Introduction

AlloMap Gene Expression Profiling is addressed by this guideline.

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan’s procedure code list for management requirements.

<table>
<thead>
<tr>
<th>Procedure addressed by this guideline</th>
<th>Procedure code</th>
</tr>
</thead>
<tbody>
<tr>
<td>AlloMap</td>
<td>81595</td>
</tr>
</tbody>
</table>

What is AlloMap

Definition

AlloMap is a non-invasive blood test that is designed to help identify heart transplant recipients with stable allograft function who have a low probability of moderate/severe acute cellular rejection at the time of testing.¹

Current uses

AlloMap is designed to help providers obtain this information without the use of endomyocardial biopsy. While endomyocardial biopsy is currently the standard of care for heart transplant recipients, it is an invasive procedure with associated risks.

Description

AlloMap is a panel of 20 genes. The assay uses gene expression of RNA isolated from peripheral blood mononuclear cells.¹

Results

Using data from the gene expression of these genes, an AlloMap score is calculated. The lower the score, the lower the probability of acute cellular rejection at the time of testing.¹
Intended use

AlloMap is intended for use in heart transplant recipients 15 years of age or older who are at least 2 months post heart transplant.¹

Test information

Introduction

The AlloMap assay measures the gene expression of RNA of 20 genes. 11 of these genes are thought to be informative for the assay, while the remaining 9 are used for quality control.¹

Risk score

The data collected from these genes is translated into a risk score. Scores range from 0-40 and are compared to post-transplant patients in the same post-transplant period. The lower the score, the lower the probability of acute cellular rejection at the time of testing.¹

Guidelines and evidence

Introduction

This section includes relevant guidelines and evidence pertaining to AlloMap testing.

International Society of Heart and Lung Transplantation

The International Society of Heart and Lung Transplantation (2010)² stated the following:

“Gene Expression Profiling (AlloMap) can be used to rule out of the presence of acute cellular rejection (ACR) of grade 2R or greater in appropriate low risk patients, between 6 months and 5 years after HT.”

Class IIa

Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.

Level of evidence: B – data derived from a single randomized clinical trial or large non-randomized studies.

U.S. Food and Drug Administration (FDA)

In 2008, the U.S. Food and Drug Administration (FDA) cleared AlloMap as a Class II Medical Device.³
Peer Reviewed Literature

Several studies have evaluated the clinical performance of AlloMap testing to assess allograft rejection in heart transplant recipients.4-9 The evidence base includes clinical validity studies evaluating diagnostic accuracy and several randomized controlled trials evaluating clinical utility. Two clinical validity studies (CARGO, CARGO II) evaluated the diagnostic performance of AlloMap for detecting moderate-to-severe rejection and reported relatively high NPV of at least 88%.6,7 Positive predictive values (PPVs) were low for 2 to 6 months post-transplant and for more than 6 months post-transplant. Direct evidence on the clinical utility of using the AlloMap test is derived from a large RCT comparing AlloMap with an endomyocardial biopsy for detecting rejection. Study results showed that use of AlloMap was non-inferior to endomyocardial biopsy; however, the evidence is insufficient regarding the prognostic use of AlloMap to establish future risk of acute cellular rejection (ACR).

Limitations of these studies include inconsistent thresholds for defining a positive AlloMap test and few cases of allograft rejection, which may have contributed to imprecision when computing diagnostic accuracy. Results are conflicting across the available studies regarding the appropriate frequency of testing intervals. Some studies reported frequency of testing (which did not include testing in consecutive months after 6 months post-transplant), while other studies did not. One RCT evaluating outcomes across multiple centers stated that each center was responsible for determining the frequency of interval testing, indicating that test frequency was not addressed by the study protocol.5

Criteria

Introduction

Requests for AlloMap Gene Expression Profiling are reviewed using these criteria.

Criteria

AlloMap is considered medically necessary when ALL of the following criteria are met:

• Medical records indicate that member has been under the care of the ordering provider within the past 30 days, and
• Member is not acutely symptomatic,2 and
• Member does not have recurrent rejection,2 (defined as having a documented prior rejection and currently having signs/symptoms of rejection), and
• Member is not currently receiving 20 mg or more of daily oral prednisone,2 and
• Member has not received high-dose intravenous corticosteroids or myeloablative therapy in the past 21 days,2 and
• Member has not received blood products or hematopoietic growth factors in the past 30 days,2 and
• Member is not pregnant,\textsuperscript{2} and
• Member is at least 2 months post-transplant,\textsuperscript{2,4} and
• Member is less than 5 years post-transplant,\textsuperscript{2} and
• Member is at least 15 years of age\textsuperscript{2}

\textbf{Recommended frequency of AlloMap testing}

This table describes the recommended frequency of AlloMap testing.

<table>
<thead>
<tr>
<th>Months post-transplant</th>
<th>Frequency of AlloMap testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 to 6 months</td>
<td>every 2 to 4 weeks</td>
</tr>
<tr>
<td>6 to 12 months</td>
<td>every 2 months</td>
</tr>
<tr>
<td>12 to 24 months</td>
<td>every 3 months</td>
</tr>
<tr>
<td>24 months to 60 months</td>
<td>every 6 months</td>
</tr>
<tr>
<td>greater than 60 months</td>
<td>every 12 months</td>
</tr>
</tbody>
</table>

\textbf{Exceptions to testing frequency}

AlloMap may be used as a substitute for endomyocardial biopsy in surveillance of stable patients. Exceptions to the above testing frequencies may be considered as warranted by an individual patient’s clinical presentation.\textsuperscript{2,4,6} AlloMap testing is not routinely covered in individuals greater than 5 years post-transplant. Requests for exceptions to this criteria will be evaluated on a case by case basis.

\textbf{Exclusions}

Coverage for AlloMap testing has some exclusions.

\textbf{Exclusion for prognostic purposes}

The use of AlloMap for prognostic purposes is specifically excluded by this guideline. Studies on the ability of the test to predict future clinical events do not provide enough evidence to warrant coverage at this time.

\textbf{References}

\textbf{Introduction}

These references are cited in this guideline.

1. Allomap website. Available at: \texttt{http://www.allomap.com/}. 


