Medical Policy
Immune Cell Function Assay

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

Policy Number: 182
BCBSA Reference Number: 2.04.56
NCD/LCD: N/A

Related Policies
None

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

Use of the immune cell function assay to monitor and predict immune function after solid organ transplantation is considered INVESTIGATIONAL.

Use of the immune cell function assay to monitor and predict immune function after hematopoietic stem cell transplantation is considered INVESTIGATIONAL.

Use of the immune cell function assay for all other indications is considered INVESTIGATIONAL.

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 Codes

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.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The following CPT code is considered investigational for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

<table>
<thead>
<tr>
<th>CPT codes:</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>86352</td>
<td>Cellular function assay involving stimulation (e.g., mitogen or antigen) and detection of biomarker (e.g., ATP)</td>
</tr>
</tbody>
</table>

**Description**

Currently, immunosuppression is determined by testing for clinical toxicity (e.g., leukopenia, renal failure) and by therapeutic drug monitoring (TDM) when available. However, drug levels are not a surrogate for overall drug distribution or efficacy because pharmacokinetics often differ among individuals due to clinical factors such as underlying diagnosis, age, sex, and race; circulating drug levels may not reflect the drug concentration in relevant tissues; and serum level of an individual immunosuppressant drug may not reflect the cumulative effect of other concomitant immunosuppressants. The main value of TDM is the avoidance of toxic levels and monitoring patient compliance. Further, the appropriate level of immunosuppression may vary from person to person. Individual immune profiles, such as an immune cell function assay, could support clinical decision making and help to manage the risk of infection from excessive immunosuppression and the risk of rejection from inadequate immunosuppression in immunosuppressed patients.

ImmuKnow® measures the concentration of adenosine triphosphate (ATP) in whole blood after a 15- to 18-hour incubation with the mitogenic stimulant, phytohemagglutinin. In cells that respond to stimulation, increased ATP synthesis occurs during incubation. Concurrently, whole blood is incubated in the absence of stimulant for the purpose of assessing basal ATP activity. CD4+ T lymphocytes are immunoselected from both samples using anti-CD4 monoclonal antibody-coated magnetic particles. After washing the selected CD4+ cells on a magnet tray, a lysis reagent is added to release intracellular ATP. A luminescence reagent added to the released ATP produces light measured by a luminometer, which is proportional to the concentration of ATP. The characterization of the cellular immune response of a specimen is made by comparing the ATP concentration for that specimen with fixed ATP production ranges.

Pleximmune™ measures CD154 expression on T-cytotoxic memory cells in patient’s peripheral blood lymphocytes. CD154 is a marker of inflammatory response. To characterize risk of rejection, the patient’s inflammatory response to (transplant) donor cells is expressed as a fraction of the patient’s inflammatory response to third-party cells. This fraction or ratio is called the Immunoreactivity Index (IR). If the donorinduced response exceeds the response to third-party cells, the individual is at increased risk for rejection. Cells are cultured and then analyzed with fluorochrome-stained antibodies to identify the cells expressing CD154. For posttransplant blood samples, an IR greater than 1.1 indicates increased risk of rejection, and an IR less than 1.1 indicates decreased risk of rejection. For pretransplant samples, the threshold for IR is 1.23.
Summary
Careful monitoring of lifelong immunosuppression is required to ensure long-term viability of solid organ allografts without incurring an increased risk of infection. The monitoring of immunosuppression parameters attempts to balance the dual risks of rejection and infection. It is proposed that individual immune profiles, such as an immune cell function assay, will help assess the immune function of the transplant recipient and individualize immunosuppressive therapy.

The evidence for immune cell function assay in patients who have a solid organ transplant includes numerous studies of the association of assay test values and subsequent rejection or infection, and 1 randomized controlled trial in liver transplant patients. Relevant outcomes are overall survival, test accuracy, other test performance measures, and morbidity events (rejection and infection). The ImmuKnow® test shows variable associations with infection and rejection depending on the type of transplant and the context of the study. The predictive characteristics of the test are still uncertain, and do not allow a strong indirect argument of clinical utility. The trial of ImmuKnow® in liver transplant patients showed improvement in overall survival; however, the trial has several shortcomings. Pleximmune™ test results correlated with rejection, but conclusions are uncertain because of extremely limited evidence deriving from a small number of patients described briefly in Food and Drug Administration approval documents. Studies of clinical utility of Pleximmune™ were not identified. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for immune cell function assay in patients who have a hematopoietic stem cell transplant includes studies correlating ImmuKnow® values with subsequent survival. Relevant outcomes are overall survival, test accuracy, other measures of test performance, and morbidity events. Small studies show that ImmuKnow® values correlate with long-term survival. This information on predictive capability could not be linked to improved outcomes. No direct studies of clinical utility were identified. The evidence is insufficient to determine the effects of the technology on health outcomes.

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/2017</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
<tr>
<td>2/2016</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
<tr>
<td>11/2015</td>
<td>Added coding language.</td>
</tr>
<tr>
<td>12/2014</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
<tr>
<td>2/2014</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
<tr>
<td>11/2011-4/1012</td>
<td>Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.</td>
</tr>
<tr>
<td>1/2011</td>
<td>References added.</td>
</tr>
</tbody>
</table>

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
- Managed Care Guidelines
- Indemnity/PPO Guidelines
- Clinical Exception Process
- Medical Technology Assessment Guidelines

References


