Clinical Policy: Genetic and Pharmacogenetic Testing

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

Policy/Criteria

I. It is the policy of Louisiana Healthcare Connections 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 Louisiana Healthcare Connections 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;
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.

III. It is the policy of Louisiana Healthcare Connections 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.

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.

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. 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	Review Date	Approval Date
Converted corporate to local policy.	08/15/2020	
References reviewed and updated. Removed section on authorization protocol. Combined criteria notes into one notes section before criteria.	10/1021	

References

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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. 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.

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