Medica Central Coverage Policy

Policy Name:	**Genetic Testing - Specialty Testing: Nephrology**
Effective Date:	**01/01/2026**

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.

OVERVIEW

This policy addresses the use of tests for known or suspected kidney disorders, including testing of asymptomatic potential living donors.

For additional information see the Rationale and References 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. Please see the Concert Platform for additional registered tests.

POLICY REFERENCE TABLE

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
Polycystic Kidney Disease			
Polycystic Kidney Disease Panels	Hereditary Cystic Kidney Diseases Panel (PreventionGenetics, part of Exact Sciences)	81403, 81404, 81405, 81406, 81407, 81408, 81479, N18, Q61	Rationale/ References
	Polycystic Kidney Disease Panel (GeneDx)		

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
Comprehensive Kidney Disease Panels			
Comprehensive Kidney Disease Panels	KidneySeq Version 5 Comprehensive Testing (Iowa Institute of Human Genetics)	81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408, 81479, N00-N08, N10-N19, Q61, R31	Rationale/ References
	RenaSight (Natera)		
	RenalZoom (DNA Diagnostic Laboratory - Johns Hopkins Hospital)		
***APOL1*-Mediated Kidney Disease**			
APOL1-Targeted Variant Analysis	Apolipoprotein L1 (APOL1) Renal Risk Variant Genotyping - 0355U (Quest Diagnostics)	81479, 0355U, N00-N08, N10-N19	Rationale/ References
	APOL1 Genotype, Varies (Mayo Clinic Laboratories)		
Other Covered Kidney Disorders			
Other Covered Kidney Disorders	See list below	81400, 81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408, 0268U	Additional References

RELATED POLICIES

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

- ***Specialty Testing: Multisystem Genetic Conditions*** for coverage criteria related to diagnostic tests for genetic disorders that affect multiple organ systems (e.g., whole exome and genome sequencing, chromosomal microarray, and multigene panels for broad phenotypes).
- ***Oncology Testing: Hereditary Cancer Susceptibility*** for coverage criteria related to von Hippel Lindau (VHL) syndrome and other hereditary cancer syndromes.
- ***Specialty Testing: Hematology*** for coverage criteria related to diagnostic tests for benign (non-cancerous) hematologic conditions including sickle cell disease, inherited anemias, and hemophilias.
- ***General Approach to Laboratory Testing*** for coverage criteria related to nephrology, including known familial variant testing, that is not specifically discussed in this or another non-general policy.

back to top

COVERAGE CRITERIA

POLYCYSTIC KIDNEY DISEASE

Polycystic Kidney Disease Panels

I. Genetic testing using a polycystic kidney disease panel to confirm or establish a diagnosis of polycystic kidney disease (PKD) is considered **medically necessary** when:

   A. The member has any of the following clinical features of PKD:

      1. Kidney cysts, **OR**

      2. Cysts in organs other than the kidneys (especially the liver, seminal vesicles, pancreas, and arachnoid membrane), **OR**

      3. Bilaterally enlarged and diffusely echogenic kidneys.

II. Genetic testing using polycystic kidney disease panels to confirm or establish a diagnosis of polycystic kidney disease (PKD) is considered **investigational** for all other indications.

view rationale

back to top

COMPREHENSIVE KIDNEY DISEASE PANELS

Comprehensive Kidney Disease Panels

I. Genetic testing for kidney disease via a comprehensive kidney disease panel is considered **medically necessary** when:

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

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

         a) Onset of chronic kidney disease under 50 years of age, **OR**

         b) One or more first-degree relatives with chronic kidney disease, **OR**

         c) Consanguineous family history, **OR**

         d) Cystic renal disease, **OR**

         e) Congenital nephropathy, **OR**

         f) Syndromic/multisystem features, **OR**

         g) There is a possibility of identifying a condition amenable to targeted treatment, **OR**

         h) The member is being wait-listed for kidney transplant, **AND**

            (1) A close relative is considering kidney donation to the member, **OR**

   B. The member is asymptomatic, **AND**

1. The member is being considered as a kidney donor, **AND**
2. The member has at least one first-degree relative with kidney disease suggestive of autosomal dominant or X-linked inheritance, **AND**
3. No causative mutation has been established yet for the kidney disease seen in the family.

II. Genetic testing for kidney disease via a comprehensive kidney disease panel is considered **investigational** for all other indications.

view rationale

back to top

APOL1-MEDIATED KIDNEY DISEASE

***APOL1*-Targeted Variant Analysis**

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

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

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

1. The member is of African ancestry, **OR**
2. The member has a close relative 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) is considered **investigational** for all other indications.

view rationale

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 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 Laboratory Testing* (see policy for coverage criteria).

NOTE: 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

RATIONALE AND REFERENCES

Polycystic Kidney Disease Panels

Kidney Disease: Improving Global Outcomes (KDIGO)

KDIGO developed a Clinical Practice Guideline for the Evaluation, Management, and Treatment of Autosomal Dominant Polycystic Kidney Disease (ADPKD) with collaborators and representatives from multiple US-based institutions. Figure 2, Chapter 1 (p. 4) supports genetic testing for ADPKD in individuals with a positive family history of the condition for the following scenarios:

1. Equivocal or atypical features on ultrasound
2. Atypical extra-renal features
3. When prognostic information is requested following an ultrasound diagnostic for ADPKD
4. When the patient's presentation is very different from the familial phenotype

Figure 3, Chapter 1 (p. 5) addresses genetic testing for ADPKD in individuals without a family history of the condition (ie, incidentally detected kidney or liver cysts on ultrasound, MRI, or CT). The guideline includes genetic testing as part of the diagnostic algorithm in the following scenarios:

1. An atypical or mild presentation leading to an uncertain ADPKD diagnosis
2. A presentation consistent with a clinical ADPKD diagnosis

Torres VE, Ahn C, Barten TRM, et al. KDIGO 2025 clinical practice guideline for the evaluation, management, and treatment of autosomal dominant polycystic kidney disease (ADPKD): executive summary. Kidney Int. 2025;107(2):234-254. doi:https://doi.org/10.1016/j.kint.2024.07.010

GeneReviews: Autosomal Recessive Polycystic Kidney Disease - PKHD1

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 e autosomal recessive polycystic kidney disease (ARPKD) is as follows:

"Autosomal recessive polycystic kidney disease – PKHD1 (ARPKD-PKHD1) should be suspected in probands with the following age-related clinical and ultrasonographic findings at presentation…:

Infantile presentation (age 4 weeks to 1 year)

- Bilaterally enlarged kidneys (in relation to age-, height-, or weight-based 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…
- 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…"

Burgmaier K, Gimpel C, Schaefer F, Liebau M. Autosomal Recessive Polycystic Kidney Disease - *PKHD1* 2001 Jul 19 [Updated 2024 Apr 4]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1326/

back to top

Comprehensive Kidney Disease Panels

Hays, et al.

"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).

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

Kidney Disease: Improving Global Outcomes (KDIGO)

KDIGO developed a Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease in 2024. Section 1.1.4 discusses evaluating the cause of chronic kidney disease (CKD) and recommends genetic testing as an important component of this evaluation. Per this guideline, testing has identified pathogenic or likely pathogenic variants in more than 10% of individuals, and results may impact medical management (p. S173).

The following are recommendations from the guideline for when genetic testing can be particularly informative:

1. High prevalence of monogenic subtypes within the clinical category
2. Early age of onset of CKD
3. Syndromic/ multisystem features
4. Consanguinity
5. Possibility of identifying a condition amenable to targeted treatment
6. 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 to include in genetic testing evaluation: *APOL1, COL4A3, COL4A4, COL4A5, NPHS1, UMOD, HNF1B, PKD1, PKD2.* The comment in Table 6 of the guidelines says that genetic testing 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).

KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International. 2024;105(Suppl 4S):S117–S314. https://kdigo.org/wp-content/uploads/2024/03/KDIGO-2024-CKD-Guideline.pdf

National Kidney Foundation (NKF)

The National Kidney Foundation (NKF) developed multiple recommendations for Advancing Genetic Testing in Kidney Disease based on working group consensus. An Algorithm was created (Figure 2, Table 2) for decision-making for genetic testing in symptomatic individuals. The specific recommendations for genetic testing include:

- Family history of CKD (refers to first-degree relatives only, unless there is evidence of autosomal recessive of X-linked inheritance in the family)
- Multi-organ syndrome of unknown etiology
- Atypical clinical disease, to guide therapeutics…
- Kidney biopsy findings suggestive of a genetic cause…
- CKD/ESKD of unknown etiology after a comprehensive clinical evaluation if any of the following are true:
    - Age <50
    - The patient is being wait listed for kidney transplant and their blood relative is considering kidney donation
    - Diagnosis may aid in management of extra-renal manifestation
- Evaluation of patients with atypical cystic kidney or liver disease and no family history

Several recommendations were also made for at-risk relatives, including the following:

- Living donors unrelated to the recipients should undergo genetic testing if they have significant family history (CKD of unknown etiology or early-onset CKD, cystic kidney disease, congenital disease with extrarenal signs, aHUS) (p. 8)

The NKF Algorithm also recommends large multi-disease kidney panel testing (p. 8).

Franceschini N, Feldman DL, Berg JS, et al. Advancing Genetic Testing in Kidney Diseases: Report From a National Kidney Foundation Working Group. Am J Kidney Dis. 2024;84(6):751-766. doi:10.1053/j.ajkd.2024.05.010

back to top

APOL1-Targeted Variant Analysis

Freedman, et al.

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).

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. doi:10.1681/ASN.2020101399

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

back to top

ADDITIONAL REFERENCES

1. Seattle (WA): University of Washington, Seattle; 1993-2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1116/
2. Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD). World Wide Web URL: https://omim.org/
3. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US). Available from: https://medlineplus.gov/genetics/.

back to top

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.

	Committee/Source	Date(s)
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