

Origination Date: 10/03	Revision Date(s): 7/04, 10/04, 11/04, 4/05, 9/05, 1/06, 7/06, 8/07, 8/08, 2/09
Developed By: Medical Criteria Committee	

Csaba Mera MD

Approved: Csaba Mera, MD

Date: 02/24/09

Description:

The broadest definition of genetic testing includes all tests that are ordered to look for evidence of inherited traits or diseases. Some genetic tests analyze DNA, the inherited chemical material. Other tests examine the chromosomes or protein. Genetic tests search DNA for specific changes. Some changes could increase a person's chance of developing a particular disease. Other changes might not affect the person, but could put his or her children at risk. Some genetic tests look for changes in proteins, which reflect changes in the DNA. Such tests look for the presence, absence or function of a protein. This information can tell doctors if the gene that makes the protein is working properly. Laboratory tests can determine whether a person carries some of the genetic alterations that can increase a person's risk of developing certain cancers. With the completion of the Human Genome Project, new genetic tests have entered the market. Disease risk testing seeks to identify individuals predisposed toward certain diseases and to identify markers for risk of future disease. However, the information obtained from genetic tests is often complex and difficult to interpret. The decision to undergo genetic testing should therefore be a personal, voluntary one and should only be made in conjunction with appropriate genetic counseling.

Criteria:

***Note:** Except for routine newborn screening tests, ODS does not cover genetic testing performed for screening purposes only. Genetic testing will be covered for individuals shown to be at risk if the results may affect the course of treatment.

ODS will cover genetic testing to plan limitations when any of the following criteria are met:

1. **Pregnancy related** (or those planning to become pregnant, as applicable):
 - a. The following will be covered for all pregnant women:
 - i. First trimester screening for Down syndrome (also known as nuchal translucency test or Ultra Screen)
 - ii. Maternal alpha-fetoprotein (MAFP);
 - b. Pregnant women who will be 35 years of age or older at the time of delivery or who have had a high MAFP test:
 - i. Amniocentesis;
 - ii. Chorionic villus sampling
 - c. Pregnant women or women planning pregnancies with a personal or family history of a genetic disorder;
 - d. Testing of both parents (i.e. chromosome analysis, karotype) after previous unexplained stillbirth or repeated (two or more) first trimester miscarriages;
 - e. When both parents' ancestry is from a part of the world where certain genetic mutations are known to be common:
 - i. Tay-sachs disease (Eastern European Ashkenazi Jews, French Canadians, Cajuns, Irish)
 - ii. Cystic fibrosis (European Ashkenazi Jews);
 - f. Genetic carrier testing for cystic fibrosis will be covered for the following individuals:
 - i. Adults with a positive family history of cystic fibrosis;
 - ii. Reproductive partners of persons with cystic fibrosis;
 - iii. Couples planning pregnancy;
 - iv. Couples seeking prenatal care;

Origination Date: 10/03	Revision Date(s): 7/04, 10/04, 11/04, 4/05, 9/05, 1/06, 7/06, 8/07, 8/08, 2/09
Developed By: Medical Criteria Committee	

2. **BRCA gene mutation** testing will be covered for the following situations:
 - a. The member has a personal history of breast cancer and **one** of the following:
 - i. Female member who is diagnosed at age 40 or younger; or
 - ii. Female member who is diagnosed at age 50 or younger and has at least one blood relative with breast or ovarian cancer diagnosed at age 50 or younger; or
 - iii. Female member who is diagnosed at any age with at least two blood relatives with breast or ovarian cancer diagnosed at any age; or
 - iv. Female member who has a male blood relative with breast cancer; or
 - v. Female member who has a personal history of breast and ovarian cancer; or
 - vi. Male or female member with a personal history of breast cancer and one blood relative who has a BRCA 1 or BRCA 2 mutation; or
 - vii. Male member with a personal history of breast cancer; or
 - viii. Multiple primary or bilateral breast cancers in the member or one family member; or
 - ix. Member is at increased risk for specific mutations due to ethnic background (i.e. Ashkenazi Jewish descent); or
 - b. The member does not have a person history of breast cancer but is considered high-risk due to **one** of the following:
 - i. Female members with three or more affected blood relatives on the same side of the family; or
 - ii. Women with 2 or more blood relatives with breast cancer, one of whom was diagnosed at age 50 or younger; or
 - iii. Female members with one or more blood relatives with multiple primary or bilateral breast cancer; or
 - iv. Female members with one or more blood relatives with breast cancer and one or more blood relatives with ovarian cancer on the same side of the family; or
 - v. Female members with one or more blood relatives who has a BRCA 1 or BRCA 2 mutation; or
 - vi. Female members with one or more male blood relatives with breast cancer; or
 - vii. Female members who are at increased risk for specific mutations due to ethnic background (i.e. Ashkenazi Jewish descent) and who have one or more blood relatives with breast or ovarian cancer diagnosed at any age.
3. **Oncotype DX gene assay** will be covered for members with stage I or II, node negative, estrogen receptor positive breast cancer. This multi-gene testing assay is able to predict recurrence risk in node negative breast cancer. It predicts which women need chemotherapy in addition to Tamoxifen for estrogen receptor positive patients. The test results suggest that women diagnosed with estrogen-dependent, lymph-node negative breast cancer are at low risk for recurrence and may not need to go through the discomfort and side effects of chemotherapy.
4. **MammaPrint gene expression assay** will be covered for members under the age of 61 with stage I or II, node negative breast cancer whose tumor is ≤ 5.0 cm in size. MammaPrint is a gene expression assay similar to Oncotype DX. MammaPrint test results are intended to be used as a prognostic tool along with other clinicopathologic factors to help predict recurrence and assess whether chemotherapy will be a beneficial treatment for the patient.
5. **HER2 gene amplification testing** will be covered for members with breast cancer. HER2 stands for human epidermal growth factor receptor 2. HER2 is a gene that helps control how cells grow, divide and repair themselves. Individuals with breast cancer, who have over expression of HER2 protein, may be less likely to respond to certain treatments. There are currently 2 FDA approved tests to determine HER2 status: immunohistochemistry (HerceptTest) or fluorescence in situ hybridization (FISH).

Origination Date: 10/03	Revision Date(s): 7/04, 10/04, 11/04, 4/05, 9/05, 1/06, 7/06, 8/07, 8/08, 2/09
Developed By: Medical Criteria Committee	

6. Pre/Post Symptomatic Testing

Genetic testing may be considered medical necessary to establish a diagnosis of an inheritable disease when all of the following are met:

- a. Members who have signs or symptoms or a genetic disease or are at direct risk of inheriting the disease due to family history; and
- b. The results of the test may confirm or deny the diagnosis when standard evaluation does not provide a definitive answer; and
- c. The results will directly impact the course of treatment

Information to be Submitted with Pre-Authorization Request:

- Physician chart notes
- Family history

References:

- Williams. Genetics and Managed Care: Policy Statement of the American College of Medical Genetics. Genetics in Medicine, November/December 2001:3:430-435.
- ACOG News Release, December 12, 2001.
- Klausner, R. Understanding Gene Testing: US Department of Health & Human Services. Access Excellence, Resource Center, www.accessexcellence.org/AE/AEPC/NIH/. Accessed October 2003.
- Higashi, Veenstra. Managed Care in the Genomics Era: Assessing the Cost Effectiveness of Genetic Tests. The American Journal of Managed Care. July 2003:9:493-500.
- Medical References: Tay - Sachs disease. March of Dimes. www.marchofdimes.com/professionals, September, 2003.
- Zoppi MA, Ibba RM, Putzolu M, et al. Nuchal translucency and the acceptance of invasive prenatal chromosomal diagnosis in women aged 35 and older. Obstetrics and Gynecology. June 2001;97(6):916-20.
- Richards CS, Haddow JE. Prenatal screening for cystic fibrosis. Clinics in Laboratory Medicine. June 2003;23(2).
- Paik S, Shak S, Wolmark N, et al. A Multigene Assay to Predict Recurrence of Tamoxifen-Treated, Node-Negative Breast Cancer. The New England Journal of Medicine, 351:2817-26. December 30, 2004.
- Carlson RW, Moench SJ, Hammond ME, et al. HER2 testing in breast cancer: NCCN task force report and recommendations. J Natl Compr Canc Netw. 2006 July; 4 Suppl 3:S1-S22.
- Invasive Breast Cancer. NCCN Practice Guidelines in Oncology. V.2.2006.
- Mammagprint as a Guide for the Management of Early Stage Breast Cancer. Submitted by Richard Bender, MD, FACP, Chief Medical Officer, Agendia, Inc. January 27, 2009.
- Buyse M, Loi S, Van't Veer L, et al. Validation and clinical utility of a 70-gene prognostic signature for women with node-negative breast cancer. Journal of the National Cancer Institute. Sept 6, 2006;98(17):1183-1192.
- Cardoso F, Van't Veer L, Rutgers E, et al. Clinical application of the 70-gene profile: the MINDACT trial. Journal of Clinical Oncology. Feb 10, 2008;26(5):729-735.
- Physician Advisors