



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Genetic Disease Screening Panels

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INSTRUCTIONS FOR USE

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Coverage Policy

CIGNA does not cover genetic testing for heritable disorders in the general population, including genetic disease screening panels such as the Ashkenazi Jewish Panel, because such screening for multiple conditions is considered not medically necessary or of unproven benefit.

CIGNA covers genetic testing for specific diseases and disorders as medically necessary when established criteria for that specific genetically transmitted disease are met. For specific criteria, please refer to the related disease specific Coverage Policies.

General Background

The National Institutes of Health Task Force on Genetic Testing (Holtzman, et al., 2006) defines a genetic test as the “analysis of human deoxyribonucleic acid (DNA), ribonucleic acid (RNA), chromosomes, proteins, and certain metabolites in order to detect heritable disease-related genotypes, mutations, phenotypes, or karyotypes for clinical purposes. Such purposes include predicting risk of disease, identifying carriers, establishing prenatal and clinical diagnosis or prognosis. Prenatal, newborn, and carrier screening, as well as testing in high-risk families, are included. Tests for metabolites are covered only when they are undertaken with high probability that an excess or deficiency of the metabolite indicates the presence of heritable mutations in single genes. Tests conducted purely for research are excluded from the definition, as are tests for somatic (as opposed to heritable) mutations, and testing for forensic purposes”.

Some but not all predictive genetic testing falls under genetic screening. The Task Force defines genetic screening as a “search in a population for persons possessing certain genotypes that (1) are already associated with disease or predisposed to disease, (2) may lead to disease in their descendants, or (3) produce other variations not known to be associated with disease. Although genetic screening typically uses the same assays as those used for genetic testing, it is distinguished from testing by its target population. Under this definition, testing an asymptomatic person in a family with several relatives affected with disease does not constitute screening but predictive genetic testing instead” (Holtzman, et al., 2006).

Despite progress, much remains unknown about the risks and benefits of genetic testing including: the lack of effective interventions available to improve the outcome of most inherited diseases; negative (normal) test results might not rule out future occurrence of disease; and/or positive test results might not mean the disease will inevitably develop. Genetic screening tests should have a high positive predictive value and should provide information that can result in either disease prevention or a useful clinical therapeutic intervention (Holtzman, et al., 2006).

Certain ethnic groups are at an increased risk for particular genetic diseases (e.g., Eastern European Ashkenazi Jewish individuals). Some laboratories are presently offering genetic testing to determine carrier status for many different diseases in one panel. The number and type of genetic diseases offered per panel varies. An example of one of these panels is an Ashkenazi Jewish screening panel. Some of the diseases that may be included in this panel are briefly described below. In most diseases, a negative carrier test decreases the likelihood that a person is a carrier but cannot completely eliminate the possibility (Klugman and Gross, 2010; American College of Obstetricians and Gynecologists [ACOG], 2009; American College of Medical Genetics [ACMG], 2008a).

Diseases Suggested for Ashkenazi Screening Panel

Bloom Syndrome: Bloom syndrome is a condition characterized by severe pre- and postnatal growth deficiency, skin sensitivity to sunlight, and immunodeficiencies. Individuals with Bloom syndrome are predisposed to develop common cancers such as breast cancer, colon cancer, and leukemia. The carrier frequency in the Ashkenazi Jewish population is approximately one in 107. Testing for one common mutation allows for a carrier detection rate that is greater than 95%.

Canavan Disease: Canavan disease, typically fatal in childhood, is a progressive disease of the central nervous system for which there is no treatment. The carrier frequency in the Ashkenazi Jewish population is about one in 40. Testing involves analysis of common mutations in the aspartoacylase (ASPA) gene, and the detection rate is about 95%.

Cystic Fibrosis (CF): CF is a chronic, progressive, genetic disease in which defective chloride transport across cell membranes causes dehydrated secretions and leads to thick, tenacious mucus in multiple organs. CF is found in all ethnic groups. It is most common among Caucasians, Jewish and non-Jewish alike, with a carrier frequency of about one in 25. By testing for some of the more common mutations, 96% of Ashkenazi Jewish CF carriers can be identified, as can 85% of non-Jewish Northern European CF carriers.

Familial Dysautonomia (FD): FD, or Riley-Day syndrome, is a disease of the autonomic nervous system. Individuals with FD may have severe gastrointestinal problems and pulmonary complications such as

pneumonia. The carrier frequency in the Ashkenazi population is one in 30. Testing for two common mutations provides a carrier detection rate of 99%.

Fanconi Anemia (FAC) (Type C): FAC type C is a chronic disease associated with short stature, bone marrow failure, congenital malformations, and a predisposition to leukemia. The carrier frequency in the Ashkenazi Jewish population is about one in 90. Testing for one common mutation provides a carrier detection rate of approximately 95%. Analysis of FAC mutations does not detect other forms of Fanconi anemia and has limited value for people who are not of Ashkenazi descent. Fanconi anemia can also be diagnosed through chromosome breakage analysis, but this analysis cannot determine carrier status.

Gaucher Disease (Type I): Gaucher disease (type I) is characterized by enlargement of the spleen and liver as well as blood abnormalities, including anemia, easy bruising, and impaired clotting. Type I Gaucher disease is the most common genetic disorder in the Ashkenazi Jewish population, with a carrier frequency of about one in 18. Analysis of common mutations allows a detection rate for carriers of about 95%.

Mucopolipidosis Type IV (MLIV): MLIV is a neurodegenerative condition that is characterized by a variable degree of growth, mental retardation, and ophthalmologic abnormalities. The carrier frequency in the Ashkenazi population is approximately one in 125. Testing for two mutations provides a carrier detection rate of 96%.

Niemann-Pick Disease: Niemann-Pick disease (NPD) is an inherited condition involving lipid metabolisms in which harmful amounts of lipids accumulate in the spleen, liver, lungs, bone marrow and brain. Approximately one in 90 Ashkenazi Jewish individuals carries the Niemann-Pick disease gene type A or B. More than 95% of Ashkenazi Jewish carriers of types A and B disease can be detected with this test. Niemann-Pick disease type C is subdivided into types C1 and C2, each caused by a different gene mutation.

Tay-Sachs Disease (TSD): Tay-Sachs is a disorder caused by a deficiency of the β -hexosaminidase A enzyme which leads to progressive degeneration of the central nervous system. About one in 30 Ashkenazi Jewish individuals is a Tay-Sachs carrier. The gene is also relatively common in the French Canadian population and the Louisiana Cajun community. Carrier screening involves analysis of the enzyme responsible for TSD. The detection rate for carriers is approximately 95%.

In summary, there has been much discussion and debate over which ethnic and racial groups should be offered genetic testing in population-based screening programs. Some maintain that screening should be limited to those groups in which both the carrier frequency and the detectability of the majority of prevalent mutations are sufficiently high to justify efficient and cost-effective screening. Others contend that the marked and growing ethnic admixture in the United States makes it difficult to readily classify or exclude patients based on ethnic group, and that even attempting to make such determinations in a busy clinical setting would place an undue burden on the primary care physician and impair the overall effectiveness and cost of the screening program.

Genetic disease screening of groups or populations may be offered because it is believed that the group has a greater chance of carrying a gene that increases the risk of disease to them or to their children. However, genetic testing for heritable disorders of specific groups, including genetic disease screening panels, is generally not recommended. Genetic testing of an asymptomatic person in a family with several relatives affected with disease does not constitute screening but predictive genetic testing. Targeted predictive genetic testing of individual diseases is appropriate when the specific indications for each test are met.

Professional Societies/Organizations

American College of Obstetricians and Gynecologists (ACOG): In their recommendations for preconception and prenatal carrier screening in individuals of Eastern European Jewish descent, the ACOG Committee on Genetics (2009) stated carrier screening for Tay-Sachs Disease, Canavan disease, cystic fibrosis, and familial dysautonomia "should be offered to Ashkenazi Jewish individuals before conception or during early pregnancy so that a couple has an opportunity to consider prenatal diagnostic testing options. If the woman is already pregnant, it may be necessary to screen both partners simultaneously so that the results are obtained in a timely fashion to ensure that prenatal diagnostic testing is an option". If only one of the couple is Ashkenazi Jew, that person should be screened first. ACOG also states that patients may inquire regarding carrier screening for mucopolipidosis IV, Niemann-Pick disease type A, Fanconi anemia group C, Bloom syndrome, and Gaucher disease and urges providing educational material to the patient so an informed decision regarding testing can be

made. Individuals with a positive family history of any one of these diseases should be offered carrier screening for the specific disorder.

American College of Medical Genetics (ACMG): In practice guidelines for carrier screening in individuals of Ashkenazi Jewish descent, ACMG (2008a) recommended that carrier screening for cystic fibrosis, Canavan disease, familial dysautonomia, Tay-Sachs disease, Fanconi anemia (Group C), Niemann-Pick (Type A), Bloom syndrome, mucopolysaccharidosis IV, or Gaucher disease along with genetic counseling be offered to all individuals of Ashkenazi Jewish descent ideally prior to pregnancy, but also to those who are pregnant. If only one of the couple is of Ashkenazi Jewish descent, ideally that individual would be tested first. If that test is positive, then the partner should be tested. In respect to panel testing, ACMG stated that panel testing is “practical from a technical and cost standpoint. However, the ethical concept of respect for persons necessitates that physicians only order tests for those diseases that have been consented to by the patient. If a patient does not provide informed consent for all tests included in a multiplex panel, then the requested tests should be ordered individually”.

Summary

The clinical utility of genetic testing for heritable disorders by genetic disease screening panels (e.g., Ashkenazi Jewish Panel) has not been established. The impact of such screening on meaningful health outcomes in the general population or ethnic sub-populations is not known. Genetic testing for an individual disease is considered medically necessary on a per Coverage Policy basis and covered when established criteria are met.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Experimental/Investigational/Unproven/Not Covered when used to report genetic testing for heritable disorders in the general population, including genetic disease screening panels such as the Ashkenazi Jewish Panel:

CPT [®] * Codes	Description
83080	b-Hexosaminidase, each assay
83891	Molecular diagnostics; isolation or extraction of highly purified nucleic acid, each nucleic acid type (ie, DNA or RNA)
83892	Molecular diagnostics; enzymatic digestion, each enzyme treatment
83900	Molecular diagnostics; amplification, target, multiplex, first 2 nucleic acid sequences
83901	Molecular diagnostics; amplification, target, multiplex, each additional nucleic acid sequence beyond 2 (List separately in addition to code for primary procedure)
83909	Molecular diagnostics; separation and identification by high resolution technique (eg, capillary electrophoresis), each nucleic acid preparation
83912	Molecular diagnostics; interpretation and report
83914	Mutation identification by enzymatic ligation or primer extension, single segment, each segment (eg, oligonucleotide ligation assay [OLA], single base chain extension [SBCE], or allele-specific primer extension [ASPE])
	All other codes [†]

ICD-9-CM Diagnosis Codes	Description
V82.79	Other genetic screening
V82.89	Genetic screening; other specified conditions
V82.9	Genetic screening; unspecified condition
	All other codes [†]

†Refer to related specific Genetic Testing Coverage Policies for specific codes for individual conditions.

*Current Procedural Terminology (CPT®) © 2010 American Medical Association: Chicago, IL.

References

1. Ambry Genetics. Clinical diagnostics and carrier testing. Ambry Tests®: Ashkenazi Jewish FlexPanel™. 2009. Accessed Jan 9, 2011. Available at URL address: <http://www.ambrygen.com/Ashkenazi-Jewish-FlexPanel.html>
2. American College of Medical Genetics (ACMG). Practice guideline. Carrier screening in individuals of Ashkenazi Jewish descent. Jan 2008a. Accessed Jan 9, 2011. Available at URL address: http://www.acmg.net/AM/Template.cfm?Section=Practice_Guidelines&Template=/CM/HTMLDisplay.cfm&ContentID=6043
3. American College of Medical Genetics (ACMG). Technical standards and guidelines for reproductive screening in the Ashkenazi Jewish population. Jan 2008b. Accessed Jan 9, 2011. Available at URL address: http://www.acmg.net/AM/Template.cfm?Section=Laboratory_Standards_and_Guidelines&Template=/CM/HTMLDisplay.cfm&ContentID=4216
4. American College of Obstetricians and Gynecologists (ACOG) Committee on Genetics. ACOG committee opinion. Number 442, Oct 2009. Preconceptional and prenatal carrier screening for genetic diseases in individuals of Eastern European Jewish descent. *Obstet Gynecol.* 2009 Oct;114(4):950-953Flicka890.
5. Holtzman NE, Watson MS, editors. Promoting Safe and Effective Genetic Testing in the United States. Final Report of the Task Force on Genetic Testing. 1997. Reviewed Apr 2006. Accessed Jan 9, 2011. Available at URL address: <http://www.genome.gov/page.cfm?pageID=10001733>
6. Kaback M. Gene Tests. Hexosaminidase A deficiency. Updated May 19, 2006. Accessed Jan 9, 2011. Available at URL address: <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=tay-sachs>
7. Khoury M, McCabe L, McCabe E. Population screening in the age of genomic medicine. *N Engl J Med.* 2003;348(1):50-8.
8. Klugman S, Gross SJ. Ashkenazi Jewish screening in the twenty-first century. *Obstet Gynecol Clin North Am.* 2010 Mar;37(1):37-46.
9. Laboratory Corporation of America (LabCorp). Ashkenazi Jewish carrier profile plus. 2011. Accessed Jan 9, 2011. Available at URL address: <https://www.labcorp.com/datasets/labcorp/html/chapter/mono/mg004500.htm>
10. Matalon R. Gene Tests. Canavan Disease. Oct 1, 2009. Accessed Jan 9, 2011. Available at URL address: <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=canavan>
11. National Human Genome Research Institute. National Institutes of Health. Genetic testing report – chapter 1. Promoting safe and effective genetic testing in the United States. 2005. Accessed Jan 9, 2011. Available at URL address: <http://www.genome.gov/10002405>
12. Pastores G. Gene Tests. Gaucher Disease. Updated Mar 13, 2008. Accessed Jan 9, 2011. Available at URL address: <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=gaucher>
13. Patterson M. Niemann-Pick Disease, Type C. Gene Tests. Updated Jul 22, 2008. Accessed Jan 9, 2011. Available at URL address: <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=npcc>

14. Quest diagnostics. Ashkenazi Jewish Panel. 2009. Accessed Jan 9, 2011. Available at URL address: <http://www.questdiagnostics.com/hcp/topics/ashkenazi/ashkenazi.html>
15. Slatkin M. A population genetic test of founder effects and implications for Ashkenazi Jewish diseases. *Am J Hum Genet.* 2004;75:282-93.
16. Shobat M. Familial Dysautonomia. *Gene Tests.* Jun 1, 2010. Accessed Jan 9, 2011. Available at URL address: <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=fd>
17. Strom C, Crossley B, Redman J, Quan F, Buller A, McGinniss M, Sun W. Molecular screening for diseases frequent in Ashkenazi Jews: Lessons learned from more than 100,000 tests performed in a commercial laboratory. *Genet Med* 2004 May/June;6(3):145-152.
18. Taniguchi, T. *Gene Tests.* Fanconi Anemia. Mar 27, 2008. Accessed Jan 9, 2011. Available at URL address: <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=fa>

Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	2/15/2008	0280	Genetic Disease Screening Panels

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