Medical Policy
Myocardial Sympathetic Innervation Imaging in Patients with Heart Failure

Table of Contents
- Policy: Commercial
- Policy: Medicare
- Authorization Information
- Coding Information
- Description
- Policy History
- Information Pertaining to All Policies
- References

Policy Number: 576
BCBSA Reference Number: 6.01.56

Related Policies
- Homocysteine Testing in the Screening, Diagnosis, and Management of Cardiovascular Disease, #016
- Measurement of Lipoprotein-Associated Phospholipase A2 - Lp-PLA2 - in the Assessment of Cardiovascular Risk, #558
- KIF6 Genotyping for Predicting Cardiovascular Risk or Effectiveness of Statin Therapy, #129
- Gene Expression Testing to Predict Coronary Artery Disease, #349

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity
Medicare HMO BlueSM and Medicare PPO BlueSM Members

Myocardial sympathetic innervation imaging with 123Iodine meta-iodobenzylguanidine (MIBG) is INVESTIGATIONAL for patients with heart failure.

Prior Authorization Information
Pre-service approval is required for all inpatient services for all products.
See below for situations where prior authorization may be required or may not be required for outpatient services.
Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

<table>
<thead>
<tr>
<th>Outpatient</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial Managed Care (HMO and POS)</td>
<td>This is not a covered service.</td>
</tr>
<tr>
<td>Commercial PPO and Indemnity</td>
<td>This is not a covered service.</td>
</tr>
<tr>
<td>Medicare HMO BlueSM</td>
<td>This is not a covered service.</td>
</tr>
<tr>
<td>Medicare PPO BlueSM</td>
<td>This is not a covered service.</td>
</tr>
</tbody>
</table>
CPT Codes / HCPCS Codes / ICD-9 Codes
The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes

<table>
<thead>
<tr>
<th>CPT codes:</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0331T</td>
<td>Myocardial sympathetic innervations imaging, planar qualitative and quantitative assessment;</td>
</tr>
<tr>
<td>0332T</td>
<td>Myocardial sympathetic innervations imaging, planar qualitative and quantitative assessment; with tomographic SPECT</td>
</tr>
</tbody>
</table>

HCPCS Codes

<table>
<thead>
<tr>
<th>HCPCS codes:</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A9582</td>
<td>Iodine I-123 iobenguane, diagnostic, per study dose, up to 15 millicuries</td>
</tr>
</tbody>
</table>

Diagnosis Codes

Investigational for all diagnoses.

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 $^{123}$Iodine meta-iodobenzylguanidine (known as MIBG) over several hours after injection of the agent is a potential marker of sympathetic neuronal activity and may correlate with the severity of heart failure. 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

An estimated 5.7 million adults in the United States have heart failure, and heart failure is the main cause of death for approximately 55,000 Americans each year. (1) Underlying causes of heart failure include coronary artery disease (CAD), hypertension, valvular disorders, and primary cardiomyopathies. These conditions reduce myocardial pump function and decrease left ventricular ejection fraction (LVEF). 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 in order 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 space for storage or catabolic disposal that terminates the synaptic response by the uptake-1
pathway. The increased release of NE is usually accompanied by decreased NE reuptake, thereby further increase circulating NE levels.

Guanethidine is a false neurotransmitter that is an analogue of NE; it is also taken up by the uptake-1 pathway. \textsuperscript{1,2,3} Iodine meta-iodobenzylguanidine (known as \textsuperscript{123}I-MIBG or MIBG) is guanethidine that is chemically modified and labeled with radioactive iodine. MIBG moves into the synaptic cleft and then is taken up and stored in the presynaptic nerve space 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.\textsuperscript{2} 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 myocardial imaging has been in use in Europe and Japan and standardized procedures for imaging have been proposed by European organizations.\textsuperscript{3} Administration of MIBG is recommended by slow (1 to 2 minutes) injection. Planar images of the thorax are acquired 15 minutes (early image) and 4 hours (late image) after injection. In addition, optional single-photon emission computed tomography (SPECT) imaging can be performed following the early and late planar images. MIBG uptake is semi-quantified by determining the average count per pixel in regions of interest (ROI) drawn over the heart and the upper mediastinum in the planar anterior view. There is no single universally used myocardial MIBG index. The most commonly used myocardial MIBG indices are the early heart to mediastinum (H/M) ratio, late H/M ratio and the myocardial MIBG washout rate. The H/M ratio is calculated by taking the average count per pixel in the myocardium divided by the average count per pixel in the mediastinum. The myocardial washout rate is expressed as the rate of decrease in myocardial counts over time between early and late imaging (normalized to mediastinal activity).

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.

\textbf{Summary}

Imaging using \textsuperscript{123}Iodine meta-iodobenzylguanidine (known as MIBG) is a technique that allows direct measurement of myocardial sympathetic innervation. There is evidence from numerous studies that MIBG findings predict outcomes in patients with heart failure. While available studies vary in their patient inclusion criteria and methods for analyzing MIBG parameters, the highest quality studies demonstrate a significant association of MIBG results with adverse cardiac events, including cardiac death. Moreover, MIBG findings have been shown to improve the ability of the Seattle Heart Failure Model (SHFM) to predict mortality. There is no direct published evidence on the clinical utility of MIBG i.e., whether findings of the test would lead to patient management changes that improve health outcomes. Moreover, there is 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 superior outcomes compared to management without MIBG imaging. As a result, the use of MIBG myocardial imaging for patients with heart failure is considered investigational.

\textbf{Policy History}

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/2016</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
<tr>
<td>8/2015</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
<tr>
<td>9/2014</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
</tbody>
</table>

\textbf{Information Pertaining to All Blue Cross Blue Shield Medical Policies}

Click on any of the following terms to access the relevant information:

Medical Policy Terms of Use
References

Iodine-123-meta-iodobenzylguanidine scintigraphy in evaluating the effectiveness of pharmacological
2013;17(1):56-68. PMID 23329524

innervation maps to assess substrate and successful ablation sites for ventricular tachycardia: a
feasibility study for a novel paradigm of innervation imaging. Circ Arrhythm Electrophysiol. Jun
2015;8(3):583-591. PMID 25713216

working group on the translation of cardiovascular molecular imaging. Circulation. May 17
2011;123(19):2157-2163. PMID 21576680

failure: executive summary: a report of the American College of Cardiology Foundation/American
PMID 23741057