MEDICAL POLICY – 6.01.56
Myocardial Sympathetic Innervation Imaging in Patients with Heart Failure

BCBSA Ref. Policy: 6.01.56
Effective Date: Nov. 1, 2017
Last Revised: Oct. 19, 2017
Replaces: N/A

RELATED MEDICAL POLICIES:
2.04.509 Cardiovascular Risk Panels
12.04.72 Gene Expression Testing to Predict Coronary Artery Disease

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | CODING | RELATED INFORMATION
EVIDENCE REVIEW | REFERENCES | HISTORY

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

An MIBG scan involves injecting a radioactive material (iodine-123-meta-iodobenzylguanidine) into the body. This radioactive material — known as a tracer — gathers in specific nerve endings in the heart. The tracer gives off gamma rays, which can be detected by a special type of scanner. The goal is to try to determine the severity of heart failure and who could be at high risk of dying from it in 1 to 2 years. It’s also been proposed that MIBG scans could someday help guide treatment for and monitoring of heart failure. Medical studies have not been able to determine if MIBG test results lead to better health outcomes. For this reason MIBG scans are considered investigational (unproven) for patients with heart failure.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria
Myocardial sympathetic innervation imaging with Iodine123 meta-iodobenzylguanidine (MIBG) is considered investigational for patients with heart failure.

### Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>Myocardial sympathetic innervation imaging; planar qualitative and quantitative assessment</td>
</tr>
<tr>
<td>0331T</td>
<td>Myocardial sympathetic innervation imaging, planar qualitative and quantitative assessment; with tomographic SPECT</td>
</tr>
<tr>
<td>A9582</td>
<td>Iodine I-123 iobenguane, diagnostic, per study dose, up to 15 millicuries</td>
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### Related Information

N/A

### Evidence Review

### Description

In patients with heart failure, activation of the sympathetic nervous system is an early mechanism to compensate for decreased myocardial function. The concentration of Iodine-123 meta-iodobenzylguanidine (MIBG) over several hours after injection of the agent is a potential marker of sympathetic neuronal activity. MIBG activity is proposed as a prognostic marker in
patients with heart failure to aid in the identification of patients at risk of 1- and 2-year mortality. The marker could also potentially be used to guide treatment decisions or to monitor the effectiveness of heart failure treatments.

Background

Heart Failure

An estimated 5.7 million adults in the United States have heart failure, and heart failure is the main cause of death for approximately 58,300 Americans each year. Underlying causes of heart failure include coronary artery disease, hypertension, valvular disorders, and primary cardiomyopathies. These conditions reduce myocardial pump function and decrease left ventricular ejection fraction. An early mechanism to compensate for this decreased myocardial function is activation of the sympathetic nervous system. The increased sympathetic activity initially helps compensate for heart failure by increasing heart rate and myocardial contractility to maintain blood pressure and organ perfusion. However, over time, this places additional strain on the myocardium, increasing coronary perfusion requirements, which can lead to worsening of ischemic heart disease and or myocardial damage. As the ability of the heart to compensate for reduced myocardial function diminishes, clinical symptoms of heart failure develop. Another detrimental effect of heightened sympathetic activity is an increased susceptibility to potentially fatal ventricular arrhythmias.

Overactive sympathetic innervation associated with heart failure involves increased neuronal release of norepinephrine (NE), which is the main neurotransmitter of the cardiac sympathetic nervous system. In response to sympathetic stimulation, vesicles containing NE are released into the neuronal synaptic cleft. The released NE binds to post-synaptic beta-1, beta-2, and alpha receptors, enhances adenyl cyclase activity, and brings about the desired cardiac stimulatory effects. NE is then taken back into the presynaptic axon by the uptake-1 pathway for storage or catabolic disposal that terminates the synaptic response. The increased release of NE is usually accompanied by decreased NE reuptake, thereby further increasing NE levels in the synaptic cleft.

Diagnostic Imaging

Guanethidine is a false neurotransmitter that is an analog of NE; it is also taken up by the uptake-1 pathway. $^{123}$Iodine meta-iodobenzylguanidine ($^{123}$I-MIBG or MIBG) is chemically
modified guanethidine labeled with radioactive iodine. MIBG moves into the synaptic cleft and then is taken up and stored in the presynaptic nerve ending in a manner that is similar to NE. However, unlike NE, MIBG is not catabolized and thus concentrates in myocardial sympathetic nerve endings. This concentrated MIBG can be imaged with a conventional gamma camera. The concentration of MIBG over several hours after injection of the agent is thus a reflection of sympathetic neuronal activity, which in turn may correlate with the severity of heart failure.

MIBG activity is proposed as a prognostic marker in patients with heart failure, to be used in conjunction with established markers or prognostic models to identify heart failure patients at increased risk of short-term mortality. MIBG activity could also potentially be used to guide treatment decisions or to monitor the effectiveness of heart failure treatments.

Summary of Evidence

For individuals with heart failure who receive imaging with MIBG for prognosis, the evidence includes numerous studies that MIBG cardiac imaging findings predict outcomes in patients with heart failure. Relevant outcomes are overall survival, disease-specific survival, functional outcomes, health status measures, quality of life, hospitalizations, and medication use. While the available studies vary in their patient inclusion criteria and methods for analyzing MIBG parameters, the highest quality studies have demonstrated a significant association between MIBG imaging results and adverse cardiac events, including cardiac death. Moreover, MIBG findings have been shown to improve the ability of the Seattle Heart Failure Model and other risk models to predict mortality. However, there is no direct published evidence on the clinical utility of MIBG (ie, whether findings of the test would lead to patient management changes that improve health outcomes) and no clear chain of indirect evidence of clinical utility. Management changes made as a result of MIBG imaging are uncertain, and it is not possible to determine whether management changes based on MIBG results lead to improved health outcomes compared with management without MIBG imaging. The evidence is insufficient to determine the effects of the technology on health outcomes.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 1.
Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NCT02656329a</td>
<td>International Study to Determine if AdreView Heart Function Scan Can be Used to Identify Patients With Mild or Moderate Heart Failure (HF) That Benefit From Implanted Medical Device (AMIRE-ICD)</td>
<td>2216</td>
<td>Aug 2019</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.
a Denotes industry-sponsored or cosponsored trial.

Practice Guidelines and Position Statements

**National Heart, Lung, and Blood Institute**

In 2011, the National Heart, Lung, and Blood Institute published a report on translation of cardiovascular molecular imaging.23 In regard to imaging the heart with meta-iodobenzylguanidine (MIBG), the report cited the AMIRE-HF trial,8 and stated that additional clinical trials would be needed to determine the efficacy of heart failure management strategies with MIBG compared with usual care without MIBG imaging.

**American College of Cardiology Foundation and the American Heart Association**

In 2013, the American College of Cardiology Foundation and the American Heart Association published updated guidelines on the management of heart failure.24 These guidelines included recommendations on the use of noninvasive cardiac imaging in the management of heart failure but did not address the use of MIBG imaging in heart failure management.

**Medicare National Coverage**

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.
Regulatory Status

In September 2008, AdreView® (Iobenguane I 123) Injection (GE Healthcare) was approved by the Food and Drug Administration’s (FDA) the new drug application (NDA) process (NDA 22-290) for the detection of primary or metastatic pheochromocytoma or neuroblastoma as an adjunct to other diagnostic tests.\(^4\)

In March 2013, the FDA approved a supplemental application (NDA 22-290/S-01) for AdreView® and expanded the labeled indication to include scintigraphic assessment of sympathetic innervation of the myocardium by measurement of the heart to mediastinum (H/M) ratio of radioactivity uptake in patients with New York Heart Association (NYHA) class II or class III heart failure and left ventricular ejection fraction (LVEF) <35%.\(^5\)

References


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<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>08/11/14</td>
<td>Annual Review. Policy updated with literature review through May 13, 2014; references 8, 12, 15, 16 added; others renumbered/removed. Policy statements unchanged. Related Policies updated; 2.04.32 removed; it has been archived.</td>
</tr>
<tr>
<td>01/19/16</td>
<td>Coding Update. New CPT code 0399T, effective 1/1/16, added to policy.</td>
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<tr>
<td>03/31/16</td>
<td>Coding Update. CPT code 0399T removed, CPT code previously added in error.</td>
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<tr>
<td>06/01/16</td>
<td>Update Related Policies. Removed 12.04.67 as it was deleted; information moved to 2.04.509.</td>
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</table>

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