Concert Genetic Testing: Kidney Disorders

Reference Number: LA.CP.CG.11
Date of Last Revision ~~06/24~~01/25
Revision Log

Coding implications

See Important Reminder **at the end of this policy for important regulatory and legal information.**

OVERVIEW

Inherited kidney disorders and inherited disorders that indirectly affect the kidneys can be ~~more~~ common, such as autosomal dominant polycystic kidney disease, or ~~more rarely~~rare, such as Lowe syndrome and Fabry disease. Identifying the genetic cause of an inherited kidney disorder can help direct treatment, inform family members, and contribute to the overall understanding of the genetic etiology of chronic kidney disease. More advanced next-generation sequencing, such as exome sequencing and comprehensive genetic testing panels, are emerging as a first-line diagnostic method for patients with chronic kidney disease.

With the use of donor-derived cell-free DNA (ddcfDNA), biomarker tests have been developed as an alternative to more invasive procedures for post-renal transplant care to optimize graft longevity while avoiding side effects and toxicity of immunosuppressive therapies.

POLICY REFERENCE TABLE

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2023, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only and may not support medical necessity. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

The tests ~~and~~, associated laboratories, CPT codes, and CPT codes contained within this document serve only as examples to help users navigate claims and corresponding criteria; as such, they are not comprehensive and are not a guarantee of coverage or non-coverage. Please see the ~~Concert Genetics Platform~~Concert Platform for a comprehensive list of registered tests.

NOTE: Coverage is subject to each requested code's inclusion on the corresponding LDH fee schedule. Non-covered codes are denoted (*) and are reviewed for Medical Necessity for members under 21 years of age on a per case basis. The non-covered codes will only be denoted in the table below and not throughout the policy. Please only reference the policy reference table for covered and non-covered codes.

Criteria Sections	Example Tests (Labs)	Common CPT Codes	Common ICD Codes	Ref
~~Polycystic Kidney Disease~~Polycystic Kidney Disease				
~~Targeted Variant Analysis~~Polycystic Kidney Disease Panels	Hereditary Cystic Kidney Diseases Panel (PreventionGenetics, part of Exact Sciences)~~Targeted Mutation Analysis for a Known Familial Variant~~	81404*, 81405*, 81406*, 81407*, 81408*, 81479~~81403*~~	Q61, N18	1, 2~~, 8~~
	~~Autosomal Dominant~~ Polycystic Kidney Disease ~~(ADPKD) via the GANAB Gene (PreventionGenetics, part of Exact Sciences~~Panel (GeneDx)			
		~~81404*, 81405*, 81406*, 81407*, 81408*, 81479~~		
Comprehensive Kidney Disease Panels				
~~Comprehensive Kidney Disease Panels~~Comprehensive Kidney Disease Panels	RenaSight (Natera)	81401*, 81402*, 81403*, 81404*, 81405*,	N00-N08, N10-N19, Q61, R31	3, 8

		81406*, 81407*, 81408*, 81479		
	KidneySeq Version 5 Comprehensive Testing (Iowa Institute of Human Genetics)			
	RenalZoom (DNA Diagnostic Laboratory - Johns Hopkins Hospital)			
***APOL1*-Mediated Kidney Disease**				
~~*APOL1* Targeted Variant Analysis~~*APOL1*-Targeted Variant Analysis	Apolipoprotein L1 (APOL1) Renal Risk Variant Genotyping (Quest Diagnostics)	0355U*	N00-N08, N10-N19	~~9~~7
	APOL1 Genotype, Varies (Mayo Clinic Laboratories)	81479		
Donor-Derived Cell ~~Free~~-free DNA for Kidney Transplant Rejection				
~~Donor-Derived Cell-Free DNA for Kidney Transplant Rejection~~Donor-Derived Cell-free DNA for Kidney Transplant Rejection	Allosure Kidney (CareDx, Inc.)	81479	T86.11, T86.12, Z94.0	~~7~~9, 10, 11
	Prospera ~~Kidney~~ (Natera)	0493U*		
	Viracor TRAC Kidney dd-cfDNA (Viracor Eurofins)	0118U*		
	VitaGraft Kidney Baseline + 1st Plasma Test (Oncocyte Corporation)	0508U*		
	VitaGraft Kidney Subsequent (Oncocyte Corporation)	0509U*		
Other Covered Kidney Disorders				
~~Other Covered Kidney Disorders~~Other Covered Kidney Disorders	See list below	81400*, 81401*, 81402*, 81403*, 81404*, 81405*, 81406*, 81407*, 81408~~*, 0268U~~*		4, 5, 6

OTHER RELATED POLICIES

This policy document provides criteria for hereditary kidney disorders. Please refer to:

- ***Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability, and Developmental Delay*** for criteria related to genetic disorders that affect multiple organ systems
- ***Genetic Testing: Hereditary Cancer Susceptibility*** for criteria related to von Hippel Lindau (VHL) syndrome and other hereditary cancer syndromes.
- ***Genetic Testing: General Approach to Genetic and Molecular Testing*** for criteria related to genetic testing for kidney disease that is not specifically discussed in this or another non-general policy, including known familial variant testing.
- ***Genetic Testing Hematologic Conditions Non-Cancerous*** for criteria related to hematologic disorders that affect the kidneys.

back to top

CRITERIA

It is the policy of Louisiana Healthcare Connections that the specific genetic testing noted below is **medically necessary** when meeting the related criteria:

POLYCYSTIC KIDNEY DISEASE PANELS

~~**Targeted Variant Analysis**~~

~~***PKD1, PKD2, GANAB,* or *DNAJB11* targeted variant analysis (81403) to establish~~**Polycystic Kidney Disease Panels**

~~I.~~ Genetic testing using a ~~diagnosis of autosomal dominant~~ polycystic kidney disease ~~is considered **medically necessary** when:~~

~~A. The member/enrollee has a~~ close relative ~~with a known pathogenic or likely pathogenic variant in *PKD1*, *PKD2*, *GANAB*, or *DNAJB11*.~~

~~II. *PKHD1* targeted variant analysis (81403) to establish a diagnosis of autosomal recessive polycystic kidney disease is considered **medically necessary** when:~~

~~A. The member/enrollee has a biological~~ full sibling ~~with known biallelic pathogenic or likely pathogenic variants in *PKHD1*.~~

~~III. *PKD1*, *PKD2*, *GANAB*, *DNAJB11*, or *PKHD1* targeted variant analysis (81403) to establish a diagnosis of autosomal dominant or autosomal recessive polycystic kidney disease is considered **investigational** for all other indications.~~

~~Single Gene or Multigene Panel~~

I. ~~*PKD1* (81407, 81479), *PKD2* (81406, 81479), *GANAB* (81479), *DNAJB11* (81479), *PKHD1* (81408, 81479) sequencing and/or deletion/duplication analysis or multigene~~ panel ~~analysis~~ (81404, 81405, 81406, 81407, 81408, 81479) to confirm or establish a diagnosis of polycystic kidney disease is considered **medically necessary** when:

A. The member/enrollee has any of the following clinical features of polycystic kidney disease:

1. Multiple bilateral renal cysts, **OR**
2. Cysts in organs other than the kidneys (especially the liver, seminal vesicles, pancreas, and arachnoid membrane), **OR**
3. Hypertension in an individual younger than age 35, **OR**

~~1. Intracranial aneurysm, **OR**~~

4. Bilaterally enlarged and diffusely echogenic kidneys~~, **OR**~~

~~2. Poor corticomedullary differentiation, **OR**~~

~~3. Hepatobiliary abnormalities with progressive portal hypertension, **OR**~~

~~4. Congenital hepatic fibrosis (CHF) with portal hypertension.~~

II. ~~*PKD1* (81407, 81479), *PKD2* (81406, 81479), *GANAB* (81479), *DNAJB11* (81479), *PKHD1* (81408, 81479) sequencing and/or deletion/duplication analysis or multigene panel analysis~~Genetic testing using polycystic kidney disease panels (81404, 81405, 81406, 81407, 81408, 81479) to confirm or establish a diagnosis of polycystic kidney disease is considered **investigational** for all other indications.

back to top

COMPREHENSIVE KIDNEY DISEASE PANELS

Comprehensive Kidney Disease Panels

I. Genetic testing for kidney disease via a comprehensive kidney disease panel (81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408, 81479) is considered **medically necessary** when:

A. The member/enrollee has chronic kidney disease with an undetermined cause after undergoing standard-of-care workup studies (examples: history and physical examination, biochemical testing, renal imaging, or renal biopsy), **AND**

B. The member/enrollee meets at least one of the following:

1. Onset of chronic kidney disease under 40 years of age, **OR**
2. One or more first- or second-degree relatives with chronic kidney disease, **OR**
3. Consanguineous family history, **OR**
4. Cystic renal disease, **OR**
5. Congenital nephropathy~~.~~, **OR**
6. Syndromic/multisystem features, **OR**
7. There is a possibility of identifying a condition amenable to targeted treatment.

II. Genetic testing for kidney disease via a comprehensive kidney disease panel (81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408, 81479) is considered **investigational** for all other indications.

back to top

APOL1-MEDIATED KIDNEY DISEASE

~~*APOL-1*~~APOL1 Targeted Variant Analysis

I. Targeted variant analysis for the *APOL1* high-risk genotype (i.e., G1/G1, G1/G2, or G2/G2) (0355U, 81479) is considered **medically necessary** when:

A. The member/enrollee has kidney disease, **AND**

B. The member/enrollee meets at least one of the following:

1. The member/enrollee is of African ancestry, **OR**
2. The member/enrollee has a family member with a confirmed *APOL1* high-risk genotype (i.e., G1/G1, G1/G2, or G2/G2).

II. Targeted variant analysis for the *APOL1* high-risk genotype (i.e., G1/G1, G1/G2, or G2/G2) (0355U, 81479) is considered **investigational** for all other indications.

back to top

DONOR-DERIVED CELL-FREE DNA FOR KIDNEY TRANSPLANT REJECTION

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 (81479, 0493U, 0118U, 0508U, 0509U) is considered **medically necessary** when:

A. The member/enrollee 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.

~~I.~~II. The use of peripheral blood measurement of donor-derived cell-free DNA in the management of patients after renal transplantation (81479, 0493U, 0118U, 0508U, 0509U) is considered **investigational** for all other indications~~, including but not limited to:~~.

~~A. Detection of acute renal transplant rejection~~

~~B. Detection of renal transplant graft dysfunction~~

back to top

OTHER COVERED KIDNEY DISORDERS

Other Covered Kidney Disorders

The following is a list of conditions that have a known genetic association. Due to their relative rareness, it may be appropriate to cover these genetic tests to establish or confirm a diagnosis.

I. Genetic testing to establish or confirm one of the following genetic kidney disorders to guide management is considered **medically necessary** when the member~~/enrollee~~

demonstrates clinical features* consistent with the disorder (the list is not meant to be comprehensive, see II below):

A. Alport Syndrome
B. C3 Glomerulopathy
C. Congenital nephrotic syndrome
D. Cystinosis
E. Cystinuria
F. Fabry Disease
G. Genetic (familial) atypical hemolytic-uremic syndrome (aHUS)
H. Primary Hyperoxaluria

II. Genetic testing to establish or confirm the diagnosis of all other kidney disorders not specifically discussed within this or another medical policy will be evaluated by the criteria outlined in *General Approach to Genetic and Molecular Testing* (see policy for criteria).

*Clinical features for a specific disorder may be outlined in resources such as GeneReviews, OMIM, National Library of Medicine, Genetics Home Reference, or other scholarly source.

back to top

DEFINITIONS

1. **Close relatives** include first, second, and third degree blood relatives on the same side of the family:
    a. **First-degree relatives** are parents, siblings, and children
    b. **Second-degree relatives** are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half siblings
    c. **Third-degree relatives** are great grandparents, great aunts, great uncles, great grandchildren, and first cousins

~~1. **Full siblings** are individuals who share the same biological parents.~~

back to top

BACKGROUND AND RATIONALE

Polycystic Kidney Disease ~~- Targeted Variant Analysis~~Panels

~~*Genetic Support Foundation*~~

~~The Genetic Support Foundation's Genetics 101 information on genetic testing says the following about testing for familial pathogenic variants:~~

> ~~Genetic testing for someone who may be at risk for an inherited disease is always easier if we know the specific genetic cause. Oftentimes, the best way to find the genetic cause is to start by testing someone in the family who is known or strongly suspected to have the disease. If their testing is positive, then we can say that we have found the familial pathogenic (harmful) variant. We can use this as a marker to test other members of the family to see who is also at risk.~~

GeneReviews: Polycystic Kidney Disease, Autosomal Dominant and Autosomal Recessive Polycystic Kidney Disease~~, Autosomal Recessive~~

~~GeneReviews is an expert-authored review of current literature on a genetic disease, and goes through a rigorous editing and peer review process before being published online.~~

~~Per GeneReviews, autosomal recessive polycystic kidney disease (ARPKD) is due to biallelic mutations in the~~ - *PKHD1* ~~gene. Testing is possible for siblings of an affected individual in whom both of the causative mutations are identified~~

~~Polycystic Kidney Disease - Single Gene or Multigene Panel~~

~~GeneReviews: Polycystic Kidney Disease, Autosomal Dominant and Polycystic Kidney Disease, Autosomal Recessive~~

GeneReviews is an expert-authored review of current literature on a genetic disease, and goes through a rigorous editing and peer review process before being published online.

The recommended polycystic kidney disease testing for autosomal dominant polycystic kidney disease (ADPKD) and autosomal recessive polycystic kidney disease (ARPKD) is as follows:

"ADPKD should be suspected in individuals with the following:

- Multiple bilateral renal cysts and the absence of manifestations suggestive of a different renal cystic disease
- Cysts in other organs, especially the liver, but also seminal vesicles, pancreas, and arachnoid membrane…
- Hypertension in an individual younger than age 35 years
- ~~An intracranial aneurysm…"~~

"Autosomal recessive polycystic kidney disease – PKHD1 (ARPKD-PKHD1) should be suspected in ~~individuals~~probands with ~~bilaterally enlarged, diffusely echogenic kidneys…[and] one or more of~~ the following~~:...Clinical/laboratory signs of congenital hepatic fibrosis (CHF) that leads~~ age-related clinical and ultrasonographic findings at presentation…:

Infantile presentation (age 4 weeks to ~~portal hypertension…"~~1 year)

~~"The renal diagnostic criteria for ARPKD detected by ultrasonography are:~~

- ~~Increased renal size~~Bilaterally enlarged kidneys (in relation to ~~normative size~~ age-, height-, or weight-based ~~on age and size of the affected individual);~~normal range) that usually retain their typical shape

  Note: (1) Bilaterally enlarged kidneys can be interspersed with macrocysts. (2) During later disease stages relative kidney length may decrease again.

- Increased echogenicity~~;~~…
- ~~Poor~~High-resolution ultrasonography may demonstrate innumerable very small cysts (rarely exceeding 1-2 mm) in the cortex and medulla.

Childhood/Young Adulthood Presentation (age >1 year)

- Imaging findings typically are the following:
  - Enlarged kidneys with multiple macrocysts, increased echogenicity, and reduced or absent corticomedullary differentiation~~"~~…"

~~"[In] Childhood and young adulthood…The hepatobiliary abnormalities with progressive portal hypertension are often the prominent presenting features."~~

Comprehensive Kidney Disease Panels

Hays et al (2020)

"We propose the following approach, based on a review of current literature and our practical experience. This approach assumes individuals have already undergone an initial nephrologic workup, including biochemical and serologic testing, imaging of the kidneys, and renal biopsy if indicated.

…[A]fter a negative or inconclusive initial workup, a patient is considered to have KDUE [kidney disease of unknown etiology] and may then be stratified according to the probability of a genetic disease. We consider higher probability patients as those with the following risk factors: early-onset disease (age <40 years), a positive family history of CKD [chronic kidney disease], consanguinity, extrarenal anomalies, cystic renal disease, or congenital nephropathy". (p. 594)

~~***APOL1* Mediated~~ *Kidney Disease: Improving Global Outcomes (KDIGO)*

KDIGO developed a Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease in 2024. The guideline states the following:

"Genetic testing is emerging as a valuable component for evaluation of cause. In some studies, >10% of people with CKD, regardless of family history, were observed to carry genetic pathogenic and likely pathogenic variant(s) that represent a plausible molecular cause for the development or progression of CKD. In some cases, identification of actionable genes through

genetic testing can impact the clinical management of people with CKD. A recent KDIGO Controversies Conference listed the following recommendations for when genetic testing can be particularly informative: (i) high prevalence of monogenic subtypes within the clinical category, (ii) early age of onset of CKD, (iii) syndromic/ multisystem features, (iv) consanguinity, (v) possibility of identifying a condition amenable to targeted treatment, and (vi) CKD/ kidney failure of unknown etiology when kidney biopsy would not be informative due to advanced disease." (p. S173)

Additionally, the guideline lists the following genes as examples for genetic testing evaluation: APOL1, COL4A3, COL4A4, COL4A5, NPHS1, UMOD, HNF1B, PKD1, PKD2. It goes on to say this is "evolving as a tool for diagnosis, increased utilization is expected. Recognition that genetic causes are more common and may present without classic family history". (p. S150)

APOL1 Targeted Variant Analysis

Freedman et al (2021)

A multidisciplinary group of experts and patient advocates performed a systematic review and created consensus-based guidelines in 2021 to guide health care providers in *APOL1*-associated neuropathy. The guidelines recommend the following:

"...*APOL1* testing should be considered in all patients of African ancestry with kidney disease and in any patient with kidney disease and a family member with a confirmed *APOL1* high-risk genotype." (p. 1768)

Regarding the definition of "high-risk phenotype": "Two copies of the *APOL1* variants (G1/G1, G1/G2, G2/G2) are commonly referred to as a 'high-risk' genotype…" (p. 1765)

Donor-Derived Cell-Free DNA for Kidney Transplant Rejection

~~*Knight et al (2019)*~~

~~A publication in the journal Transplantation~~ *Centers for Medicare and Medicaid Services*

The CMS local coverage determination (LCD) entitled "~~Donor-specific Cell-free DNA as a Biomarker in~~ MolDX: Molecular Testing for Solid Organ ~~Transplantation. A Systematic Review" stated~~Allograft Rejection" states the following~~:~~

~~In summary,~~ regarding donor-derived ~~cfDNA shows promise as a biomarker for the detection of acute transplant graft injury. It has potential to reduce the need for protocol biopsy surveillance, allowing for a more targeted diagnostic approach. Detection of injury occurs before clinical manifestation, meaning that there is a window for earlier detection and treatment of AR [acute rejection] and other causes of graft injury with the potential to improve outcomes. It may also~~

~~facilitate the detection of under immunosuppression and find use as a tool for monitoring during immunosuppression minimization. Further studies are required to validate the thresholds for further investigation and intervention, determine the optimum frequency for monitoring, and to identify whether prospective monitoring using dd-cfDNA can indeed improve transplant outcomes compared to current practice.~~cell-free DNA tests in individuals who have had solid organ transplantation: ~~(p. 280)~~

"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

The European Society of Organ Transplantation (ESOT, published in 2024) 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 a statement on donor derived cell-free DNA (dd-cfDNA) in 2023. At this time, there are no evidence-based screening recommendations for frequency of testing mentioned in this statement.

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.

back to top

Reviews, Revisions, and Approvals	Revision Date	Approval Date	Effective Date
Converted corporate to local policy.	09/23	11/27/23	
Semi-annual review. Updated title to reflect V1.2024 version. Overview, coding, reference-table, background and references updated. Throughout policy: replaced "coverage criteria" with "criteria. For Policy Reference Table; under Single gene of Multigene Panel: added "PreventionGenetics, part of Exact Sciences" throughout; added "APOL1-Mediated Kidney Disease…"; under Other Covered Kidney Disorders: added "81400, 81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408, 0268U".	12/23	2/27/24	
Semi-annual review. Updated title to reflect V2.2024 version. In *APOL-1* Targeted Variant Testing criteria, criteria set name changed (formerly "Targeted Variant Analysis"). Minor rewording for clarity throughout. Coding, reference-table, background and references updated.	06/24	8/19/24	9/19/24
Semi-annual review. Updated title to reflect 1.2025 version. Donor-Derived Cell-Free DNA for Kidney Transplant Rejection: Coverage status changed from non-covered to covered based on LCD and society guidelines; Added covered PLA codes to be consistent with LCD; Corrected minor typo in Policy Reference Table; Updated references. Comprehensive Kidney Disease Panels: Added the following criteria based on literature and new guidelines; *Syndromic/multisystem features; * There is a possibility of identifying a condition amenable to target treatment; Added new reference and support in Background and Rationale. Polycystic Kidney Disease - Targeted Variant Analysis: RETIRED; Tests for this condition will now be reviewed using the General policy. Polycystic Kidney Disease Panels: Removed the following criteria; - Intracranial aneurysm- Poor corticomedullary differentiation - Hepatobiliary abnormalities with progressive portal hypertension - Congenital hepatic fibrosis (CHF) with portal hypertension; Former criteria name: "PKD1, PKD2, GAANAB, DNAJB11, PKHD1 Sequencing and/or Deletion/Duplication Analysis or Multigene Panel Analysis"; Updated example tests, CPT codes, and common ICD codes in Policy Reference Table;	11/25		

Reviews, Revisions, and Approvals	Revision Date	Approval Date	Effective Date
Streamlined portions of Background and Rationale section for brevity; Updated references. Other Covered Kidney Disorders: Updated dates in references.			

REFERENCES

1. Harris PC, Torres VE. Polycystic Kidney Disease, Autosomal Dominant. 2002 Jan 10 [Updated 2022 Sep 29]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-~~2023~~2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1246/
2. ~~Sweeney WE, Avner ED.~~Burgmaier K, Gimpel C, Schaefer F, Liebau M. . Autosomal Recessive Polycystic Kidney Disease~~, Autosomal Recessive.~~ - *PKHD1* 2001 Jul 19 [Updated ~~2019 Feb 14~~2024 Apr 4]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-~~2023~~2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1326/
3. Hays T, Groopman EE, Gharavi AG. Genetic testing for kidney disease of unknown etiology. Kidney Int. 2020;98(3):590-600. doi:10.1016/j.kint.2020.03.031
4. Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-~~2023~~2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1116/
5. Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD). World Wide Web URL: https://omim.org/
6. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US). Available from: https://medlineplus.gov/genetics/.
1. ~~Knight SR, Thorne A, Lo Faro ML. Donor-specific cell-free DNA as a biomarker in solid organ transplantation. A systematic review. *Transplantation*. 2019;103(2):273-283.~~
2. ~~Genetic Support Foundation. Genetics 101 Genetic Testing: Familial Pathogenic Variant. Accessed 10/4/2022. https://geneticsupportfoundation.org/genetics-101/#~~
7. Freedman BI, Burke W, Divers J, et al. Diagnosis, education, and care of patients with APOL1-associated nephropathy: a Delphi consensus and systematic review. JASN. 2021;32(7):1765-1778.

8. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International (2024). Volume 105 (Suppl 4S), S117–S314. https://kdigo.org/wp-content/uploads/2024/03/KDIGO-2024-CKD-Guideline.pdf
9. Centers for Medicare & Medicaid Services. Medicare Coverage Database: Local Coverage Determination. MolDX: Molecular Testing for Solid Organ Allograft Rejection (L38582). Available at: https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=38582

10. Park S, Sellares J, Tinel C, Anglicheau D, Bestard O, Friedewald JJ. European Society of Organ Transplantation Consensus Statement on Testing for Non-Invasive Diagnosis of Kidney Allograft Rejection. *Transpl Int*. 2024;36:12115. Published 2024 Jan 4. doi:10.3389/ti.2023.12115
11. ASTS Statement on donor derived cell-free DNA (dd-cfDNA), ASTS.org, Approved March 6, 2023.https://asts.org/docs/default-source/position-statements/dd-cfdna-position-statement.pdf

~~back to top~~

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of member/enrollees. This clinical policy is not intended to recommend treatment for member/enrollees. Member/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.

This clinical policy is the property of LHCC. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, member/enrollees, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, member/enrollees and their representatives agree to be bound by such terms and conditions by providing services to member/enrollees and/or submitting claims for payment for such services.

back to top