Medica Central Coverage Policy

Policy Name:	**Genetic Testing – Specialty Testing: Transplant MP9798**
Effective Date:	**07/01/2025**

Important Information – Please Read Before Using This Policy

These services may or may not be covered by all Medica Central plans. Coverage is subject to requirements in applicable federal or state laws. Please refer to the member's plan document for other specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare, Medicaid, and other government programs, this policy will apply unless these programs require different coverage.

Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions may call the Provider Service Center. Please use the Quick Reference Guide on the Provider Communications page for the appropriate phone number. https://mo-central.medica.com/Providers/SSM-employee-health-plan-for-IL-MO-OK-providers

Medica Central coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care, and treatment.

Coverage Policy

OVERVIEW

This policy addresses the use of tests for diagnosis and screening during the process of solid organ transplantation, either using tissue or peripheral blood.

For additional information see the Rationale section.

The tests, CPT codes, and ICD codes referenced in this policy are not comprehensive, and their inclusion does not represent a guarantee of coverage or non-coverage.

POLICY REFERENCE TABLE

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	REF
Heart Transplant Tests			
Donor-Derived Cell-free DNA for Heart Transplant Rejection	AlloSure (CareDx)	81479, 0055U, 0118U, 0493U, Z48.21, Z94.1	7, 8
	Prospera - 0493U (Natera)		
	myTAIHEART - 0055U (TAI Diagnostics)		

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	REF
	Viracor TRAC Heart dd-cfDNA - 0118U (Eurofins)		
Post Heart Transplant Gene Expression Panels for Rejection Risk via Peripheral Blood	AlloMap - 81595 (CareDx)	81595, Z48.21, Z94.1	7
Post Heart Transplant Gene Expression Panels for Rejection Risk via Tissue	Molecular Microscope MMDX - Heart - 0087U (Kashi Clinical Laboratories)	0087U, Z48.21, Z94.1	7
Kidney Transplant Tests			
Donor-Derived Cell-free DNA for Kidney Transplant Rejection	Allosure Kidney (CareDx, Inc.)	81479, 0118U, 0493U, 0508U, 0509U, T86.11, T86.12, Z94.0	6, 8, 9
	Prospera - 0493U (Natera)		
	Viracor TRAC Kidney dd-cfDNA - 0118U (Viracor Eurofins)		
	VitaGraft Kidney Baseline + 1st Plasma Test - 0508U (Oncocyte Corporation)		
	VitaGraft Kidney Subsequent - 0509U (Oncocyte Corporation)		
Lung Transplant Tests			
Evidence-Based Donor-Derived Cell-free DNA for Lung Transplant Rejection	Prospera Lung (Natera) AlloSure Lung (CareDx)	81479, T86.810, Z48.24, Z94.2	6
Emerging Evidence Donor-Derived Cell-free DNA for Lung Transplant Rejection	Eurofins TRAC dd-cfDNA - 0118U (Transplant Genomics Inc)	0118U, T86.810, Z48.24, Z94.2	6
HLA Typing for Transplantation			

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	REF
HLA Typing for Transplantation	HLA-A,B Intermediate Resolution (Versiti)	81370, 81371, 81372, 81373, 81376, 81378, 81379, 81380, 81382, C25, C81-C96, D46, D61, Z52.20, Z52.3, Z52.4 Z52.89, N17, N18, N19, I12, E08-E13	1, 2, 3, 4, 5
	HLA-B Low Resolution (Versiti)		
	HLA-DQB1,DQA1 Intermediate Resolution (Versiti)		
	HLA-A, B, C, DRB1 and DQ High Resolution (Quest Diagnostics)		
	HLA A,B,C Profile (High Resolution) (Labcorp)		
	HLA-A High Resolution (Versiti)		

RELATED POLICIES

This policy document provides coverage criteria for testing related to transplantation. Please refer to:

- ***Oncology Testing: Hematologic Malignancy Molecular Diagnostics*** for coverage criteria related to molecular profiling of a known or suspected blood cancer (e.g. broad molecular profiling, including Minimal Residual Disease (MRD) Testing, Tumor Mutational Burden (TMB), and cytogenetic / fusion testing).
- ***Oncology Testing: Solid Tumor Molecular Diagnostics*** for coverage criteria related to molecular profiling of a known or suspected cancer (e.g. broad molecular profiling, including Minimal Residual Disease (MRD) Testing, Tumor Mutational Burden (TMB), and cytogenetic / fusion testing).
- ***Specialty Testing: Cardiovascular*** for coverage criteria related to diagnostic tests for inherited and sporadic cardiovascular conditions.
- ***Specialty Testing: Nephrology*** for coverage criteria related to diagnostic tests for suspected kidney disorders, including testing of asymptomatic potential living donors.
- ***Specialty Testing: Respiratory*** for coverage criteria related to diagnostic tests for disorders that affect the lungs, including cystic fibrosis.
- ***General Approach to Laboratory Testing*** for coverage criteria related to transplantation, that is not specifically discussed in this or another non-general policy.

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COVERAGE CRITERIA

HEART TRANSPLANT TESTS

Donor-Derived Cell-free DNA for Heart Transplant Rejection

I. The use of peripheral blood measurement of donor-derived cell-free DNA in the management of patients after heart transplantation is considered **medically necessary** when:

   A. The member has undergone a heart transplant, **AND**

   B. Peripheral blood measurement of donor-derived cell-free DNA testing has not been performed in the past twelve months.

II. The use of peripheral blood measurement of donor-derived cell-free DNA in the management of patients after heart transplantation is considered **investigational** for all other indications.

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Post Heart Transplant Gene Expression Panels for Rejection Risk via Peripheral Blood

I. The use of post heart transplant gene expression panels for rejection risk via peripheral blood to determine management of patients after heart transplantation is considered **medically necessary** when:

   A. The member is age 18 or older, **AND**

   B. The member has undergone heart transplant, **AND**

   C. The member is at low-risk for organ rejection, **AND**

   D. The member's heart transplant was performed at least 2 months ago and less than 5 years ago.

II. The use of post heart transplant gene expression panels for rejection risk via peripheral blood to determine management of patients after heart transplantation is considered **investigational** for all other indications.

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Post Heart Transplant Gene Expression Panels for Rejection Risk via Tissue

I. The use of post heart transplant gene expression panels for rejection risk via tissue is considered **investigational** for all indications.

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KIDNEY TRANSPLANT TESTS

Donor-Derived Cell-free DNA for Kidney Transplant Rejection

I. The use of peripheral blood measurement of donor-derived cell-free DNA in the management of patients after renal transplantation is considered **medically necessary** when:

   A. The member has undergone kidney transplantation, **AND**

B. The test has not been performed in the previous 12 months, **AND**

C. The member meets at least one of the following:

1. The member has clinical signs of acute rejection, **OR**
2. A biopsy was done to check for signs of acute rejection and is inconclusive, **OR**
3. The member is being monitored for adequate immunosuppression.

II. The use of peripheral blood measurement of donor-derived cell-free DNA in the management of patients after renal transplantation is considered **investigational** for all other indications.

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LUNG TRANSPLANT TESTS

Evidence-Based Donor-Derived Cell-free DNA for Lung Transplant Rejection

I. The use of peripheral blood measurement of donor-derived cell-free DNA tests with sufficient evidence of clinical utility and validity in the management of patients after lung transplantation is considered **medically necessary** when:

A. The member has undergone lung transplantation, **AND**

B. The test has not been performed in the last 12 months, **AND**

C. The member meets at least one of the following:

1. The member has clinical signs of acute rejection, **OR**
2. A biopsy was done and is inconclusive for rejection, **OR**
3. The member is being monitored for adequate immunosuppression.

II. The use of peripheral blood measurement of donor-derived cell-free DNA tests in the management of patients after lung transplantation is considered **investigational** for all other indications.

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Emerging Evidence Donor-Derived Cell-free DNA for Lung Transplant Rejection

I. Donor-derived cell-free DNA tests with insufficient evidence of clinical validity in the management of patients after lung transplantation are considered **investigational** for all indications.

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HLA TYPING FOR TRANSPLANTATION

HLA Typing for Transplantation

I. HLA typing for transplantation is considered **medically necessary** when the member meets the following:

A. The member is being considered for any of the following:

1. Recipient of bone marrow transplantation, **OR**

2. Donor for bone marrow transplantation, **OR**
3. Recipient of solid organ transplantation, **OR**
4. Donor for solid organ transplantation.

II. HLA typing for transplantation is considered **investigational** for all other indications.

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PRIOR AUTHORIZATION

Prior authorization is not required. However, services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial may result if criteria are not met.

RATIONALE

Donor-Derived Cell-free DNA for Heart Transplant Rejection

American Society of Transplant Surgeons

In their position statement approved in March 2023 and updated October 2024, the American Society of Transplant Surgeons (ASTS) stated the following: “We recommend that dd-cfDNA [donor-derived cell-free DNA] may be utilized to rule out subclinical rejection for heart transplant recipients” (p. 5).

International Society of Heart and Lung Transplantation

The 2023 ISHLT guidelines were reviewed to assess the recommended frequency for dd-cfDNA testing. Included in the guidelines is an example of a biopsy schedule for follow-up visits post-transplant. The 2023 updated guideline states that noninvasive testing (such as Allomap) may be included in these follow-up visits. However, we did not identify any clear evidence-based recommendations in ISHLT for the use of dd-cfDNA testing as a serial monitoring tool.

Concert Note

For routine monitoring of patients post-transplant, absent clear, specific and evidence-based guideline recommendations for a particular regimen of screening, a default frequency of coverage of once every 12 months will be adopted.

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Post Heart Transplant Gene Expression Panels for Rejection Risk via Peripheral Blood

International Society of Heart and Lung Transplantation

The 2023 International Society of Heart and Lung Transplantation (ISHLT) Guidelines for the Care of Heart Transplant Patients include recommendations for the non-invasive monitoring of acute cellular rejection (ACR) after heart transplant [HT]. They specifically address Allomap and state that peripheral blood testing “can be used in low-risk patients between 2 months and 5 years after HT to identify adult recipients who have low risk of current ACR to reduce the frequency of EMB [endomyocardial biopsy]”. At this time, the recommendation is specific to adults given data in children does not allow for a general recommendation for GEP (p. e38).

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Post Heart Transplant Gene Expression Panels for Rejection Risk via Tissue

International Society of Heart and Lung Transplantation

The 2023 International Society of Heart and Lung Transplantation (ISHLT) guidelines for the Care of Heart Transplant Patients states that gene expression testing of allograft tissue (e.g., Molecular Microscope, MMDx) may allow for "improved discrimination between T-cell mediated or antibody mediated rejection and tissue injury". However, the test is not routinely used or may not be clinically available at this time (p. e33-34).

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Donor-Derived Cell-free DNA for Kidney Transplant Rejection

Centers for Medicare and Medicaid Services

The CMS local coverage determination (LCD) entitled "MolDX: Molecular Testing for Solid Organ Allograft Rejection" states the following regarding donor-derived cell-free DNA tests in individuals who have had solid organ transplantation:

"This Medicare contractor will provide limited coverage for molecular diagnostic tests used in the evaluation and management of patients who have undergone solid organ transplantation. These tests can inform decision making along with standard clinical assessments in their evaluation of organ injury for active rejection (AR).

These tests may be ordered by qualified physicians considering the diagnosis of AR affiliated with a transplant center, helping to rule in or out this condition when assessing the need for or results of a diagnostic biopsy. They should be considered along with other clinical evaluations and results and may be particularly useful in patients with significant contraindications to invasive procedures.

The intended use of the test must be:

- To assist in the evaluation of adequacy of immunosuppression, wherein a non-invasive or minimally invasive test can be used in lieu of a tissue biopsy in a patient for whom information from a tissue biopsy would be used to make a management decision regarding immunosuppression, OR
- As a rule-out test for AR in validated populations of patients with clinical suspicion of rejection with a non-invasive or minimally invasive test to make a clinical decision regarding obtaining a biopsy, OR
- For further evaluation of allograft status for the probability of allograft rejection after a physician-assessed pretest, OR
- To assess rejection status in patients that have received a biopsy, but the biopsy results are inconclusive or limited by insufficient material."

European Society of Organ Transplantation (2024)

The European Society of Organ Transplantation (ESOT) published a Consensus Statement on Testing for Non-Invasive Diagnosis of Kidney Allograft Rejection, which states the following:

"Recommendation 1.1: We suggest that clinicians consider measuring serial plasma dd-cfDNA in patients with stable graft function to exclude the presence of subclinical antibody mediated rejection (p. 5).

Recommendation 2.1: We recommend that clinicians measure plasma dd-cfDNA in patients with acute graft dysfunction to exclude the presence of rejection, particularly antibody mediated rejection" (p. 6).

American Society of Transplant Surgeons (ASTS)

The ASTS issued an updated statement on donor derived cell-free DNA (dd-cfDNA) in October of 2024. Included in the statement is a section on the current state of evidence supporting a frequency schedule for dd-cfDNA testing in kidney transplant recipients. Overall, the ASTS states that "the optimal surveillance testing frequency is unknown". In their summary of evidence, they state that additional research is needed to determine the optimal frequency for dd-cfDNA surveillance testing (p. 3-4).

Concert Note

Although the ASTS recommendations include a suggestion for "serial dd-cfDNA" testing in kidney transplant recipients, there is currently not a clear, specific, and evidence-based guideline recommendation for a particular regimen of screening. Therefore, a default frequency of coverage of once every 12 months will be adopted.

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Evidence-Based Donor-Derived Cell-free DNA for Lung Transplant Rejection

Centers for Medicare and Medicaid Services

The CMS local coverage determination (LCD) entitled "MolDX: Molecular Testing for Solid Organ Allograft Rejection" states the following regarding donor-derived cell-free DNA tests in individuals who have had solid organ transplantation:

"This Medicare contractor will provide limited coverage for molecular diagnostic tests used in the evaluation and management of patients who have undergone solid organ transplantation. These tests can inform decision making along with standard clinical assessments in their evaluation of organ injury for active rejection (AR).

These tests may be ordered by qualified physicians considering the diagnosis of AR affiliated with a transplant center, helping to rule in or out this condition when assessing the need for or results of a diagnostic biopsy. They should be considered along with other clinical evaluations and results and may be particularly useful in patients with significant contraindications to invasive procedures.

The intended use of the test must be:

- To assist in the evaluation of adequacy of immunosuppression, wherein a non-invasive or minimally invasive test can be used in lieu of a tissue biopsy in a patient for whom information from a tissue biopsy would be used to make a management decision regarding immunosuppression, OR
- As a rule-out test for AR in validated populations of patients with clinical suspicion of rejection with a non-invasive or minimally invasive test to make a clinical decision regarding obtaining a biopsy, OR
- For further evaluation of allograft status for the probability of allograft rejection after a physician-assessed pretest, OR
- To assess rejection status in patients that have received a biopsy, but the biopsy results are inconclusive or limited by insufficient material."

Concert Note

For monitoring patients post lung transplantation, absent clear, specific and evidence-based guideline recommendations for a particular regimen of screening, a default frequency of once every 12 months will be adopted.

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Emerging Evidence Donor-Derived Cell-free DNA for Lung Transplant Rejection

Tests that have limited established clinical utility or validity as defined in the Concert policy for General Approach to Genetic and Molecular testing do not meet the threshold for coverage. Evidence for validity may include a Technology Assessment conducted by an independent third party (e.g.MolDx Tech, ECRI, Optum Genomic) and/or evidence-based guidelines published by professional societies. Such evidence was not identified for the tests referenced by this policy.

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HLA Typing for Transplantation

UpToDate: Human leukocyte antigens (HLA): A roadmap

For patients who are undergoing or being evaluated for hematopoietic stem cell transplantation, full HLA typing is required.

UpToDate: Donor selection for hematopoietic cell transplantation

Donor and recipient HLA typing for HLA-A, -B, -C, and -DR is an important and necessary part of successful hematopoietic cell transplantation (HCT). T

NMDP, formerly known as the National Marrow Donor Program and Be The Match

“These guidelines were developed jointly by NMDP and the American Society for Transplantation and Cellular Therapy (ASTCT). The guidelines are based on current clinical practice, medical literature, National Comprehensive Cancer Network (NCCN) Guidelines for the treatment of cancer and evidence-based reviews.”

“If allogeneic transplant is potentially indicated, you should perform HLA typing of the patient and potential family donors at diagnosis. In addition, a preliminary unrelated donor search of the NMDP Registry should be completed.”

Organ Procurement and Transplantation Network (OPTN)

The OPTN (effective date: 10/31/2024) includes a section titled “Requirements for Performing and Reporting HLA Typing”, in which it states:

“Laboratories must perform HLA typing on a kidney, kidney-pancreas, pancreas, or pancreas islet candidate and report results for HLA A, B, Bw4, Bw6, and DR to the transplant program prior to registration on the waiting list” (p. 52).

Additionally, the document states:

“Laboratories performing histocompatibility testing for kidney transplants or multi-organ transplants in which a kidney is to be transplanted must perform a final crossmatch and report the results to the Transplant Program before transplant (p. 55).

Tait, et al

In 2013, Tait et al. created a list of technical test recommendations for pre and post solid organ transplantation. Per the article:

“HLA typing of donor and recipient must be performed at a level required for accurate antibody interpretation. When a patient is sensitized, precise characterization of HLA antibodies and complete HLA typing of the donor pretransplantation must be performed” (p. 37).

Of note, there is no mention of performing HLA Typing post-transplantation.

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REFERENCES

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3. 2024 CONSULTATION GUIDELINES Recommended Timing for Transplant Consultation. Published jointly by NMDPSM and the American Society for Transplantation and Cellular Therapy (ASTCT). Available at: https://www2.bethematchclinical.org/ConsultationGuidelines

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Note: The Health Plan uses the genetic testing clinical criteria developed by Concert Genetics, an industry-leader in genetic testing technology assessment and policy development.

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