

Clinical Policy: Genetic and Pharmacogenetic Testing

Reference Number: CP.MP.89

Last Review Date: 03/20

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

This policy includes criteria for making medical necessity determinations for genetic tests when specific criteria are not available for the requested genetic or pharmacogenetic test. Genetic testing is the analysis of human DNA, RNA, or chromosomes in order to detect heritable disease-related genotypes, mutations, phenotypes, or karyotypes for clinical purposes. Such purposes include predicting risk of disease, identifying carriers, and establishing prenatal and clinical diagnosis or prognosis. There are currently more than 1000 genetic disorders for which genetic testing is available on a clinical or research basis. A pharmacogenetic test is a specific type of genetic test that is performed in order to predict which patients are at risk for adverse medication reactions and/or lack of efficacy. These test results are used to guide drug therapy decisions.

Note: This policy should only be used if there is no specific clinical decision support criteria available for the requested genetic test.

Policy/Criteria

- I. It is the policy of health plans affiliated with Centene Corporation® that genetic testing is **medically necessary** when *all* the following criteria are met:
 - A. The member displays clinical features, or is at direct risk of inheriting the mutation in question, *and*
 - B. The test results will be used to develop a clinically useful approach or course of treatment, or to cease unnecessary monitoring or treatments for the individual being tested. Clinically useful test results allow providers to do at least one of the following:
 1. Inform interventions that could prevent or delay disease onset,
 2. Detect disease at an earlier stage when treatment is more effective,
 3. Manage the treatable progression of an established disease,
 4. Treat current symptoms significantly affecting a member's health,
 5. Guide decision making for the member's current or planned pregnancy; *and*
 - C. The genetic disorder could not be diagnosed through completion of conventional diagnostic studies, pedigree analysis and genetic counseling consistent with the community standards;
 - D. The member has not previously undergone genetic testing for the disorder, unless significant changes in testing technology or treatments indicate that test results or outcomes may change due to repeat testing;
 - E. Technical and clinical performance of the genetic test is supported by published peer-reviewed medical literature.

- II. It is the policy of health plans affiliated with Centene Corporation® that *pharmacogenetic testing* is **medically necessary** when all the following criteria are met:
 - A. Targeted drug therapy is reasonable and necessary for the treatment of the diagnosis;
 - B. Targeted drug therapy is associated with a specific gene biomarker or mutation;

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- C. The test results will be used to guide drug therapy decisions (e.g., drug choice, dose, evaluate adverse effects or non-responsiveness);
- D. Previous pharmacogenetic testing has not been done for the gene biomarker or mutation, unless significant changes in testing technology or treatments indicate that test results or outcomes may change due to repeat testing;
- E. Technical and clinical performance of the genetic test is supported by published peer-reviewed medical literature.

Note: All requests for genetic or pharmacogenetic testing reviewed under this policy require medical director review.

Note: When using testing panels, including but not limited to, multiple genes or multiple conditions, and in cases where a tiered approach/method is clinically available, testing would be covered ONLY for the number of genes or tests deemed medically necessary to establish a diagnosis.

III. It is the policy of health plans affiliated with Centene Corporation that all other requests for *genetic or pharmacogenetic testing* not meeting the above stated criteria, including direct-to-consumer testing and genetic banking/DNA storage, are considered **not medically necessary**.

Authorization Protocol

Requests for prior authorization will be accepted up to 10 business days following specimen collection and will be reviewed for medical necessity based on the above stated criteria.

Testing in Children

Testing in children should take into account the availability of evidenced based risk reduction strategies and the probability of developing a serious medical condition during childhood. Unless there is a clinical intervention appropriate in childhood, parents should be encouraged to defer genetic testing for adult-onset conditions until adulthood. Advocating for the best interests of the child is necessary until he/she is able to make the personal choice to have genetic testing.⁵

Background

Genetic testing identifies changes in chromosomes, genes or proteins. Genetic testing results can confirm or rule out a suspected genetic condition or can help determine a person's chance of developing or passing on a genetic disorder. Test results can direct a person towards appropriate prevention, monitoring and treatment options. There are three methods used for genetic tests: gene tests, chromosomal tests and biochemical tests. Gene tests look at DNA or RNA taken from blood or body fluids such as saliva or other tissue. These tests can look for large changes, such as missing or added sections of a gene, or small changes, such as a missing, added, or altered chemical base within a DNA strand. They can also detect genes with too many copies, those that are too active, turned off, or lost entirely. Genes can be tested using DNA probes or rely on DNA or RNA sequencing.

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Chromosomal tests look at features of chromosomes for changes such as pieces being deleted, expanded, or switched to a different chromosomal location. There are two types of chromosomal tests, karyotype and FISH (florescent *in situ* hybridization) analysis. A karyotype test gives a picture of all of a person's chromosomes and can identify changes in chromosome number and large changes in DNA structure. FISH analysis can identify irregularities in certain regions of chromosomes using fluorescent DNA probes. Additionally, FISH analysis can identify small changes that can be missed by overall karyotype testing.

Biochemical tests measure the amount or activity of proteins or particular enzymes. Genes contain the DNA code for making proteins. An abnormal amount or activity of proteins can indicate that genes are not working normally. These tests are most commonly used for newborn screening to detect conditions such as phenylketonuria (PKU).

Pharmacogenetic testing is available for a limited number of drug classes and may enable physicians to understand why patients respond differently to various drugs and to make better decisions about therapy.

Pharmacogenomic influences on drug response have traditionally been divided into four categories based upon the impact of genetic variability on the pharmacologic properties of a drug:

- Effect on drug pharmacokinetics, which may include the drug's absorption, distribution, metabolism, and/or elimination;
- Effects on pharmacodynamics (the therapeutic response of a target, often a receptor, to the drug);
- Effect on idiosyncratic reactions (eg, increased frequency of allergic reactions in individuals with certain genotypes);
- Effect on disease pathogenesis, which in turn may make the disease more or less responsive to a specific therapy.⁹

Pharmacogenomic information is currently contained in about 10 percent of labels for drugs approved by the FDA, however, just a few include labeling specifically requiring or recommending testing of genetic biomarkers prior to instituting therapy (e.g., Maraviroc, Abacavir, Cetuximab, etc). An updated listing of pharmacogenetic biomarkers cited in drug labels in the United States is available on the FDA website. Other resources include the Pharmacogenomics Knowledge Base hosted by the National Institute of General Medical Sciences of the National Institutes of Health and the Clinical Pharmacogenetics Implementation Consortium.

Despite the labeling changes implemented by the FDA and the increasing number of pharmacogenetic studies in the published literature, integration of pharmacogenetic testing into clinical care has been slow, and many of the tests recommended by the FDA for individual drugs are not in routine use.⁹ Limitations to testing include, but are not limited to, study design limitations, regulatory and ethical concerns, lack of cost effectiveness analyses, lack of available pharmacogenetic tests and guidelines for test implementation, lack of education regarding pharmacogenetic testing, and potential for delay in therapy while awaiting results of genotyping.

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Per the FDA, there are some FDA-approved drug and genetic test labels, and labels of FDA-cleared genetic tests that provide general information about the impact of DNA variations on drug levels, but do not describe how that genetic information can be used for determining therapeutic treatment. These labels are intended to be informational, but do not indicate that there is evidence to support making treatment decisions based on the information provided by the genetic test. Information regarding therapeutic treatment recommendations for patients with certain genetic variations can be found in the warnings (Boxed Warning, or Warnings and Precautions), Indications and usage, Dosage and Administration, or Use in Specific Populations sections of the FDA approved drug labeling, as appropriate.¹¹

Reviews, Revisions, and Approvals	Date	Approval Date
Policy developed and approved	11/13	11/13
Updated genetic testing description Removed adequately interpreted from criteria Clarified use of results criteria point to point out ‘clinically useful’ testing	01/15	02/15
Added for “the member’s current or planned” pregnancy to policy/criteria section B	06/15	06/15
Converted to new template. Added “to inform interventions that could prevent or delay disease onset, to detect disease at an earlier stage when treatment is more effective” to criteria. Added recommendation that unless there is an intervention appropriate in childhood, parents defer genetic testing for adult onset conditions until adulthood per ASHG guidelines.	06/16	06/16
References reviewed and updated. Added the following note: “When using testing panels, including but not limited to, multiple genes or multiple conditions, and in cases where a tiered approach/method is clinically available, testing would be covered ONLY for the number of genes or tests deemed medically necessary to establish a diagnosis.”	06/17	06/17
References reviewed and updated. Added I.D: member has not previously undergone genetic testing for the disorder. Added statement that direct-to-consumer genetic testing is not medically necessary.	04/18	04/18
References reviewed and updated. Specialist reviewed.	03/19	04/19
Changed period in which authorizations can be requested from 5 days post-service to 10 days.	05/19	
Added note that this criteria should only be used if there is no specific clinical decision support criteria available.	07/19	
Added note that all genetic testing requests reviewed under this policy will require medical director review.	09/19	
Added that technical and clinical performance of the genetic test is supported by published peer-reviewed medical literature.	11/19	11/19
Added general criteria for pharmacogenetic testing. Updated background on pharmacogenetic testing. Changed title to reflect pharmacogenetic criteria. References reviewed and updated.	03/20	03/20

References

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4. Next-Gen Sequencing: Expanded genetic testing the real world. Medscape. Sept 15, 2014.
5. The American Society of Human Genetics Board of Directors and the American College of Medical Genetics Board of Directors. “Points to Consider: Ethical, Legal, and Psychosocial Implications of Genetic Testing in Children and Adolescents. “Am J Hum Genet. 2015.97(1); 6-21. Accessed Mar 03, 2020 at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4570999/pdf/main.pdf>
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8. American College of Obstetricians and Gynecologists. Counseling About Genetic Testing and Communication of Genetic Test Results. Committee Opinion. Number 693. April 2017. Reaffirmed 2019
9. Tantisira K, Weiss ST. Overview of pharmacogenomics. In: UpToDate. Raby BA (Ed), UpToDate, Waltham, MA. Accessed Feb. 27, 2020
10. Clinical Pharmacogenetics Implementation Consortium. Guidelines. Available at: <https://cpicpgx.org/guidelines/>
11. U.S. Food and Drug Administration. Safety Communication. The FDA Warns Against the use of Many Genetic Tests with Unapproved Claims to Predict Patient Response to Specific Medications: FDA Safety Communication. October 31, 2018. Accessed 3/2/20: <https://www.fda.gov/medical-devices/safety-communications/fda-warns-against-use-many-genetic-tests-unapproved-claims-predict-patient-response-specific>
12. U.S. Food and Drug Administration. Table of pharmacogenomic biomarkers in drug labels. Content current as of 2/05/20. Accessed 3/2/20: <https://www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling>

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.

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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.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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 members. This clinical policy is not intended to recommend treatment for members. Members 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 the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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

Note: For Medicaid members, 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 members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, 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.

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