



Evidence Based Guideline

Immune Cell Function Assay in Solid Organ Transplantation

File Name: immune_cell_function_assay_in_solid_organ_transplantation
Policy Number: EBG.MED1222
Origination: 11/2009
Last CAP Review: Not Applicable
Next CAP Review: 4/2011
Last Review: 10/2009

Description of Procedure or Service

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 Evidence Based Guideline is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Evidence Based Guideline for Immune Cell Function Assay in Solid Organ Transplantation

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.

Medical Evidence regarding Immune Cell Function Assay in Solid Organ Transplantation indicates:

Use of the immune cell function assay to monitor and predict immune function after solid organ transplantation is not recommended.

Clinicaltrials.gov lists five studies assessing the ImmuKnow® assay's ability to predict or monitor the development of infection or rejection in solid organ and hematopoietic stem-cell transplant recipients and in multiple sclerosis patients. None of the studies include modifications of immunosuppressive medication regimens based on ATP level.

Without clinical trials demonstrating improved patient outcomes, specifically, reduced incidence of infection, rejection and adverse medication-related effects as a direct consequence of ImmuKnow® assay results and subsequent treatment, the evidence is insufficient to permit conclusions concerning the effect of this procedure on health outcomes. Therefore, the ImmuKnow® cell function assay is considered investigational.

Benefits Application

Please refer to certificate for availability of benefit. This guideline relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore certificate language should be reviewed before applying the terms of the guideline.

Billing/Coding/Physician Documentation Information

This guideline 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. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: There is no specific code for this service.

Providers may be submitting claims using CPT codes 86353 and/or 82397.

Scientific Background and Reference Sources

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]. 2.04.57, 8/13/09

Policy: Immune Cell Function Assay in Solid Organ Transplantation

Senior Medical Director - 10/2009

Policy Implementation/Update Information

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)

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