FIRST COAST SERVICE OPTIONS
MAC - PART A/B
LOCAL COVERAGE DETERMINATION

LCD Database ID Number
L33985

Contractor Name
First Coast Service Options, Inc.

Contractor Number
09101 – Florida
09201 – Puerto Rico/Virgin Islands
09102 – Florida
09202 – Puerto Rico
09302 – Virgin Islands

Contractor Type
MAC – Part A and B

LCD Title
Transplantation Immune Cell Function Assay (ImmuKnow®)

AMA CPT Copyright Statement

CPT only copyright 2002-2017 American Medical Association. All rights reserved. CPT is a registered trademark of the American Medical Association. Applicable FARS/DFARS Apply to Government Use. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. The Code on Dental Procedures and Nomenclature (Code) is published in Current Dental Terminology (CDT). Copyright (c) American Dental Association. All rights reserved. CDT and CDT-2010 are trademarks of the American Dental Association.

CMS National Coverage Policy

Language quoted from CMS National Coverage Determination (NCDs) and coverage provisions in interpretive manuals are italicized throughout the Local Coverage Determination (LCD). NCDs and coverage provisions in interpretive manuals are not subject to the LCD Review Process (42 CFR 405.860[b] and 42 CFR 426 [Subpart D]). In addition, an administrative law judge may not review an NCD. See §1869(f)(1)(A)(i) of the Social Security Act.

Unless otherwise specified, italicized text represents quotation from one or more of the following CMS sources:

CMS Internet-Only Manual, Pub. 100-08, Medicare Program Integrity Manual, Chapter 13, §13.5.1- Reasonable and Necessary Provisions in LCDs
The purpose of this local coverage determination (LCD) is to communicate that after review of the strongest available evidence, it has been determined that the Transplantation Immune Cell Function Assay (ImmuKnow®) does not meet reasonable and necessary criteria as defined in Section 1862 (a)(1)(A) of the Social Security Act.

Section 1862(a)(1)(A) of the Social Security Act precludes program payment for services not deemed to be medically reasonable and necessary.

A service or item is considered to be reasonable and necessary if it is:

**Safe and effective:**

*Appropriate, including the duration and frequency that is considered appropriate for the service, in terms of whether it is:*

- Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient’s condition or to improve the function of a malformed body member;
- Furnished in a setting appropriate to the patient’s medical needs and condition;
- Ordered and furnished by qualified personnel;
- One that meets, but does not exceed, the patient’s medical need; and
- At least as beneficial as an existing and available medically appropriate alternative.

**Background**

Both solid organ (kidney, heart, liver, lung, integument) and hematopoietic stem cell transplantation are interventions which place beneficiaries at high risk. Among the risks are opportunistic infection, induction of malignancy, and the multi-system morbidity of immune transplant rejection.
Transplantation Immune Cell Function Assay (ImmuKnow®)

Laboratory tests to predict rejection (incompatibility) between transplant donors and recipients measure two separate aspects of immunity to predict future graft success: humoral immunity (measuring circulating antibodies directed against the graft) and cell-mediated immunity or CMI (measuring cellular anti-transplant rejection risk by lymphocytes, macrophages, and other cell types which reside in the marrow, spleen, lymph nodes, and circulation).

A variety of tests of CMI are in common use for testing the immune systems of potential and post-operative transplant recipients. The most popular and informative are the CD4- and CD8-cytotoxic CMI tests, which have high sensitivity, specificity, positive and negative predictive value for the patient's risk of "cellular rejection."

It is common practice in transplant centers to test transplant candidates for risk of cellular rejection pre- and post-transplant. In addition, when a transplant recipient exhibits signs of inflammation and acute illness, it is critical to differentiate three different potential processes, which mandate different therapeutic approaches: acute infection (which may be of an uncommon, “opportunistic” type), medication toxicity (especially the inflammatory syndromes caused by Cyclosporine toxicity), and true graft rejection.

The precision of tests to differentiate these graft- and life-threatening processes is critical. Transplant physicians must stratify test selection based on informative properties. Any lab test(s) which fail to provide maximum resolution among the above syndromes must be disqualified from use for pre-transplant candidates or recipients.

Assessment of the Transplantation Immune Cell Function Assay (ImmuKnow®)

The following summarize studies which endeavored to establish correlation between ImmuKnow test results and transplant and/or infection risks:

- A large series reported by Cadillo-Chavez, et al (2006) failed to demonstrate statistically significant relationships between ImmuKnow ATP levels and risk of infection and/or rejection episodes.
- Another report (Batal, et al, 2008) likewise failed to establish a predictive correlation between ImmuKnow levels, viral infection events, and risk of rejection.
- Serban, et al (2009) assayed the range of ATP values generated by ImmuKnow testing and failed to demonstrate a correlation to clinical rejection and likewise failed to be informative for immunosuppression dosing changes.
- Rossano, et al (2009) tested for correlation between the ImmuKnow assay and the risk of pediatric heart transplant rejection events. The authors failed to demonstrate a correlation and concluded the test cannot be recommended for routine use in this critical setting for these vulnerable patients.
- Torio, et al (2011) did demonstrate a correlation between ImmuKnow test outcomes in infected and non-infected transplant patients; however, the test exhibited no predictive value for transplant organ rejection risk.

ImmuKnow is not reasonable and necessary for the management of organ transplant rejection. There is insufficient evidence of the effectiveness of the ImmuKnow assay in the management of organ transplant rejection in individuals undergoing immunosuppressive therapy post solid organ transplant and for the identification of individual risk for rejection prior to kidney or any other solid organ transplant.

The use of ImmuKnow assay is not reasonable and necessary to indicate risk of underlying active infection. ImmuKnow has not been proven to be at least as beneficial as an existing and available medically appropriate alternative. Both active infection and cellular rejection may be more accurately assessed by alternative, proven and superior lab testing modalities. ImmuKnow is not reasonable and necessary for the individualized titration of immunosuppressive therapy. There is insufficient evidence that the results of immune cell function testing will result in improved clinical outcome in individuals following solid organ transplant. ImmuKnow is not reasonable and necessary to identify individuals at risk for rejection prior to kidney or any other solid organ transplant or for the management of other conditions. The utility of the assay is unproven for these uses.
Transplantation Immune Cell Function Assay (ImmuKnow®)

Use of the Immune Cell Function Assay to monitor and predict immune function after solid organ transplantation and to detect or predict risk of active infection does not attain reasonable and necessary criteria for coverage.

**Type of Bill Codes**

012X  Hospital Inpatient (Medicare Part B only)
013X  Hospital Outpatient
014X  Hospital - Laboratory Services Provided to Non-patients
085X  Critical Access Hospital

**Revenue Codes**

030X  Laboratory - General Classification

**CPT/HCPCS Codes**

86352  Cellular function assay involving stimulation (eg, mitogen or antigen) and detection of biomarker (eg, ATP)

**ICD-10 Codes that Support Medical Necessity**

N/A

**Diagnoses that Support Medical Necessity**

N/A

**ICD-10 Codes that DO NOT Support Medical Necessity**

N/A

**Diagnoses that DO NOT Support Medical Necessity**

N/A

**Associated Information**

**Documentation Requirements**

In order for the non-covered service listed in this Local Coverage Determination (LCD) to be evaluated for coverage, a reconsideration request must be submitted in writing to First Coast Service Options Inc., Medical Policy Department. Copies of published full-text evidence (e.g., peer-reviewed medical literature, published studies, etc.) must also be included with the reconsideration request.
Transplantation Immune Cell Function Assay (ImmuKnow®)

Utilization Guidelines

N/A

Sources of Information and Basis for Decision

First Coast Service Options reference LCD number(s) – L33015


Centers for Medicare & Medicaid Services (CMS) General Background on Transplant Patient Management:


Lab Tests Online; a peer-reviewed, non-commercial lab test resource. HLA Testing; Retrieved from http://labtestsonline.org/understanding/analytes/hla-testing/tab/test.
Transplantation Immune Cell Function Assay (ImmuKnow®)


**Start Date of Comment Period**

N/A

**End Date of Comment Period**

N/A

**Start Date of Notice Period**

04/01/2014

**Revision History**

**Revision History Number: R1**

Revision Number: 1
Publication: June 2017 Connection
LCR A/B2017-023

Explanation of Revision: Based on CR 8776, the following verbiage was removed from the “CPT/HCPCS Codes” section of the LCD: “Per CR 8572, beginning in CY 2014, payment for most laboratory tests (except for molecular pathology tests) will be packaged under the OPPS, therefore the clinical laboratory tests listed below, for TOB 13X (outpatient hospital), are packaged in this setting.” The effective date of this revision is for claims processed on or after 05/12/2017, for dates of service on or after 01/01/2014.

**Revision Number:** Original

This LCD replaces all previous LCD versions (refer to “Sources of Information and Basis for Decision” section of the LCD) and publications on this subject to comply with ICD-10-CM based on Change Request 8112. The effective date of this LCD is based on date of service.

**Related Documents**

N/A

**LCD Attachments**

N/A