Clinical Use Guidelines

Genetic Testing to Diagnose Non-Cancer Conditions

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Description

Diagnostic testing is performed in patients with clinical signs or symptoms of a non-cancer genetic condition. The genetic test may confirm or rule out a clinical diagnosis. In some cases, genetic testing is the gold standard for making a diagnosis based on evidence- or consensus-based guidelines. In others, it may be used to confirm a clinical diagnosis, offer prognostic information that impacts management, rule out a diagnosis in the differential, or confirm a positive newborn screening result. Often, diagnostic testing of an affected individual will offer results that are relevant to the testing of other family members.

- **This guideline does not include risk assessment or predictive testing for at-risk, asymptomatic individuals. Please refer to *Genetic Testing to Predict Disease Risk* for that purpose.**
- **Diagnostic testing of a pregnancy or an embryo is addressed by guidelines on *Genetic Testing for Prenatal Screening and Diagnostic Testing* and *Preimplantation Genetic Screening and Diagnosis*, respectively.**
- **In addition, testing for hereditary cancer syndromes is addressed separately under *Genetic Testing for Cancer Susceptibility and Hereditary Cancer Syndromes*.**

Criteria

Criteria: General Coverage Guidance

Individuals may be considered for diagnostic genetic testing when ALL of the following conditions are met:

- **Clinical signs and symptoms in the individual are consistent with the diagnosis in question.**
- **Technical and clinical validity: The test must be accurate, sensitive and specific, based on sufficient, quality scientific evidence to support the claims of the test.**
- **Clinical utility: Healthcare providers can use the test results to provide significantly better medical care for the individual.**

- **Reasonable use: The usefulness of the test is not significantly offset by negative factors, such as expense, clinical risk, or social or ethical challenges.**

Limits:

- **Testing will be considered only for the number of genes or tests necessary to establish mutation status. A tiered approach to testing, with reflex to more detailed testing and/or different genes, will be required when clinically possible.**
- **Diagnostic genetic testing will be allowed once per lifetime per condition. Exceptions may be considered if technical advances in testing demonstrate significant advantages that would support a medical need to retest.**

Criteria: Special Circumstances

Diagnostic testing of an individual to inform reproductive planning and testing for parents or testing for siblings

Diagnostic genetic testing may be requested in a symptomatic individual with a known genetic condition. While diagnostic testing may not impact management of the affected individual, the information gained from genetic testing may be needed to perform accurate carrier testing in the parent(s), genetic diagnosis in a pregnancy, or genetic diagnosis in a sibling.*

In these diagnostic genetic testing in a symptomatic individual may be considered when ALL of the following conditions are met:

- **The diagnosis of the disease in the affected individual is certain or highly probable based on clinical signs and symptoms, history, imaging, and/or results of other laboratory testing.**
- **The results of the genetic test in the symptomatic individual must be required in order to perform accurate carrier testing in the parent(s), genetic diagnosis in a pregnancy, or genetic diagnosis in a sibling.**
- **Technical and clinical validity: The test must be accurate, sensitive and specific, based on sufficient, quality scientific evidence to support the claims of the test.**
- **Clinical utility: Healthcare providers can use the test results to provide informative genetic testing for the sibling, parents, or for a current or future at-risk pregnancy.**
- **Reasonable use: The usefulness of the test is not significantly offset by negative factors, such as expense, clinical risk, or social or ethical challenges.**

Limits:

- **Testing will be indicated only for the number of genes or tests necessary to establish the familial mutation(s). A tiered approach to testing, with reflex to more detailed testing and/or different genes, will be required when clinically possible.**
- **Diagnostic genetic testing will be allowed once per lifetime per condition. Exceptions may be considered if technical advances in testing demonstrate significant advantages that would support a medical need to retest.**

***Parent or sibling must also be a covered member under the same health plan.**

Diagnostic testing of an individual to confirm newborn screening results

Newborn Screening (NBS) is state-mandated testing performed in the first days of life, using blood spots obtained from a heel stick. Biochemical studies are used, and often supplemented with molecular analysis, in order to screen for a number of different disorders. The goal of NBS is to identify affected infants before they become symptomatic, since these disorders may cause significant morbidity or mortality unless treatment is initiated in the neonatal period. Diagnostic genetic testing may be requested for infants with positive, borderline, or inconclusive results. The American College of Medical Genetics and Genomics (ACMG) ACT Algorithms contain an overview of the steps involved in determining a final diagnosis, and can be found here.

Diagnostic genetic testing in an individual for the purposes of confirming newborn screening results may be considered when the following conditions are met:

- **The individual has had a newborn screening result that is positive, borderline, or inconclusive for a specific disorder for which confirmatory genetic testing is required, AND**
- **The requested testing has not been previously performed, AND**
- **The member will benefit from information provided by the requested gene testing based on at least one of the following:**
  - **All criteria are met from a test-specific guideline, if one is available, or**
  - **The ACMG ACT Algorithm associated with the suspected disorder includes genetic testing, and all preliminary studies recommended in the algorithm have been completed (however, the genetic test must not simply be listed as "optional", or as an intervention that may be considered), or**
  - **There is uncertainty in the diagnosis, despite further evaluation by an appropriate provider, and genetic testing is needed to clarify the diagnosis, or**
  - **An individual has a confirmed biochemical diagnosis of the disorder for which testing is requested, but healthcare providers can use the**

genetic test results to directly impact medical care for the individual (e.g. change in surveillance or treatment plan).

Limits:

- **Testing will be indicated only for the number of genes or tests necessary to establish the diagnosis. A tiered approach to testing, with reflex to more detailed testing and/or different genes, will be required when clinically possible.**
- **Diagnostic genetic testing will be allowed once per lifetime per condition. Exceptions may be considered if technical advances in testing demonstrate significant advantages that would support a medical need to retest.**

Criteria: Test-specific Guidelines

Test-specific guidelines are available for some tests designed to diagnosis non-cancer conditions.