Revision log
Coding_Implications

CONCERT GENETIC TESTING: NEPHROLOGY

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 section.

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 2024, 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. 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, 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.

CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	REF
Polycystic Kidney Disease			

Polycystic Kidney Disease Panels	Hereditary Cystic Kidney Diseases Panel (PreventionGenetics, part of Exact Sciences) Polycystic Kidney Disease Panel (GeneDx)	81404, 81405, 81406, 81407, 81408, 81479, N18, Q61	1, 9
Comprehensive Kidney Disease Panels			
Comprehensive Kidney Disease Panels	KidneySeq Version 5 Comprehensive Testing (Iowa Institute of Human Genetics) RenaSight (Natera) RenalZoom (DNA Diagnostic Laboratory - Johns Hopkins Hospital)	81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408, 81479, N00-N08, N10-N19, Q61, R31	2, 7, 8
***APOL1*-Mediated Kidney Disease**			
APOL1-Targeted Variant Analysis	Apolipoprotein L1 (APOL1) Renal Risk Variant Genotyping - 0355U (Quest Diagnostics) APOL1 Genotype, Varies (Mayo Clinic Laboratories)	0355U, 81479, N00-N08, N10-N19	6
Other Covered Kidney Disorders			
Other Covered Kidney Disorders	See list below	81400, 81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408	3, 4, 5

RELATED POLICIES

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

- ***Specialty Testing: Multisystem Genetic Conditions*** for 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 criteria related to von Hippel Lindau (VHL) syndrome and other hereditary cancer syndromes.
- ***Specialty Testing: Hematology*** for 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 criteria related to nephrology, including known familial variant testing, that is not specifically discussed in this or another non-general policy.

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CRITERIA

It is the policy of health plans affiliated with Centene Corporation® that the specific genetic testing noted below is **medically necessary** when meeting the related 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/enrollee 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. Current evidence does not support genetic testing using polycystic kidney disease panels to confirm or establish a diagnosis of polycystic kidney disease (PKD) for all other indications.

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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/enrollee 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/enrollee 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/enrollee is being wait-listed for kidney transplant, **AND**

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

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

1. The member/enrollee is being considered as a kidney donor, **AND**
2. The member/enrollee 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. Current evidence does not support genetic testing for kidney disease via a comprehensive kidney disease panel for all other indications.

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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/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 close relative with a confirmed *APOL1* high-risk genotype (i.e., G1/G1, G1/G2, or G2/G2).

II. Current evidence does not support targeted variant analysis for the *APOL1* high-risk genotype (i.e., G1/G1, G1/G2, or G2/G2) for all other indications.

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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 Laboratory Testing* (see policy for 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.

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RATIONALE

Polycystic Kidney Disease Panels

Kidney Disease: Improving Global Outcomes (2025)

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

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…"

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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).

Kidney Disease: Improving Global Outcomes (KDIGO) (2024)

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:

3. High prevalence of monogenic subtypes within the clinical category
4. Early age of onset of CKD
5. Syndromic/ multisystem features
6. Consanguinity
7. Possibility of identifying a condition amenable to targeted treatment
8. 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).

National Kidney Foundation (2024)

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).

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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).

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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

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Reviews, Revisions, and Approvals	Revision Date	Approval Date
Policy developed.	03/23	03/23
Semi-annual review. Updated title to reflect V1.2024 version. Overview, coding, reference-table, background and references updated. Throughout policy: replaced	10/23	10/23

Reviews, Revisions, and Approvals	Revision Date	Approval Date
"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".		
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.	04/24	04/24
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; Streamlined portions of Background and Rationale section for brevity; Updated references. Other Covered Kidney Disorders: Updated dates in references.	11/24	11/24
Annual review. Policy name changed from "Concert Genetic Testing: Kidney Disorders" to "Concert Genetic Testing: Nephrology." Polycystic Kidney Disease Panels criteria: The criterion "Hypertension in an individual younger than age 35" was removed; minor update to criterion A.1 based on a recent KDIGO guideline; the phrase "Multiple bilateral renal" was removed and replaced with "Kidney" to capture the variety of imaging findings that could lead to genetic testing. Changed "investigational" policy statements to state "current evidence does not support…" References, rationale, background, and coding updated.	11/25	12/25

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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. The Health Plan

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. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

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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.

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conditions by providing services to member/enrollees and/or submitting claims for payment for such services.

Note: For Medicaid member/enrollees, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare member/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs and LCDs and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.