

AlloMap®

Policy Number: **M110415115**
Effective Date: **7/1/2011**
Sponsoring Department: **Health Care Services**
Impacted Department(s): **Health Care Services**

Type of Policy: Internal External

Data Classification: Confidential Restricted Public

Applies to (Line of Business):

- Corporate (All)
- State Products, if yes which plan(s): MediSource; MediSource Connect; Child Health Plus Essential Plan
- Medicare, if yes, which plan(s): MAPD; PDP; ISNP; CSNP
- Commercial, if yes, which type: Large Group; Small Group; Individual
- Self-Funded Services (*Refer to specific Summary Plan Descriptions (SPDs) to determine any pre-authorization or pre-certification requirements and coverage limitations. In the event of any conflict between this policy and the SPD of a Self-Funded Plan, the SPD shall supersede the policy.*)

Excluded Products within the Selected Lines of Business (LOB)

Applicable to Vendors? Yes No

Purpose and Applicability:

To set forth medical necessity criteria for laboratory testing for monitoring acute rejection in cardiac transplant patients.

Policy:

Commercial, Self-Funded and Medicare Advantage:

Independent Health covers genetic testing for monitoring acute rejection in cardiac transplant patients using AlloMap®.

All the following criteria must be met:

- Clinically stable cardiac transplant recipient,
- Age ≥ 15 years,
- Transplant occurred ≥ 6 months previously, and less than 5 years after transplant occurred,
- Thorough history and physical is obtained/performed by an appropriately trained transplant physician,
- A non-invasive assessment of cardiac allograft function utilizing echocardiography is performed to evaluate allograft function,
- Low probability of moderate or severe rejection as demonstrated by BOTH of the following:
 - no history or evidence of acute cellular rejection that required treatment.
 - no history or evidence of antibody mediated rejection.

Medicare Advantage:

There is currently a Local Coverage Determination (LCD) and a Local Coverage Article (LCA) for Allomap. Please refer to the links listed in the Reference section for Medicare Advantage members.

MediSource, MediSource Connect, Child Health Plus and Essential Plan:

AlloMap® is covered by MediSource, MediSource Connect and Essential Plan when ordered by the transplant surgeon or a midlevel that he or she supervises utilizing the Commercial criteria above.

AlloMap® is covered for Child Health Plus members aged 15 years-17 years utilizing the Commercial criteria above.

Background:

Cardiac transplantation is considered the definitive therapy for end-stage heart disease. Continuing advancements have reduced morbidity and mortality in the early post-transplant patient. The majority of cardiac transplant recipients experience at least one episode of rejection in the first year after transplantation. Tissue biopsy evidence of rejection usually is present before other clinical signs and symptoms of myocardial compromise, and rejection is often asymptomatic. Endomyocardial biopsy is the gold standard for assessing heart transplant rejection, monitoring, and drug titration management. Less invasive procedures of early rejection have been studied but all have limited sensitivity and specificity compared to endomyocardial biopsy.

AlloMap® is a 20-gene gene expression assay that measures the activity of the immune system with respect to the risk of cardiac allograft rejection. The AlloMap® test combines 11 genes that correlate with the presence or absence of acute cellular rejection with 9 genes included for quality control, of which 6 also function as normalization genes. Reverse transcription polymerase chain reaction (RT-PCR) is used to measure the relative expression of these 20 genes in peripheral blood mononuclear cells. This provides a score ranging from 0 to 40, with lower scores being associated with a very low likelihood of moderate/severe cardiac allograft rejection, as defined by Grade 2R

according to the revised International Society of Heart and Lung Transplantation (ISHLT) classification. The clinician uses the AlloMap® test score, along with other standard clinical assessments, to evaluate the member's probability of rejection and the need for additional diagnostic evaluations. In March 2014, XDx, Inc., the manufacturer of AlloMap®, changed its name to CareDx, Inc.

An evaluation of the peer-reviewed scientific literature, including but not limited to subscription materials, has provided Independent Health the basis for its medical necessity coverage outlined above.

Pre-Authorization Required? Yes No

Preauthorization is required for this service.

Definitions

AlloMap® Molecular Expression Testing is an In Vitro Diagnostic Multivariate Index Assay (IVDMIA) test service, performed in a single laboratory, assessing the gene expression profile of Ribonucleic Acid (RNA) isolated from peripheral blood mononuclear cells.

Gene means a functional unit of heredity found in the body cells.

Deoxyribonucleic Acid (DNA) is the hereditary material in humans and almost all other organisms. Nearly every cell in a person's body has the same DNA.

Gene Expression means the process by which inheritable information from a gene, such as the DNA sequence is made into a functional gene product, such as protein or RNA.

Molecular Diagnostic Services (MoIDX) Program identifies tests, determines coverage, and determines reimbursement as administered by Palmetto GBA, a CMS contractor.

Rejection means the process where the immune system fails to accept a transplanted organ as a part of the body.

Ribonucleic acid (RNA) is an important hereditary molecule with long chains of nucleotides. A nucleotide contains a nitrogenous base, a ribose sugar, and a phosphate.

International Society of Heart and Lung Transplantation (ISHLT) classification was originally published in 1990, and revised in 2004:

- Grade 0R* – no rejection
 - Grade 1R (1990 grades 1A, 1B, and 2) – mild rejection, with interstitial and/or perivascular infiltrate with up to 1 focus of myocyte damage
 - Grade 2R (1990 grade 3A) – moderate rejection with 2 or more foci of infiltrate with associated myocyte damage
 - Grade 3R (1990 grades 3B and 4) – severe rejection, with diffuse infiltrate with multifocal myocyte damage ± edema, ± hemorrhage ± vasculitis
- R* indicates revised grade.

References

Related Policies, Processes and Other Documents

N/A

Non-Regulatory references

California Technology Assessment Forum. Gene Expression Profiling for The Diagnosis of Heart Transplant Rejection. December 2010.

CareDx, Inc. [web site]. AlloMap® Testing Overview. Available at: <https://caredx.com/products-and-services/transplant-services/heart/heartcare#what-is-allomap> Accessed January 25, 2024.

Costanzo MR, Dipchand A, Starling R, et al.; International Society of Heart and Lung Transplantation Guidelines. The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients. J Heart Lung Transplant. 2010 Aug;29(8):914-56.

Hayes, Inc. Genetic Test Evaluation Report AlloMap® Molecular Expression (XDx Inc.) for Detection of Heart Transplant Rejection; Lansdale PA: November 2016.

Pham MX, Deng MC, Kfoury AG et al. Molecular testing for long-term rejection surveillance in heart transplant recipients: design of the Invasive Monitoring Attenuation Through Gene Expression (IMAGE) trial. J Heart Lung Transplant 2007; 26(8):808-14.

Pham MX, Teuteberg JJ, Kfoury AG, et al.; IMAGE Study Group. Gene-expression profiling for rejection surveillance after cardiac transplantation. N Engl J Med. 2010 May 20;362(20):1890-900.

Starling RC, Pham M, Valentine H, et al; Working Group on Molecular Testing in Cardiac Transplantation. Molecular testing in the management of cardiac transplant recipients: initial clinical experience. J Heart Lung Transplant. 2006 Dec;25(12):1389-95.

Stewart S, Winters GL, Fishbein MC, et al. Revision of the 1990 working formulation for the standardization of nomenclature in the diagnosis of heart rejection. J Heart Lung Transplant. 2005;24(11):1710-1720.

Velleca A, Shullo MA, Dhital K, et al. The International Society for Heart and Lung Transplantation (ISHLT) guidelines for the care of heart transplant recipients. J Heart Lung Transplant. 2023 May;42(5):e1-e141.

XDx, Inc. [web site]. News Release XDx Announces Name Change to CareDx; Available at: https://s201.g4cdn.com/458786462/files/doc_news/2014/03/28/757634.pdf Accessed January 25, 2024.

Regulatory References

Centers for Medicare and Medicaid (CMS) [web site]. Local Coverage Article Billing and Coding: Molecular Pathology Procedures (A56199). Available at: <https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleid=56199&ver=99&keyword=&keywordType=starts&areaid=all&doctype=6,3,5,1,F,P&contractOption=name&contractorName=1&hcpcsOption=code&hcpcsStartCode=81595&hcpcsEndCode=81595&sortBy=title&bc=1> Accessed January 25, 2024.

Centers for Medicare and Medicaid (CMS) [web site]. Local Coverage Determination (LCD): Molecular Pathology Procedures (L35000) Available at: <https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=35000&ver=140&> Accessed January 25, 2024.

New York State Department of Health [web site]. New York State Medicaid Program Laboratory Procedure Codes. Version 2023. Available at: https://www.emedny.org/ProviderManuals/Laboratory/PDFS/Laboratory_Procedure_Codes.pdf Accessed January 25, 2024.

United States Food and Drug Administration (FDA) [web site]. Device Classification under Section 513(f)(2)(denovo) Available at: <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm?ID=DEN080007> Accessed January 25, 2024.

This policy contains medical necessity criteria that apply for this service. Please note that payment for covered services is subject to eligibility criteria, contract exclusions and the limitations noted in the member's contract at the time the services are rendered.

Version Control

Signature / Approval on File? Yes No

Revision Date	Owner	Notes
4/1/2024	Health Care Services	Reviewed
1/1/2024	Health Care Services	Revised
4/1/2023	Health Care Services	Revised
5/1/2022	Health Care Services	Revised
6/1/2021	Health Care Services	Revised
7/1/2020	Health Care Services	Revised
8/1/2019	Medical Management	Reviewed
10/1/2018	Medical Management	Reviewed
2/1/2018	Medical Management	Reviewed
3/1/2017	Medical Management	Revised
3/1/2016	Medical Management	Revised
7/1/2015	Medical Management	Revised
6/1/2014	Medical Management	Revised
6/1/2013	Medical Management	Revised
6/1/2012	Medical Management	Revised