BlueCross BlueShield of Alabama

Name of Policy:

Genetic Testing for Inherited Cancer Predisposition and/or Pharmacogenetics related to Cancer Treatment

Policy #: 133
Category: Laboratory

Latest Review Date: October 2018
Policy Grade: D

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

A genetic disorder is a disease caused in whole or in part by a mutation of a gene. Genetic disorders can be passed on to family members who inherit the genetic abnormality. A number of disorders are caused by a mistake in a single gene. Genetic testing can be diagnostic, prenatal, presymptomatic, predispositional, and pharmacogenetic.

Genetic tests attempt to identify abnormalities in an individual's genes, which include the presence or absence of key proteins whose production is directed by specific noncoding RNAs. These abnormalities in either the presence or absence of proteins could indicate an inherited disposition for a disorder.

Genetic testing includes gene, DNA or RNA testing and biochemical or protein testing. Gene tests are performed on DNA taken from blood, body fluids or tissues and examined for the abnormality. Abnormalities may be large or small involving either a piece of a chromosome or an entire chromosome may be missing or added. Genes may be amplified, over-expressed, inactivated or lost. In some instances, genes may become switched, transposed or discovered in the wrong location. Biochemical testing evaluates the presence or absence of key proteins and metabolites that may indicate abnormal or malfunctioning genes. One of the greatest advances in biomedical research is the identification of germline gene mutations associated with cancer.

Policy:

Inherited Cancer Predisposition

Genetic testing meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage and **ALL** of the following are met:

- The individual displays clinical features or is at direct risk of inheriting the mutation in question based on family history or ethnic background; and
- The result of the test will directly impact the treatment or management of the individual or other family members.

The following conditions are established for the individual diagnoses. Testing is performed in a setting that has adequately trained health care providers who can give appropriate pre-and post-test counseling and that has a qualified laboratory. (See Key Points).

In the absence of specific information regarding advances in the knowledge of mutation characteristics for a particular disorder, the current literature indicates that **genetic tests for each individual mutation** need only be conducted **once per lifetime of the patient.**

Genetic testing in the home or home genetics tests do not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage and are considered **investigational**.

Genetic testing using the Know Error® DNA Specimen Provenance Assay to assign specimen provenance or purity when making the diagnosis of cancer and other histopathological conditions **does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered **investigational.**

Solid Organ Cancers

Breast/Ovarian Cancer

Refer to Medical Policy #513, Genetic Testing for Hereditary Breast and/or Ovarian Cancer

Refer to Medical Policy #180, Assays of Genetic Expression in Tumor Tissue as a Technique to Determine Prognosis in Patients with Breast Cancer

Colon Cancer

Refer to Medical Policy #587, Multigene Expression Assay for Predicting Recurrence in Colon Cancer

Refer to Medical Policy #720, Genetic Testing for Lynch Syndrome and Other Inherited Colon Cancer Syndromes

Head and Neck Cancers

Refer to Medical Policy #582, Analysis of MGMT Promoter Methylation in Malignant Gliomas

Refer to Medical Policy #585, Gene Expression Profiling for Uveal Melanoma

Genetic testing for retinoblastoma meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage when the following criteria are met:

- The individual displays clinical features or is at direct risk of inheriting the mutation in question based on family history or ethnic background;
- **The result of the test will directly impact the treatment or management of the individual or other family members;**
- After history, physical examination, pedigree analysis, genetic counseling, completion of appropriate conventional diagnostic studies and a definitive diagnosis remains uncertain.

Multiple Organ Cancers

Refer to Medical Policy #581, Genetic Testing for PTEN Hamartoma Tumor Syndrome (includes Cowden Syndrome, Bannayan-Riley-Ruvalcaba Syndrome, Proteus Syndrome, and Proteus-Like Syndrome)

Refer to Medical Policy #602 Genetic Testing for Li-Fraumeni Syndrome

Multiple Endocrine Neoplasia Type 1

Genetic testing for MEN 1/MENIN mutations meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage for the following patients:

- Individuals with a personal history of 2 of the 3 main MEN 1 related cancers: pancreatic (islet cell) cancer, parathyroid (hyperplasia) and/or pituitary adenoma; **OR**
- Individual with at least 1 main MEN 1 related cancer and a positive family history of 2 cases of pancreatic (islet cell) cancer, parathyroid (hyperplasia) and/or pituitary adenoma (can be the same person); **OR**;

- Unaffected individuals who have a family history of a documented MEN 1 gene mutation in a first or second degree relative.

Von-Hippel-Lindau (VHL)
VHL is characterized by lesions which can include two or more hemangioblastomas of the retina or brain, or a single hemangioblastoma in association with a visceral manifestation, such as kidney or pancreatic cysts; renal cell carcinoma; adrenal or extra-adrenal pheochromocytomas, and, less commonly, endolymphatic sac tumors, papillary cystadenomas of the epididymis or broad ligament, or neuroendocrine tumors of the pancreas.

Genetic testing for VHL gene mutations meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage for the following patients:
- Any individual who has 1 or more characteristic lesions with or without a family history, **OR**;
- Unaffected individuals who have a family history of a documented VHL gene mutation in a first or second degree relative.

Peutz-Jeghers Syndrome
Refer to Medical Policy #720, Genetic Testing for Lynch Syndrome and Other Inherited Colon Cancer Syndromes

Pancreatic Cancer
Genetic testing for inherited BRCA2 mutation meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage in the following conditions:
- Individuals with a personal history of pancreatic cancer; **OR**
- Unaffected individuals (male or female) with a relative (first or second degree) with a documented BRCA2 mutation; **OR**
- Unaffected individuals (male or female) with two or more first degree relatives with pancreatic cancer; **OR**
- Unaffected individuals with one first-degree relative diagnosed with pancreatic cancer at an early age (under the age of 50); **OR**
- Unaffected individuals with two or more second degree relatives with pancreatic cancer, one of whom developed it at an early age (under the age of 50).

Skin Cancers
Refer to Medical Policy #591, Genetic Testing for Familial Cutaneous Malignant Melanoma

Thyroid Cancer
Genetic testing for RET proto-oncogene point mutation (associated with inheritance of MEN2A, MEN2B and FMTC) for medullary thyroid cancer **meets** Blue Cross and Blue Shield of Alabama's medical criteria for coverage when **one** of the following criteria is met:
- Asymptomatic members of well-characterized families with defined RET gene mutations; **OR**
- Members of families known to be affected by inherited medullary thyroid carcinoma, but not previously evaluated for RET mutations; **OR**

- Patients with apparently sporadic medullary thyroid carcinoma; **OR**
- Patients with first-degree relatives with apparently sporadic medullary thyroid carcinoma.

Pharmacogenetics Testing Related to Cancer Treatment

Solid Organ Cancer Treatment

Breast Cancer Treatment

Refer to Policy #586, Genetic Testing for Tamoxifen Treatment

Refer to Policy # 425, Cytochrome p450 for additional information regarding coverage of testing for drugs for non-cancerous conditions.

Colon Cancer Treatment

Refer to policy #365, KRAS, NRAS and BRAF Variant Analysis in Metastatic Colorectal Cancer

Genetic testing for the UGT1A1 gene in patients with metastatic colorectal cancer to determine tolerance to irinotecan (Camptosar®) **does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage.

Lung Cancer Treatment

Refer to Policy #468, Molecular Analysis for Targeted Therapy of Non-Small-Cell Lung Cancer (NSCLC)

Hematologic Cancer Treatment

Leukemia Treatment

Refer to Policy # 583, Genetic Testing for FLT3 and NPM1 Mutations in Acute Myeloid Leukemia.

IgV(H) gene mutation analysis meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage **in the management of chronic lymphocytic leukemia (CLL).**

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

Testing for cancer-related gene mutations can identify those at high risk and help them to reduce their risk and reduce the burden of cancer. Many inherited cancers have no evidence-based preventive measures available, and for some cancers, the prevention consists of removal of at-risk organs.

Most cancer screening tests detect but do not predict disease. Cancer screening tests provide information about the individual tested. Screening tests are for all symptom-free individuals, and if a negative test results will need to be repeated at intervals. Genetic tests are performed on those with or without disease and have a family or personal medical history or belong to an ethnic group with high probability of mutation. Genetic testing can identify cancer-related germline mutations in disease-free individuals or in patients with the disease who have unaffected family members and may be candidates for testing. Disease-free individuals that have positive test results are candidates for aggressive primary preventive measure.

The following critical issues should be addressed when genetic testing is to be performed responsibly and effectively in the care of patients with a possible inherited genetical cancer predisposition:

1. Cancer-risk counseling should be integrated into the role of the clinical oncologist or clinical medical geneticist.
    - During the evaluation and management or consultation of these patients, the following services should occur:
        - Documentation of a family history for the possible inherited cancer;
        - Counseling regarding familial cancer and options for prevention and early detection;
        - Recognition of those families for which genetic testing may serve as an aid in appropriate counseling.
2. Counseling should be performed by a specialist who is appropriately sanctioned by a genetics credentialing organization (e.g. American Board of Genetic Counseling, Inc.) and who has been trained in the following:
    - Quantitative risk assessment;
    - Genetic testing;
    - Pre and post-test genetic counseling.
3. Proper informed consent must be obtained. Basic elements for informed consent include the following:
    - Information on the specific test being performed.
    - Implication of a positive or negative test result.
    - Possibility that the test will not be informative.
    - Options for risk estimation without genetic testing.
    - Risk of passing a mutation or predisposition to children.
    - Technical accuracy of the test.
    - Fees involved in testing and counseling.
    - Risks of psychological distress.
    - Risks of insurance or employer discrimination.
    - Confidentiality issues.

- Options and limitations of medical surveillance and screening following the testing.

4. Indications for counseling and testing:
    - The patient has a strong family history of cancer (specific criteria is required for each genetic test to satisfy this requirement),
    - The test can be adequately interpreted,
    - Result will influence medical management of the patient and/or family member.
5. Proper medical management, post-testing and counseling:
    - Discuss possible risks and benefits of cancer early detection and prevention modalities, which have presumed but unproven efficacy for individuals at the highest hereditary risk.
    - Encourage long-term research of outcome studies and/or cooperative studies or registries.

Know Error® DNA Specimen Provenance Assay

The Know Error® system, produced by Diagnostic ID LLC, provides DNA confirmation between patients and their biopsy tissue sample ensuring that when patients' biopsy results arrive, the results are of the tested patient. The system's testing sequence includes a comparison of short tandem repeat, or STR, profiles of both the patient and the biopsy sample cells. The error-elimination system is designed for prostate cancer and breast cancer biopsy samples. Before a biopsy procedure, a reference sample of the patient's DNA is taken by swabbing the inside of the patient's cheek. The swab is sent to an independent forensic DNA lab for testing. When the patient's biopsy result comes back, DNA from the biopsy is double-checked against DNA from the patient's cheek swab.

Short tandem repeat (STR) analysis has emerged as the method of choice for testing to resolve specimen source contamination and identify problems that arise in surgical pathology. Pfeifer, et al (2011), studied a series of consecutive cases referred for STR typing during a five-year period to document the usefulness of the approach and to describe the broadening scope of testing. The series demonstrates that STR-based typing can be applied in virtually any setting in which specimen source confirmation is requested, that STR-based typing is informative in 92% of cases, but that exceptions occasionally arise that complicate test interpretation. The series also demonstrates that in addition to traditional uses of STR typing, testing is now performed in the absence of any direct indication that a specimen mix-up or contamination may have occurred, namely, when the pathologic findings are unexpected or the clinical setting is atypical. The case series underscores the ability of STR testing to detect errors that cannot be captured by current laboratory protocols, a finding that has important implications for patient safety.

Retinoblastoma

Retinoblastoma (RB) is a malignancy of the retinal cell layer of the eye and is the most common eye cancer in children and usually presents itself before the age of five. In about 40% of the cases RB is hereditary. RB is quite rare and occurs in approximately one in every 20,000 births and can occur unilaterally or bilaterally. Those with retinoblastoma of the inherited type have an increased frequency of second malignancies and are most often bone tumors. RB is treated by surgery (enucleation, chemotherapy, cryotherapy, light coagulation, and radiation). Current statistics have an 80-90% five year survival rate.

IgV(H) Gene Mutation and Chronic Lymphocytic Leukemia (CLL)
Chronic lymphocytic leukemia (CLL) accounts for approximately 11% of hematologic neoplasms and at any time in the United States, approximately 100,000 individuals are living with CLL. Patients with CLL follow heterogeneous clinical courses. Some survive for prolonged periods without definitive therapy, while others die rapidly, despite aggressive treatment. Chin et al (2006) described that CLL patients can be divided into two basic groups on the basis of the mutational status of the immunoglobulin heavy-chain variable-region (IgV(H)) gene in leukemic cells. Patients with the IgV(H) gene mutations have a longer survival than those without. Thus, mutation analysis may be useful for assessing prognosis of patients with CLL and planning management strategies.

Thyroid Cancer
Thyroid cancer represents approximately 1% of malignancies occurring in the United States, resulting in 22,000 cancer diagnoses and 1,400 cancer deaths per year. Carcinoma of the thyroid is an uncommon cancer and is the most common malignancy of the endocrine system. Differentiated tumors (papillary or follicular) are highly treatable and usually curable. Poorly differentiated cancers (medullary or anaplastic) are much less common, are aggressive, metastasize early, and have a much poorer prognosis. Thyroid cancer affects women more than men and the majority of the cases are between the ages of 25 and 65.

Three to four percent of thyroid cancer is medullary thyroid cancer (MTC). MTC arises from the parafollicular calcitonin-secreting cells of the thyroid cells of the thyroid gland. MTC occurs in sporadic and familial forms. Familial cases may indicate the presence of multiple endocrine neoplasia Type 2 (MEN2), a group of autosomal dominant genetic disorders caused by inherited mutations in the RET oncogene. This disorder is classified into three subtypes based on the presence of other clinical complications: MEN2A, familial medullary thyroid carcinoma (FMTC) and MEN2B. All three subtypes have a high risk of developing MTC. DNA-based testing of the RET gene identifies disease-causing mutation in 95% of individuals with MEN2A and MEN2B and in about 85% of individuals with FMTC. Genetic testing is considered an important part of the management for at-risk family members. The criteria outlined by the American Society of Clinical Oncology has stated that genetic testing for MEN2 meets the criteria for at-risk individuals for first-degree relatives (parents, siblings, and children) of a person known to have MEN2.

Key Words:
Genetic testing, genetic test, genetic disorder, mutation, replication error phenotype, RER, thyroid cancer, carcinoma of the thyroid, RET proto-oncogene, medullary thyroid cancer, medullary thyroid carcinoma, MTC, multiple endocrine neoplasia type 2, MEN2, RET oncogene, MEN2A, MEN2B, familial medullary thyroid carcinoma, FMTC, RET gene, sporadic medullary thyroid carcinoma, germline alterations, fecal occult blood test, FOBT, DNA, DNA replication, microchip array, tumor gene expression, retinoblastoma, gefitinib, Iressa, non-small cell lung cancer, IgV(H), chronic lymphocytic leukemia, CLL, single-nucleotide polymorphisms (SNF), TMPRSS, Know Error® DNA specimen provenance assay, (DSPA), UGT1A1

Approved by Governing Bodies:

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. If applicable, testing should have the appropriate U.S. Food and Drug Administration (FDA) approvals/clearances.

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.
ITS: Home Policy provisions apply
FEP contracts: FEP does not consider investigational if FDA approved and will be reviewed for medical necessity. Special benefit consideration may apply. Refer to member's benefit plan.

Current Coding:

CPT codes:

81261	IGH@ (immunoglobulin heavy chain locus) (e.g., leukemias and lymphomas, b-cell), gene rearrangement analysis to detect abnormal clonal population(s); amplified methodology (e.g., polymerase chain reaction)
81262	; direct probe methodology (e.g., southern blot)
81263	IGH@ (immunoglobulin heavy chain locus) (e.g. leukemia and lymphoma, B-cell), variable region somatic mutation analysis
81264	IGK@ (immunoglobulin kappa light chain locus) (e.g. leukemia and lymphoma, B-cell), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)
81315	PML/RAR-alpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (e.g., promyelocytic leukemia) translocation analysis; common breakpoints (e.g., intron 3 and intron 6), qualitative or quantitative
81316	; single breakpoint (e.g., intron 3, intron 6 or exon 6), qualitative or quantitative
81340	TRB@ (T cell antigen receptor, beta) (e.g., leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using amplification methodology (e.g., polymerase chain reaction)
81341	; using direct probe methodology (e.g., Southern Blot)
81342	TRG@ (T cell antigen receptor, gamma) (e.g. leukemia and lymphoma), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)
81350	UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (e.g. irinotecan metabolism), gene analysis, common variants (e.g. *28, *36, *37)
81403	Molecular pathology procedure, Level 4 (NEW TESTING)

81405 Molecular pathology procedure, Level 6. KRAS (Kristen rat sarcoma viral oncogene homolog) (e.g. Noonan syndrome), full gene sequence
81479 Unlisted molecular pathology procedure
81599 Unlisted multianalyte assay with algorithmic analysis
84999 Unlisted chemistry procedure

HCPCS:

S3840 DNA analysis for germline mutation of the RET proto-oncogene for susceptibility to multiple endocrine neoplasia type 2
S3841 Genetic testing for retinoblastoma

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Policy History:

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Medical Policy Group, June 2005 **(3)**
Medical Policy Administration Committee, July 2005
Available for comment July 28-September 10, 2005
Medical Policy Group, October 2005 **(1)**
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Medical Policy Group, January 2007 **(1)**
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Medical Policy Administration Committee, July 2009
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Medical Policy Administration Committee, October 2009
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Medical Policy Group, October 2009 **(1)**

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Medical Policy Group, June 2010 **(1):** Added information regarding PathFinderTG® testing, no change in coverage
Medical Policy Group, August 2010 **(1):** Updated Description of Procedure or Service
Medical Policy Group, September 2010 **(1):** Added new non-coverage statement cutaneous malignant melanoma, Key Points
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Medical Policy Group, December 2010 **(1):** Coding update, added 88363, effective January 1, 2011
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Available for comment February 23 through April 11, 2011
Medical Policy Group, March 2011 **(1):** Policy, Key Points, Key Words and References for IgV(H) testing for CLL
Medical Policy Administration Committee, March 2011
Available for comment April 4 – May 18, 2011
Medical Policy Group, March 2011 **(1):** Entire policy reformatted and criteria dating 2005 and before removed from policy and archived
Medical Policy Group, April 2011 **(1):** Updated Key Points and References for tamoxifen;
Medical Policy Administration Committee, May 2011
Medical Policy Group, May 2011 **(1):** Updated Policy, Key Points, Key Words and References for DecisionDx-UM for uveal melanoma
Medical Policy Administration Committee, May 2011
Available for comment May 11 – June 27, 2011
Medical Policy Group, May 2011 **(1):** Updated Policy, Key Points, Key Words and References for Know Error® DNA specimen provenance assay
Medical Policy Administration Committee, May 2011
Available for comment May 11 – June 27, 2011
Medical Policy Group, June 2011 **(1):** Removed all coverage criteria related to OnDose™ testing for 5-FU and created reference statement to policy #253
Medical Policy Group, June 2011 **(1):** Update to Key Points for PathFinderTG® testing
Medical Policy Group, September 2011 **(1):** Added coverage criteria for genetic testing related to drugs crizotinib and vemurafenib under pharmacogenetics section; Changed "hereditary" to "familial" related to genetic testing for familial cutaneous malignant melanoma, no change in policy statement; Update to Key Points, Key Words and References related to crizotinib, vemurafenib and FCMM
Medical Policy Administration Committee, October 2011
Available for comment October 19 through December 5, 2011
Medical Policy Group, December 2011 **(1):** 2012 Coding Update – added, deleted, changed codes for 2012
Medical Policy Group, February 2012 **(3):** 2012 Coding Update – deleted 'S' codes effective 4/1/12
Medical Policy Group, October 2012 **(1):** Removed all aspects of Breast and Ovarian cancer related to BRCA testing to new policy #513; removed items with dates of 2006 and earlier

Medical Policy Group, December 2012 **(3):** 2013 Coding Updates: Deleted Codes 83890 through 83914; Moved codes 84999, 88299, & 99199 to Previous Codes with no deletion date; Added 81201, 81202, 81203, 81321, 81322, 81323, 81403, 81405, 81479 and 81599 effective 01/01/2013.
Medical Policy Group, July 2013 **(1):** Removed all aspects of BCR-ABL1 mutation testing related to CML and created new policy #533; removed all aspects of prostate cancer and created new policy #534; no other changes noted to policy
Medical Policy Group, December 2013 **(1):** Update to Policy, Key Points, Coding, Key Words and References with addition of MGMT gene methylation related to GBM, testing is considered investigational; 2014 Coding Update: addition of new code 81287, effective 01/01/2014
Medical Policy Administration Committee, December 2013
Available for comment December 17, 2013 through January 30, 2014
Medical Policy Group, January 2014 **(1):** Removed all aspects of BRAFV600E mutation testing related to metastatic melanoma and created new policy #541; removed all aspects of PathFinderTG molecular testing related to integrating molecular findings into pathology diagnosis and created new policy #544; no other changes noted to policy.
Medical Policy Group, March 2014 **(1):** Removed all aspects of under the curve 5-FU genetic testing and moved to policy #253; no other changes noted to policy
Medical Policy Group, November 2014**:** 2015 Annual Coding update. Added codes 81288, 81435 and 81436 to current coding. Changed verbiage on codes 81403 and 81405.
Medical Policy Group, January 2015: Added CPT code 84999 to coding section.
Medical Policy Group, April 2015 **(3):** Removed all aspects of genetic testing for tamoxifen treatment and created individual policy #586; no other changes to policy.
Medical Policy Group, April 2015 **(3):** Removed all aspects of gene expression profiling for uveal melanoma and created individual policy #585; no other changes to policy.
Medical Policy Group, April 2015 **(3):** Removed all aspects of genetic testing for FLTE and NPMI Mutations in AML and created individual policy #583; no other changes to policy.
Medical Policy Group, April 2015 **(3):** Removed all aspects of analysis of MGMT promoter methylation in malignant gliomas and created individual policy #582; no other changes to policy.
Medical Policy Group, April 2015 **(3):** Removed all aspects of genetic testing for PTEN hamartoma tumor syndrome and created individual policy #581; no other changes to policy.
Medical Policy Group, April 2015 **(3):** Removed all aspects of genetic testing for familial cuteaneous malignant melanoma and created individual policy #591; no other changes to policy.
Medical Policy Group, April 2015 **(3)**: Removed all aspects of genetic testing for patients with non-small-cell lung cancer – EGFR, KRAS, ALK and merged into policy #468; reordered remaining information for flow and clarification purposes; no other changes to policy
Medical Policy Group, November 2015: 2016 Annual Coding Update. Revised CPT codes 81405, 81435, and 81436.
Medical Policy Group, January 2016 **(3)**: Removed all aspects of genetic testing for OncotypeDX for colon cancer and merged into policy #587. No other policy changes.
Medical Policy Group, June 2017 **(3)**: Editing review; literature review on topics contained within policy underway; removed previous coding for those deleted 01/01/2014 and prior; no changes in policy statements at this time.
Medical Policy Group, July 2017 **(3)**: Removed all aspects of genetic testing for Li-Fraumeni syndrome and created individual policy #602; updated governing bodies verbiage; no other policy statement changes

Medical Policy Administration Committee, July 2017
Medical Policy Group, September 2018 **(2)**: For clarification purposes only – revised genetic testing criteria in the Policy section to include "ALL" of the following criteria and removed the "or" and added an "and"; also removed the effective date from all the codes in the coding section
Medical Policy Group, October 2018 **(9)**: Removed all aspects of genetic testing for Lynch Syndrome and Peutz-Jeghers syndrome and created individual policy #720.
