Medical Coverage Policy | Immune Cell Function Assay

EFFECTIVE DATE: | |
POLICY LAST UPDATED: 06|17|2015

OVERVIEW
This policy documents the coverage determination for use of immune cell function assays. 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.

MEDICAL CRITERIA
Not applicable

PRIOR AUTHORIZATION
Not applicable

POLICY STATEMENT
BlueCHiP for Medicare and Commercial products

Use of the immune cell function assay to monitor and predict immune function after solid organ transplantation, hematopoietic stem-cell transplantation and all other indications is considered not medically necessary as there is insufficient peer-reviewed literature that demonstrates that the service is effective.

COVERAGE
Benefits may vary between groups/contracts. Please refer to the appropriate Evidence of Coverage or Subscriber Agreement for limitations of benefits/coverage when services are not medically necessary.

BACKGROUND
Currently, immunosuppression is determined by testing for clinical toxicity (eg, 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 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.

Regulatory Status

ImmuKnow® (Cylex, recently acquired by Viracor-IBT Laboratories Inc., Lee's Summit, MO) is an immune cell function assay cleared for marketing by FDA in April 2002 to detect cell-mediated immunity (CMI) in an immunosuppressed patient population. In April 2002, Cylex obtained 510(k) clearance from FDA to market the Immune Cell Function Assay based on substantial equivalence to 2 flow cytometry reagents ("predicate devices") manufactured by Becton Dickinson, the TriTestTM CD4 FITC/CD8 PE/CD3 PerCP Reagent and the MultiTestTM CD3 FITC/CD8 PE/CD45 PerCP/CD4 APC Reagent. These reagents are used to determine CD4+ Tlymphocyte counts in immunocompromised patients. The FDA-indicated use of the Immune Cell Function Assay is for the detection of CMI in an immunosuppressed population. A subsequent 510(k) marketing clearance for a device modification was issued by FDA for this assay in 2010. There were no changes to the indications or intended use.

Published studies to date have primarily been small single-center retrospective studies. Studies indicate that adenosine triphosphate (ATP) levels vary among transplant recipients who have evidence of acute infection or transplant rejection, compared with clinically stable patients. Sensitivity and specificity of immune cell function assay have varied in studies reporting these parameters. Based on results from two 2012 systematic reviews of observational studies of ImmuKnow® in adult transplant recipients, estimates of sensitivity range from 52% to 88% for infection and 34% to 75% for rejection. Estimates of specificity, on the other hand, range from 66% to 79% for infection and 72% to 84% for rejection. Given the significant heterogeneity observed across studies, performance characteristics of ImmuKnow® 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 stimulation variably or whether cutoff values require adjustment for various clinical scenarios. Prospective trials are needed to better define the predictive ability of ImmuKnow® compared with current methods of assessing immune status.

Clinical utility of ImmuKnow® to impact net health outcome in comparison with current methods of care for solid organ transplant recipients has not been evaluated using prospective trials with multiple time point measurements of ATP production. Thus, it is unknown how current methods of assessing immune status in solid organ transplant recipients, eg, immunosuppressant drug-level monitoring or empiric use of anti-infective agents, might be changed by use of ImmuKnow®. Therefore, the ImmuKnow® cell function assay is considered not medically necessary as there is insufficient peer-reviewed literature that demonstrates that the service is effective.

CODING

BlueCHiP for Medicare and Commercial products

The following service is considered not medically necessary:
86352

RELATED POLICIES

None

PUBLISHED

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