAD) and to assess patients with cardiac arrhythmias. The MultiFunction Cardiogram™ (MCG) (Premier Heart, Port Washington, NY), a computerized ECG device that uses algorithmic analysis, has been proposed as a non-invasive alternative for the evaluation of known or suspected coronary artery disease.

Another device, the PRIME ECG® (Heartscape Technologies, Ltd, United Kingdom) records ECG signals on the body surface via an electrode array (vest). The PRIME diagnostic algorithm uses multiple parameters of ECG potentials and ECG morphology to make a recommendation on whether the patient has a normal, abnormal or acute MI condition.

Body surface maps have been used to localize and to size areas of myocardial ischemia, localize ectopic foci or accessory pathways, differentiate aberrant supraventricular conduction from ventricular origin, to identify patients prone to development of arrhythmias, and possibly to understand the mechanisms involved. Published evidence evaluating body surface mapping is limited, and the clinical usefulness of these procedures has not yet been established. In addition, the technique is cumbersome and the analysis is complex (Bonow: Braunwald's Heart Disease, 2011).

There is insufficient evidence to demonstrate that ECG based signal analysis technologies impact diagnostic decision-making or result in improved outcomes, compared to standard diagnostic techniques. A technology assessment developed for the Agency for Healthcare Research and Quality (AHRQ (Coeytaux et al., 2010) evaluated ECG-based signal analysis, including MCG and PRIME ECG, and concluded that "further research is needed to determine in what circumstance, if any, these devices might precede, replace, or add to the standard ECG for the diagnosis of CAD among patients who present with chest pain in the outpatient setting".

U.S Food and Drug Administration (FDA)
Signal-Averaged Electrocardiography (SAECG): Numerous electrocardiography devices are equipped with enhanced technology that allows signal averaging.

MultiFunction Cardiogram™ (MCG) (Premier Heart, Port Washington, NY): An early version of the device, the Cardiotron EKG Multiphase Information Analysis System, received FDA approval through the 510(k) process on March 21, 2000 The Premier Heart MultiFunction Cardiogram (MCG) records a simultaneous two-lead resting ECG from leads II and V5, using proprietary hardware and software. The analog MCG ECG signal is amplified, digitized, and transmitted to Premier Heart's data center via an encrypted internet connection. The data is analyzed, signal-averaging is performed, and the data is subjected to six mathematical transformations to identify functional indices. Patterns of abnormal indices are compared to abnormal index patterns in the

reference database to reach a final diagnostic output. The diagnostic output consists of a numeric score of 0–20 and the presence of local or global ischemia, indicating the level of coronary obstruction/myocardial ischemia. A report of the testing is available on the MCG unit or can be viewed through a web browser.

PRIME ECG® (Heartscape Technologies, Ltd, United Kingdom): The PRIME ECG with enhanced diagnostic algorithm, referred to as PRIME ECG, received FDA approval through the 510(k) process on September 12, 2008. An earlier version of the device, the PRIME ECG System (Meridian Medical Technologies, Ltd, Columbia, MD), was approved through the 510(k) process on March 6, 2002.

The PRIME ECG is indicated for the recording of electrocardiographic signals on the body surface. The device consists of the PRIME ECG cart, algorithm, and single-use patient vest. The cart is used to record, analyze and display ECG signals from the body surface. The system incorporates computer processing that can present conventional ECG waveforms as color images displayed on a simulated torso. Segments of the ECG waveform are translated into ranges of color based on measured values intended to allow physicians to identify areas of abnormality. The PRIME diagnostic algorithm uses multiple parameters of ECG potentials and ECG morphology to make a recommendation on whether the patient has a normal, abnormal or acute MI condition. The data recording and analysis system is attached to a single-use patient electrode array (vest) that is secured to the patient with pre-applied conductive adhesive gel.

Literature Review

Signal-averaged Electrocardiography (SAECG): The Cardiac Arrhythmias and Risk Stratification after Acute Myocardial Infarction (CARISMA) study (Huikuri et al., 2009) was conducted to evaluate the power of various invasive and non-invasive risk markers to predict arrhythmias with the potential to be treated with an ICD. Of 5869 consecutive patients screened two to seven days following acute myocardial infarction (AMI) in ten European centers, 312 patients with a mean left ventricular ejection fraction (LVEF) of 31 ± 6% were included. Reasons for exclusion included patient or physician refusal, other serious illness, planned coronary bypass graft surgery, or death. All patients received an implantable ECG loop-recorder 5–21 days following AMI to document fatal or near-fatal ventricular tachyarrhythmias, the primary endpoints of the study. Heart rate variability/turbulence, ambient arrhythmias, SAECG, T-wave alternans, and programmed electrical stimulation were performed six weeks after AMI. During the two year follow-up, 25 patients (8%) experienced fatal or near fatal tachyarrhythmias. The strongest predictor of these events was heart rate variability ($p<0.001$), as measured by Holter monitor. Induction of sustained monomorphic ventricular tachycardia during programmed electrical stimulation was also predictive of the final endpoint ($p=0.003$). QRS duration measured from the SAECG was a predictor of the primary endpoint, but when adjusted for clinical variables, the predictive power of SAECG was only of borderline significance ($p=0.04$). The authors stated that, while these results are promising, larger randomized interventional studies are needed before recommendations can be made regarding post-AMI Holter monitor screening.

A meta-analysis conducted by Bailey et al. (2001) evaluated current risk stratification tests for predicting major arrhythmic events after MI. The analysis included a total of 44 studies for which major adverse events incidence and predictive accuracy could be inferred. Tests reviewed included SAECG, heart rate variability, severe ventricular arrhythmia on ECG, left ventricular ejection fraction and EPS. The authors concluded that combinations of the four noninvasive tests in stages may allow 90% of patients to be stratified as high-risk or low-risk, with EPS reserved for patients for whom noninvasive tests are inconclusive, but that no single test was satisfactory alone for predicting risk. The authors further concluded that a large prospective study to develop a robust prediction model is feasible and desirable.

Several case series and cohort studies have evaluated noninvasive methods of identifying patients at risk for major arrhythmias and sudden cardiac death. The effectiveness of SAECG, T-Wave Alternans (TWA), electrophysiologic studies (EPS), heart rate variability, and baroreflex sensitivity have been evaluated in various combinations (Gold, et al., 2000; Iketa, et al., 2000; Gomes, et al., 2001; Huikuri, et al., 2001). These studies did not demonstrate that SAECG alone or in combination with other noninvasive tests is effective in defining risk and determining the appropriateness of specific pharmacological therapy or ICD implantation.

MultiFunction Cardiogram (MCG): Strobeck et al. (2009) conducted a meta-analysis to compare MCG to coronary angiography in detecting the presence and recurrence of hemodynamically relevant coronary artery disease. Three published prospective trials were included in the analysis, although the included trials were not specifically named (n=1076). The study participants consisted of a convenience sample of patients already

scheduled for the reference procedure, coronary angiography, for any indication. The intent of the included studies was not to study MCG as a screening device, but to focus on the potential of the device as a diagnostic assay for coronary artery stenosis. Patients may or may not have had prior angiography and/or coronary intervention. Results were classified by two angiographers for hemodynamically relevant stenosis (>70%). A coronary ischemia severity score of 0–20 was calculated for each patient. The severity score was significantly higher for patients with relevant coronary stenosis (5.4 ± 1.8 vs. 1.7 ± 2.1). The device correctly classified 941 of the 1076 patients (sensitivity 91.2%; specificity 84.6%; negative predictive value [NPV] 0.942, positive predictive value [PPV] 0.777). Adjusted PPV and NPV were 81.9% and 92.6%, respectively.

Evidence evaluating the use of MCG is limited; studies published to date, including Weiss et al., 2002; Hosokawa, et al., 2008; Grube, et al., 2007, Grube et al., 2008, have compared the device to coronary angiography. It is difficult to draw conclusions from the available evidence because of limitations in study design. It is not possible to determine how MCG compares to coronary angiography in determining the risk of presence of coronary artery disease. In addition, there are no published studies that evaluate the efficacy of MCG compared to other available non-invasive diagnostic methods (e.g., standard 12-lead ECG, stress testing, echocardiography and other imaging techniques). There is insufficient evidence in the published medical literature to determine how the use of this test would impact patient outcomes. The clinical utility of MCG in the evaluation or treatment of individuals with known or suspected coronary artery disease has not been established.

An Agency for Healthcare Research and Quality (AHRQ) Technology Assessment (Coeyfaux et al., 2010) evaluated the available clinical and scientific evidence on ECG-based signal analysis technologies for evaluating patients with suspected coronary artery disease (CAD). The MCG (referred to in the assessment as the 3DMP) and the PRIME ECG were noted to be the only two devices cleared fro marketing by the FDA and commercially available. No studies of 3DMP met the inclusion criteria, but four studies enrolled patients with CAD or at high risk for CAD, so met the expanded inclusion criteria. The 3DMP was evaluated in 920 patients scheduled for coronary angiography. A single low-quality study compared the 3DMP to 12-lead ECG. The 3DMP was more sensitive (97% vs. 75%) and more specific (72% vs. 41%) than ECG. The authors stated that, since there were differences in the patients and reference standard, these results are not directly comparable to the PRIME ECG or to the 12-lead ECG results.

PRIME ECG: Hoekstra et al. (2009) conducted a multicenter observational study (n=1830) to evaluate the prevalence, management patterns, and clinical outcomes of patients with ST elevated myocardial infarction (STEMI) identified on 80-lead body surface mapping (PRIME ECG) but not on 12-lead ECG. Moderate to high risk patients presenting to the emergency department with chest pain received 12-lead and 80-lead ECGs as part of the initial evaluation, and received treatment according to the standard of care at each facility. Clinicians were blinded to the results of the 80-lead ECG. The primary outcome was door-to-door sheath time in STEMI patients diagnosed with 80-lead ECG alone vs. those diagnosed by 12-lead ECG. A total of 91 patients had a discharge diagnosis of STEMI and 25 patients met the STEMI criteria based on 80-lead only ECG. Of the 91 twelve-lead STEMI patients, 84 underwent cardiac catheterization, with a median door-to-sheath time of 54 minutes. Of the 25 80-lead STEMI patients, 14 underwent cardiac catheterization, with a median door-to-sheath time of 1002 minutes. Patients with 80-lead only STEMI had clinical outcomes and revascularization rates similar to those diagnosed by 12-lead ECG, but were treated with delayed or conservative invasive strategies. The authors noted that although the study was sufficiently powered to evaluate door-to sheath time; it was not adequately powered to detect differences in clinical outcomes.

O'Neil et al. (2010) conducted a secondary analysis of the Hoekstra trial, discussed above, to analyze the sensitivity and specificity of the 80 lead versus the 12 lead ECG in the detection of high-risk ECG abnormalities (ST-segment elevation or ST depression) in patients with myocardial infarction (MI) and acute coronary syndrome (ACS), after eliminating all patients diagnosed with STEMI) by 12 lead ECG. A total of 317 of the 1,830 patients enrolled in the trial were eliminated from the analysis due to STEMI diagnosis (91) missing 80L or 12L data (225) or missing discharge diagnosis (1). Of the remaining 1,513 patients, 408 had ACS, 206 had MI, and one had missing status. The sensitivity of the 80 lead for MI had a relative increase of 81% and actual increase of 8.7% ($p = 0.0014$). The sensitivity of the 80L for ACS had a relative increase of 73% and actual increase of 5.2% ($p = 0.0025$). The 80 lead ECG identified 40 patients with MI and 50 patients with ACS overall, or an incremental 18 patients with MI and 21 patients with ACS compared to the 12 lead. There was a significant reduction in the specificity of the 80L for MI compared to the 12L, with a relative reduction of 2.7% and an actual reduction of 2.5% ($p = 0.0005$). There was also a significant reduction in the specificity of the 80

lead for ACS compared to the 12 lead, with a relative reduction of 2.9% and an absolute reduction of 2.7% (p = 0.0005), although there was no significant difference in the negative likelihood ratio or positive likelihood ratio compared to the 12-lead.

An AHRQ Technology Assessment of ECG-based signal analysis technologies for evaluating patients with acute coronary syndrome (ACS) was conducted in 2012 (Coeytuax et al.) This systematic review summarized the clinical and scientific evidence for commercially available ECG-based signal analysis technologies for evaluating patients at low to intermediate risk for coronary artery disease who have chest pain or other symptoms suggestive of ACS. A meta-analysis of eight studies of PRIME ECG determined a 68.4% sensitivity and 91.4% specificity for the PRIME ECG in detecting MI compared to 40.5% sensitivity and 95.0% specificity for the standard 12-lead ECG. Differences in test performance between the PRIME ECG and the 12-lead ECG were not considered statistically significant, based on overlapping confidence intervals. The assessment concluded that existing research is insufficient to confidently inform the appropriate use of ECG-based signal analysis technologies in diagnosing coronary artery disease and/or ACS, and that further research is needed to describe the performance characteristics of these devices to determine in what circumstances, if any, they might precede, replace or add to the standard ECG (Coeytuax et al.).

The 2010 AHRQ Technology Assessment evaluating ECG-based signal analysis technologies in patients with suspected coronary artery disease (CAD) discussed above included a sensitivity analysis of the PRIME ECG, based on five studies. An abnormal PRIME ECG in a patient with a pre-test probability for clinically significant CAD of 50% would yield a post-test probability of 87%. An abnormal result would yield a post-test probability of 25%. The authors stated that the performance characteristics of the 12-lead ECG were neither clinically nor statistically significantly different from the PRIME ECG

Professional Societies/Organizations
An American Heart Association (AHA) American College of Cardiology (ACC) Foundation/Heart Rhythm Society scientific statement on noninvasive risk stratification techniques for identifying patients at risk for sudden cardiac death states that an abnormal SAECG is likely a risk factor for sudden cardiac death, based predominantly on prospective analysis The clinical utility to guide selection of therapy has been tested, but not yet demonstrated. The statement concluded that, given the high negative predictive value of the test, it may be useful for the identification of patients at low risk. Routine use of SAECG to identify patients at high risk for sudden cardiac death is not supported (Goldberger et al., 2008).

The 2013 American College of Cardiology Foundation/American Heart Association Guideline for the Management of ST-Elevation Myocardial Infarction (STEMI) (O'Gara et al.) recommends that patients with an initially reduced left ventricular ejection fraction (LVEF) who are possible candidates for ICD therapy should undergo reevaluation of LVEF 40 or more days after discharge. In the discussion section following this recommendation, the authors state that in addition to determination of LVEF, several other noninvasive strategies have been proposed to identify patients at high risk for arrhythmic events after STEMI, such as signal-averaged or high-resolution ECG, heart rate variability, baroreflex sensitivity, and T-wave alternans. These strategies have not been adopted widely because of their limited performance characteristics and are not recommended for routine use.

An ACC/AHA/European Society of Cardiology (ESC) guideline for management of patients with ventricular arrhythmias and prevention of sudden cardiac death (Zipes, et al., 2006) discusses the use of SAECG to improve the diagnosis and risk stratification of patients with ventricular arrhythmias or who are at risk of developing life-threatening ventricular arrhythmias. Similar to the ACC/AHA guideline on acute MI, this guideline also classifies SAECG as a Class IIb indication, in which the usefulness/efficacy are not well established.

The use of the MultiFunction Cardiogram (MCG) is not addressed in relevant ACC/AHA guidelines.

A scientific statement from the American Heart Association, Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology, and ACCF states that expanded lead sets include the multiple electrode arrays used for body surface mapping of the electrical activity of the heart. The authors state that details of these arrays are beyond the scope of the report. Studies of body surface maps recorded from large electrode arrays have provided useful information about localization of ECG information on the thorax, but their complexity precludes their use as a substitute for the standard 12-lead ECG for routine recording purposes..

Use Outside the U.S.
No relevant information

Summary
Signal-averaged electrocardiography (SAECG) has been proposed as a noninvasive method for arrhythmia risk stratification. There is insufficient evidence in the published medical literature, however, to demonstrate the clinical utility of SAECG used alone or in combination with other testing for any indication, including establishing the risk of ventricular arrhythmias and sudden death, diagnosis of arrhythmogenic right ventricular dysplasia/cardiomyopathy, or when used as a patient selection criterion for pharmacological therapy, implantable cardioverter defibrillator (ICD) implantation or other treatment.

Additional devices using ECG-based signal analysis have been developed in an effort to enhance ECG capabilities in the evaluation of cardiac disorders, including arrhythmia, coronary artery disease, and acute myocardial infarction (MI). The MultiFunction Cardiogram™ (MCG) is a computerized ECG device that uses algorithmic analysis. The PRIME ECG® records ECG signals on the body surface via an electrode array (vest), and uses an algorithm to evaluate ECG potentials and morphology. There is insufficient evidence to demonstrate that ECG based signal analysis technologies impact diagnostic decision-making or result in improved outcomes, compared to standard diagnostic techniques. There is insufficient evidence in the published medical literature to demonstrate the clinical utility of these techniques for any indication, or to determine how these procedures compare to other available diagnostic methods.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

Experimental/Investigational/Unproven/Not Covered:

CPT®* Codes	**Description**
93278	Signal-averaged electrocardiography (SAECG) with or without ECG
0178T	Electrocardiogram, 64 leads or greater, with graphic presentation and analysis; with interpretation and report
0179T	Electrocardiogram, 64 leads or greater, with graphic presentation and analysis; tracing and graphics only, without interpretation and report
0180T	Electrocardiogram, 64 leads or greater, with graphic presentation and analysis; interpretation and report only
0206T	Computerized database analysis of multiple cycles of digitized cardiac electrical data from two or more ECG leads, including transmission to a remote center, application of multiple nonlinear mathematical transformations, with coronary artery obstruction severity assessment

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