

## Corporate Medical Policy

# Immune Cell Function Assay in Solid Organ Transplantation

<b>File Name:</b>	immune_cell_function_assay_in_solid_organ_transplantation
<b>Origination:</b>	11/2009
<b>Last CAP Review:</b>	3/2011
<b>Next CAP Review:</b>	3/2012
<b>Last Review:</b>	3/2011

### Description of Procedure or Service

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Careful monitoring of lifelong immunosuppression is required to ensure long-term viability of solid organ allografts without incurring increased risk of infection. Monitoring of immunosuppression attempts to balance the dual risks of rejection and infection. 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 differs among individuals due to clinical factors such as underlying diagnosis, age, gender, and race; circulating drug levels may not reflect the drug concentration in relevant tissues; and levels 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 excess immunosuppression and the risk of rejection from inadequate immunosuppression in immunosuppressed patients.

ImmuKnow® (Cylex) is an immune cell function assay cleared for marketing by the U.S. Food and Drug Administration (FDA) in April, 2002 to detect cell-mediated immunity (CMI) in an immunosuppressed patient population. The assay measures the concentration of adenosine triphosphate (ATP) in whole blood following a 15- to 18-hour incubation with the mitogenic stimulant phytohemagglutinin (PHA). 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 to fixed ATP level ranges.

On April 2, 2002, Cylex obtained 510(k) clearance from the FDA to market the Immune Cell Function Assay based on substantial equivalence to two flow cytometry reagents (“predicate devices”) manufactured by Becton Dickinson, the TriTest™ CD4 FITC/CD8 PE/CD3 PerCP Reagent and the MultiTest™ CD3 FITC/CD8 PE/CD45 PerCP/CD4 APC Reagent. These reagents are used to determine CD4+ T-lymphocyte counts in immunocompromised patients. The FDA-indicated use of the Cylex Immune Cell Function Assay is for the detection of cell-mediated immunity in an immunosuppressed population.

**\*\*\*Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

# Immune Cell Function Assay in Solid Organ Transplantation

## Policy

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**Immune Cell Function Assay in Solid Organ Transplantation is considered investigational for all applications. BCBSNC does not cover investigational services or procedures.**

## Benefits Application

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This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

## When Immune Cell Function Assay in Solid Organ Transplantation is covered

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Not applicable.

## When Immune Cell Function Assay in Solid Organ Transplantation is not covered

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Use of the immune cell function assay to monitor and predict immune function after solid organ transplantation is considered **investigational**. BCBSNC does not cover investigational services.

## Policy Guidelines

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The American Society of Transplantation (AST) has published recommendations for the screening, monitoring and reporting of infectious complications in immunosuppression trials of organ transplant recipients. These recommendations define relevant infectious complications to be included in the reporting of immunosuppression trials and recommend specific laboratory monitoring and surveillance methods. The immune cell function assay is not included in these recommendations.

The studies identified compare the outcomes of treatment decisions made with the ImmuKnow® assay to those made without ImmuKnow®. That is, the clinical utility of the ImmuKnow® assay is unknown.

The analytic and clinical validity of the test have not been conclusively demonstrated. Further, it remains unclear whether different types of organ transplants or different immunosuppressive regimens affect CD4+ T-cells' response to phytohemagglutinin (PHA) stimulation variably, or whether cut-off values require adjustment for various clinical scenarios. The clinical utility of the ImmuKnow® assay to impact net health outcome in comparison to current methods of care for solid organ transplant recipients has not been evaluated.

# Immune Cell Function Assay in Solid Organ Transplantation

## Billing/Coding/Physician Documentation Information

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This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbsnc.com](http://www.bcbsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable service codes: 86352*

*\*\*\*Please note: 86352 is not specific to this policy and may be submitted for other laboratory tests.*

*Providers should **not** be submitting claims using CPT codes 86353 and/or 82397.*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

## Scientific Background and Reference Sources

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Humar A, Michaels M; AST ID Working Group on Infectious Disease Monitoring. American Society of Transplantation recommendations for screening, monitoring and reporting of infectious complications in immunosuppression trials in recipients of organ transplantation. *Am J Transplant* 2006; 6(2):262-74.

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.56, 8/13/09

Senior Medical Director - 10/2009

Senior Medical Director - 12/2009

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.04.56, 9/16/2010

Specialty Matched Consultant Advisory Panel – 3/2011

## Policy Implementation/Update Information

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- 11/9/09 New Evidence Based Guideline issued. Reviewed with Senior Medical Director 10/16/2009. "Use of the immune cell function assay to monitor and predict immune function after solid organ transplantation is not recommended." (btw)
- 1/5/10 Evidence Based Guideline converted to Corporate Medical Policy. "BCBSNC will not provide coverage for Immune Cell Function Assay in Solid Organ Transplantation because it is considered investigational. BCBSNC does not cover investigational services." Added new CPT code, 86352, to the "Billing/Coding" section. Changed the wording of "Providers may be submitting claims using CPT codes 86353 and/or 82397." to "Providers should not be submitting claims using CPT codes 86353 and/or 82397." Notice given 1/5/2010. Policy effective 4/13/2010. (btw)
- 6/22/10 Policy Number(s) removed (amw)
- 7/6/10 Added statement to "Billing/Coding" section to indicate; "*Please note: 86352 is not specific to this policy and may be submitted for other laboratory tests.*" (btw)
- 4/26/11 Specialty Matched Consultant Advisory Panel review March 30, 2011. No change to policy statement. "Policy Guidelines" updated. References added. (btw)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.