Medicare Advantage  X Commercial

AlloMap® Molecular Expression Test Policy

I. Purpose
Indiana University Health Plans (IU Health Plans) considers clinical indications when making a medical necessity determination for AlloMap® Molecular Expression Test.

II. Scope
All Utilization Management (UM) staff conducting physical and behavioral health UM review.

III. Exceptions
A. AlloMap® Molecular Expression Test is considered not medically necessary for any of the following:
   1. Patient is less than two months post-transplant
   2. Patient is between two- and six-months post-transplant without documented indications for consideration of early AlloMap® testing as described below
   3. The patient is in a hospital or long-term acute care inpatient setting
   4. Patient is unwilling to have an Endomyocardial biopsy (EMB) if indicated
   5. There are signs and symptoms of acute cellular rejection or declining graft function
   6. Patient has had multi-organ transplants
   7. There has been immunosuppressive treatment for acute rejection or other reasons within the past 21 days including any of the following:
      a. Myeloablative or myelosuppressive therapy
      b. High-dose IV steroids
      c. Oral steroids with prednisone or equivalent dosage dose > 20 mg/day
   8. Blood products given within the past 30 days
   9. Bone marrow stimulating products given within the past 30 days including but not limited to any of the following:
      a. Filgrastim (Neupogen), pegfilgastrim (Neulasta), sagromostin (Leukine)
      b. Epoetin Alfa (Procrit, Epogen), Darbepoetin Alfa (Aranesp), and Peginesatide (Omontys)
   10. Patients in whom surveillance biopsies would not be performed by current protocol (e.g., those who are stable and over three years post-transplant)
   11. Patients with 3 AlloMap® scores over 34 and did not show rejection on any of the follow-up EMBs, and it is deemed that further AlloMap® testing is not warranted
IV. Definitions

None

V. Policy Statements

A. IU Health Plans considers AlloMap® Molecular Expression Test medically necessary when one or more of the following criteria are met:

1. Patient is six months or greater from the time of the heart transplant and meets all of the following:
   a. Patient has clinically stable cardiac graft function meeting all of the following criteria:
      1) No clinical signs or symptoms of graft dysfunction or heart failure
      2) Left ventricular ejection fraction is > 40%
      3) Cardiac Index is greater than 2 L/min
      4) No history of grade 2R or greater acute cellular rejection (predominantly T-cell mediated) within the previous 6 months
      5) No history of antibody-mediated (predominantly B-cell mediated) rejection within the previous 6 months
   b. Patient must be 15 years of age or older
   c. Patient is not pregnant
   d. Patient is in an outpatient setting
   e. There are no limitations or exclusions as listed below

2. Early testing consideration (between two- and six-months post-transplant) must meet all of the following:
   a. One of the following:
      1) Difficult vascular access
      2) Intolerance to EMB
      3) Inability to pass the biotome into the right ventricle
      4) Chronic anticoagulation with high risk of interruption/Lovenox bridging required for EMB
      5) AlloMap® concurrent with EMB to establish a reference for trending acute rejection in anticipation of future limitations for EMB.
   b. All of the following:
      1) Patient has clinically stable cardiac graft function meeting all of the following criteria:
         a) No clinical signs or symptoms of graft dysfunction or heart failure
         b) Left ventricular ejection fraction is > 40%
         c) Cardiac Index is greater than 2 L/min
         d) No history of grade 2R or greater acute cellular rejection (predominantly T-cell mediated) within the previous 6 months
         e) No history of antibody-mediated (predominantly B-cell mediated) rejection within the previous 6 months
      2) Patient must be 15 years of age or older
      3) Patient is not pregnant
      4) Patient is in an outpatient setting
      5) There are no limitations or exclusions as listed below
**Background**
The most recent statistics reveal that approximately 3,500 people undergo heart transplantation every year worldwide. Out of this group, nearly 40% of the recipients experienced at least one episode of rejection during the first year after transplantation. Monitoring for acute cellular rejection is critical since reversal depends on early and accurate identification and treatment. Acute cellular rejection (ACR) is the most common complication following heart transplantation and is a major cause of graft failure.

Endomyocardial biopsy (EMB) is the gold standard for rejection monitoring, but is invasive and may only detect rejection after significant myocyte damage has occurred. AlloMap® Molecular Expression Testing was developed by XDx Expression Diagnostics and Food and Drug Administration (FDA)-approved as test for early rejection surveillance. It was first introduced in January 2005 for clinical use. It is intended for non-invasive monitoring of patients post-heart transplant in conjunction with standard clinical evaluation.

AlloMap® test translates the complex signals of the immune system’s multiple genes and pathways, specifically those associated with heart transplant ACR, into an objective, actionable score.

AlloMap® was FDA approved for use after 2 months post-transplant however; clinical trials only included patients > 6 months post-transplant. Consequently, utility of the test between 2 and 6 months is unproven and remains unclear.

According to the ISHLT Guidelines for care of heart transplant recipients: Gene Expression Profiling (Allomap) can be used to rule out the presence of ACR of grade 2R or greater in appropriate low-risk patients, between 6 months and 5 years after HT. Level of Evidence: B.

**Codes:**

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<tr>
<th>CPT Codes / HCPCS Codes / ICD-10 Codes</th>
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<tbody>
<tr>
<td>Code</td>
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**CPT codes**

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<th>Description</th>
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**ICD-10 codes covered if selection criteria are met:**

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<td>Z94.1</td>
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**VI. Procedures**

None

**VII. References/Citations**


VIII. Forms/Appendices

None

IX. Responsibility

Medical Director