



**HEART TRANSPLANT REJECTION TESTS
(HEARTSBREATH AND ALLOMAP™
MOLECULAR EXPRESSION TEST)
HS-060**



Harmony Behavioral Health, Inc.

Harmony Behavioral Health of Florida, Inc.

Harmony Health Plan of Illinois, Inc.

HealthEase of Florida, Inc.

*'Ohana Health Plan, a plan offered by
WellCare Health Insurance of Arizona, Inc.*

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WellCare Prescription Insurance, Inc.

**Heart Transplant Rejection
Tests (Heartsbreath and
Allomap™ Molecular
Expression Test**

Policy Number: HS-060

Original Effective Date: 11/20/2008

**Revised Date(s): 11/24/2009;
11/12/2010; 10/6/2011**

DISCLAIMER

The Clinical Coverage Guideline is intended to supplement certain standard WellCare benefit plans. The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this Clinical Coverage Guideline. When a conflict exists between the two documents, the Member's Benefit Plan always supersedes the information contained in the Clinical Coverage Guideline. Additionally, Clinical Coverage Guidelines relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

BACKGROUND

Heart transplantation is a widely accepted therapy for the treatment of end-stage cardiac disease. Approximately 20,000 people in the United States and more than 30,000 people throughout the world live with a transplanted heart. Even with modern drug therapy, cardiac allograft rejection (i.e., rejection of a transplanted heart) remains a constant hazard for heart transplantation patients. Allograft rejection is most frequent within the first month following cardiac transplantation and declines progressively thereafter. Patient survival depends on accurate and timely monitoring for allograft rejection and graft dysfunction. Transplant recipients must be tested repeatedly for signs of rejection, typically with an endomyocardial biopsy. Alternative noninvasive techniques to detect and monitor allograft rejection are under investigation.

Allomap™ Molecular Expression Testing

The AlloMap™ Molecular Expression Test is a noninvasive, 20-gene expression assay that measures the activity of the immune system with respect to the risk of cardiac allograft rejection. In essence, the test detects the absence of rejection in a transplanted heart. The patient's peripheral blood is drawn according to particular specifications, the sample is sent to the XDx Laboratory, and the messenger RNA (mRNA) in the sample is quantified using real-time polymerase chain reaction. Each gene is tested in triplicate. An algorithm that combines the gene expression values of genes that are linked to cardiac allograft rejection is applied to generate a clinically useful "AlloMap score." This score, which ranges from 0 to 40, indicates the immune system's response to the transplanted heart – the higher the score, the greater the risk of rejection. Additional clinical experience and independent replication of study data is necessary, if proven effective in well-designed trials, this test may allow some patients to safely reduce the number of endomyocardial biopsies required after heart transplantation. The impact of the results of this test on clinical decision making requires further evaluation (Hayes, 2006).

Heartsbreath Breath Test

The Heartsbreath test works on the principle that rejection of the transplanted heart is accompanied by oxidative stress that degrades membrane polyunsaturated fatty acids, evolving alkanes and methylalkanes that are excreted in the breath as volatile organic compounds (VOCs). The patient breathes for two minutes through a disposable mouthpiece attached to a breath collecting device, which then analyses the VOCs in alveolar and room air and interprets the values, using a proprietary algorithm to predict the probability of Grade 3 heart transplant rejection.

Based on a review of the published peer-reviewed scientific literature, there is insufficient evidence to conclude that the breath test for detection of heart transplant rejection results in improved management of heart transplant recipients. There is insufficient evidence that use of this test will result in earlier or more efficient detection of heart transplant rejection or that this test is equal to or superior than the standard test, endomyocardial biopsy. Well-designed clinical trials are needed to further evaluate the potential utility of this test and define the role of the test in management of heart transplantation.

ISHLT Standardized Cardiac Biopsy Grading: Acute Cellular Rejection

The diagnosis of rejection may be graded based upon the consensus classification for cardiac allograft rejection published by the International Society for Heart and Lung Transplantation (ISHLT). The grades were initially published in 1990 and have been subsequently updated (2004). The current standard cardiac biopsy grading is:

Grade 0	No rejection
Grade 1 R, mild	Interstitial and/or perivascular infiltrate with up to 1 focus of myocyte damage
Grade 2 R, moderate	Two or more foci of infiltrate with associated myocyte damage
Grade 3 R, severe	Diffuse infiltrate with multifocal myocyte damage ± edema ± hemorrhage ± vasculitis



POSITION STATEMENT

The Heartsbreath Breath Test (Menssana Research, Inc) **is considered experimental and investigational and NOT a covered benefit.** The Allomap™ Molecular Expression Test (XDX, Inc) **is considered experimental and investigational and NOT a covered benefit.**

CODING

CPT® Codes

Not applicable

ICD-9-CM Procedure Codes

Not applicable

Non - Covered CPT® Category III Code

0085T Breath test for heart transplant rejection

Non - Covered ICD-9-CM Diagnosis Code

V42.1 Heart replaced by transplant

*Current Procedural Terminology (CPT®) ©2011 American Medical Association: Chicago, IL.

REFERENCES

Peer Reviewed

1. Hayes Directory. (2006, August 10). Allomap™ molecular expression testing (XDX Inc. [Expression Diagnostics]) for detection of heart transplant rejection). Retrieved from <http://www.hayesinc.com>
2. Stewart, S., Winters, G.L., Fishbein, M.C., Tazelaar, H.D., Kobashigwa, J., Abrams, J., & et al. (2005). Revision of the 1990 working formulation for the standardization of nomenclature in the diagnosis of heart rejection. *Journal of Heart and Lung Transplantation*, 24(11), 1710-1720.

Government Agencies, Professional and Medical Organizations

1. Centers for Medicare and Medicaid Services. (2008). Proposed decision memo for Heartsbreath test for heart transplant rejection (CAG-00394N). Retrieved from <http://www.cms.hhs.gov/mcd/search.asp>

HISTORY AND REVISIONS

Date	Action
12/1/2011	• New template design approved by MPC.
10/6/2011	• Approved by MPC. Reformatted references; no major changes.