UnitedHealthcare®

Reimbursement Policy

Molecular Pathology/Molecular Diagnostics/Genetic Testing

Policy Number	GEN01252012RP	Approved By	UnitedHealthcare Medicare Reimbursement Policy Committee	Current Approval Date	04/23/2014

IMPORTANT NOTE ABOUT THIS REIMBURSEMENT POLICY

This policy is applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates.

You are responsible for submission of accurate claims. This reimbursement policy is intended to ensure that you are reimbursed based on the code or codes that correctly describe the health care services provided. UnitedHealthcare reimbursement policies use Current Procedural Terminology (CPT®*), Centers for Medicare and Medicaid Services (CMS), or other coding guidelines. References to CPT or other sources are for definitional purposes only and do not imply any right to reimbursement.

This reimbursement policy applies to all health care services billed on CMS 1500 forms and, when specified, to those billed on UB04 forms (CMS 1450). Coding methodology, industry-standard reimbursement logic, regulatory requirements, benefits design and other factors are considered in developing reimbursement policy.

This information is intended to serve only as a general resource regarding UnitedHealthcare's reimbursement policy for the services described and is not intended to address every aspect of a reimbursement situation. Accordingly, UnitedHealthcare may use reasonable discretion in interpreting and applying this policy to health care services provided in a particular case. Further, the policy does not address all issues related to reimbursement for health care services provided to UnitedHealthcare enrollees. Other factors affecting reimbursement may supplement, modify or, in some cases, supersede this policy. These factors may include, but are not limited to: legislative mandates, the physician or other provider contracts, and/or the enrollee's benefit coverage documents. Finally, this policy may not be implemented exactly the same way on the different electronic claims processing systems used by UnitedHealthcare due to programming or other constraints; however, UnitedHealthcare strives to minimize these variations.

UnitedHealthcare may modify this reimbursement policy at any time by publishing a new version of the policy on this Website. However, the information presented in this policy is accurate and current as of the date of publication.

Table of Contents

Molecular Pathology/Molecular Diagnostics/Genetic Testing

Application

This reimbursement policy applies to services reported using the Health Insurance Claim Form CMS-1500 or its electronic equivalent or its successor form, and services reported using facility claim form CMS-1450 or its electronic equivalent or its successor form. This policy applies to all products, all network and non-network physicians, and other health care professionals.

The HCPCS/CPT code(s) may be subject to Correct Coding Initiative (CCI) edits. This policy does not take precedence over CCI edits. Please refer to the CCI for correct coding guidelines and specific applicable code combinations prior to billing UnitedHealthcare. It is not enough to link the procedure code to a correct, payable ICD-9-CM diagnosis code. The diagnosis must be present for the procedure to be paid. Compliance with the provisions in this policy is subject to monitoring by pre-payment review and/or post-payment data analysis and subsequent medical review. The effective date of changes/additions/deletions to this policy is the committee meeting date unless otherwise indicated. Fee schedules, relative value units, conversion factors, and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein.

Summary

Overview

Hereditary Breast and Ovarian Cancer

Families can be suspected of having hereditary breast or ovarian cancer based on occurrence at an early age, in multiple generations, often bilaterally, and in a pattern suggesting an autosomal dominant pattern of inheritance. The susceptibility may be transmitted through the maternal or paternal side of the family. Germ-line alterations in two genes, BRCA1 and BRCA2, are associated with an increased risk of breast and ovarian cancer. Alterations in BRCA1 and BRCA2 explain many, but not all, of inherited forms of breast and ovarian cancer. With the identification of BRCA1 and BRCA2, it is now possible to test for abnormalities in the genes to provide information on the future risk of cancer and to make important treatment decisions in affected individuals. Approximately five- to ten-percent of all breast cancers, and a similarly small percentage of ovarian cancers, are attributed to dominantly inherited susceptibility.

Families at high risk of harboring a BRCA1 or BRCA2 mutation are those in which the incidence of breast or ovarian cancer suggests an autosomal dominant inheritance (i.e., about half the family members are affected). Men rarely develop breast cancer and, thus, there may not be an affected first-degree relative, and the size of the family may not permit analysis of possible autosomal dominant inheritance.

In patients with breast or ovarian cancer who are from high-risk families without a known BRCA1 or BRCA2 gene, the entire gene must be sequenced to identify possible mutations. In those families with a known BRCA1 or BRCA2 gene mutation, only a single mutation site sequence is required. In the case of individuals with Ashkenazi Jewish ancestry, testing for 3 mutations common in this population may be warranted even after a single mutation has been identified in their family member. (See section Hereditary Breast and Ovarian Cancer Syndromes under the coverage guideline section for specific coverage guidelines)

Oncotype Diagnostic Test for Breast Cancer Prognosis

Oncotype DX (trademark) is a patented gene panel test developed for node-negative, estrogen receptor (ER)-positive breast cancer. More recent clinical data supports its use for micro metastases and for 1-3 positive nodes. The assay can be conducted on routine paraffin-embedded breast cancer tissue. Algorithmic weighting of gene expression yields a Recurrence Score (RS) which is strongly correlated with the recurrence of breast cancer and may be used in the decision making for chemotherapy. The test is provided to Medicare beneficiaries throughout the US by the CLIA-regulated laboratory of Genomic Health, Inc. Therefore, when this test is a Part B service, most or all coverage decisions for Medicare beneficiaries are made by the Part B contractor serving Genomic Health, Inc, which is Palmetto GBA. Test results have been incorporated in one version of a nationally recognized multi-variate prognostic model for breast cancer recurrence (www.adjuvant-online.com; Ravdin, 2001).

(See section Oncotype Diagnostic Test for Breast Cancer Prognosis under the coverage guideline section for

specific coverage guidelines)

Mammaprint Test – Breast Cancer Prognosis

MammaPrint is an FDA cleared *in vitro* microarray diagnostic test that uses gene expression profiling to analyze the gene activity of the tumor itself. By analyzing the individual activity of the tumor's genes, MammaPrint enables a more accurate prognosis of breast cancer recurrence to assist physicians in dealing with their patients with breast cancer.

Patients with high risk of relapse need to be identified and treated with a systematic adjuvant therapy. However, while adjuvant therapies, such as chemotherapy and hormonal therapy, can reduce the risk of distant metastases by approximately one-third, it is estimated that many patients receiving chemotherapy may have survived without it and also avoided often unpleasant side-effects. MammaPrint, in addition to other tests and clinical factors, helps to classify the tumors into high and low risk for recurrence. Chemotherapy itself has inherent risk of morbidity, particularly in patients with comorbid conditions. When physicians make treatment decisions that chemotherapy can be safely avoided and alternative therapy (hormonal manipulation, radiation therapy) used, there can be patient benefit.

(See section Mammaprint Test – Breast Cancer Prognosis under the coverage guideline section for specific coverage guidelines)

Hereditary Colorectal and Endometrial Cancer Syndromes

Lynch Syndrome (previously denoted as Hereditary Non-Polyposis Colorectal Cancer (HNPCC) syndrome), is an autosomal dominant syndrome that accounts for about 3-5% of colorectal cancer cases. HNPCC syndrome mutations occur in the following genes: hMLH1, hMSH2, hMSH6, PMS2 and EPCAM. Colorectal cancers associated with Lynch syndrome occur at a younger age (average age of onset between 44-61 years of age) compared with the more common colorectal cancers typically found during the seventh decade of life. Other Lynch syndrome-associated cancers include endometrial, ovarian, gastric, pancreas, ureter and renal pelvis, biliary tract, brain (usually glioblastoma, and small intestine cancers, as well as sebaceous gland adenomas/carcinomas and keratoacanthomas (AKs). Female carriers of a specific Lynchgene mutation have up to a 71% risk of endometrial cancer and 12% risk of ovarian cancer, in addition to the other Lynch syndrome cancer risks. Furthermore, gynecologic cancers may precede colorectal cancer in as many as 50% of female HNPCC gene mutation carriers.

Inherited mutations in MLH1 and MSH2 account for the majority (~70%) of mutations detected with MSH6 and PMS2 found in the remainder of mutation positive cases. MSH6 mutations are responsible for approximately 15% of Lynch syndrome cases. Recent reports confirm that PMS2 mutations are a significant contributor to Lynch syndrome. Estimates of the proportion of Lynch syndrome cases due to PMS2 vary and are as high as 15%.

Familial Adenomatous Polyposis (FAP) is an autosomal dominant syndrome caused by a germ-line mutation of the APC gene. Characteristically, affected patients develop multiple adenomas diffusely throughout the colon beginning in their teens. Colorectal cancer is inevitable in patients with FAP if colectomy is not performed. The average age at symptomatic diagnosis ranges from 34 to 45 years of age. However, the average age of colonic adenoma appearance is 16 years and of cancer diagnosis is 39 years. The FAP gene mutation occurs in approximately 1/10,000 - 1/30,000 live births in the United States, affects both sexes equally, and accounts for up to 1% of colorectal cancers.

MYH-associated polyposis (MAP) is an autosomal recessive syndrome linked to germ-line mutations of the MYH gene. The full clinical picture of MYH-associated polyposis (MAP) is incompletely understood at this time. Current evidence suggests it is associated with about 0.4-1.0% of colorectal cancers.

(See section Hereditary Colorectal Cancer Syndromes under the coverage guideline section for specific coverage guidelines)

Multiple Myeloma Gene Expression Profile

MyPRS™ is a test for Multiple Myeloma Gene Expression Profile.

Multiple myeloma is an incurable malignancy of terminally differentiated antibody secreting plasma cells. The median overall survival is reported at 3-4 years. Disease sequelae associated with this malignancy includes anemia, immunodeficiency, renal insufficiency/failure, lytic bone lesions and hypercalcemia.

The classification of myeloma is inadequate with morphology alone. The Durie-Salmon Staging System was first published in 1975 and predicts tumor mass and estimates survival by using levels of immunoglobin proteins, hemoglobin and calcium, and the number of bone lesions. CMS follows this classification in NCD 110.8.1 for Autologous Stem Cell Transplantation and will continued to be followed until changed.

International classification of myeloma, first published in 2005, is based on B2 microglobulin levels and albumen proteins.

More recently, genetic testing has shown myeloma exists in a hyperdiploidy or nonhyperdiploidy states. Some chromosomal abnormalities have been shown to be associated with poor prognosis. Two genetic testing schemes, TC or Translocations / Cyclin D and Gene Expression Profiles, were discussed in Leukemia 2009 by a report of the International Myeloma Working Group molecular classification of multiple myeloma. The two schemes have generated information of multiple myeloma being a heterogenetic disease with 7 to 8 subsets with various life expectancies.

Multiple Myeloma Gene Expression Profile (MyPRS) isolates plasma cells from myeloma patients, extracts DNA, which is then subjected to MicroArray testing and application of validated software programs to identifying patterns of genetic abnormalities. Seventy highly predictive genes have been identified and correlated to myeloma early relapse. MyPRS gives a predictive risk signature as high-risk or low-risk at this time. A high risk score predicts a <20% three-year complete remission where as a low-risk predicts a five-year complete remission of > 60%. The predictive value for the stratification of therapeutic interventions allows these patients to be treated in a more personalized manner based on their own genetic profile. However, it would be inappropriate to use this test as a diagnostic tool or as a monitoring device of ongoing therapy. Other testing is available for this function. This test is used only after an initial diagnosis of multiple myeloma has been made and will be available to be used in stratification of therapeutic interventions. The coverage is set to include only two clinical settings:

1. once after initial diagnosis is made (ICD-9-CM 203.00), or
2. If relapse has occurred and a change in the therapeutic modalities is contemplated (203.02)

(See section Multiple Myeloma Gene Expression Profile under the coverage guideline section for specific coverage guidelines)

Loss-of-Heterozygosity Based Topographic Genotyping with PathfinderTG®

Evaluating tissue samples pathologically is crucial to the diagnosis and treatment of patients with malignancy. At times, standard pathologic analyses provide inconclusive information. Combining pathologic study with molecular analyses of microdissected tissue, is claimed to enhance the ability to provide more specific diagnostic information, to help guide treatment decisions. These testing combinations are generally known as topographic genotyping.

More specifically, loss-of-heterozygosity based topographic genotyping and other molecular analyses are combined in a patented technology known as PathfinderTG®. Recently, a Technology Assessment Report prepared by the Tufts Evidence-Based Practice Center, for the Agency for Healthcare Research and Quality (AHRQ), reviewed the existing scientific literature for PathfinderTG®.

The Technology Assessments conclusions noted insufficient studies measuring whether the use of PathfinderTG® Technology would improve patient relevant clinical outcomes. Questions raised included whether PathfinderTG® results affected diagnostic evaluation or treatment decisions.

However, during the comment period for the draft LCD, Highmark Medicare Services received extensive comments from physicians and providers from across the country, many from distinguished, highly reputable universities and physicians specifically on their use and results of the PathfinderTG® Technology very specifically for patients with pancreatic cysts where “traditional” fluid chemistry and/or cytology evaluations were inconclusive. Several institutions provided their own research results of their use of PathfinderTG® Technology specifically for patients with pancreatic cysts where fluid chemistries and/or cytology evaluations were inconclusive.

(See section Loss-of-Heterozygosity Based Topographic Genotyping with PathfinderTG ® under the coverage guideline section for specific coverage guidelines)

Heartsbreath

The Heartsbreath test is a Food and Drug Administration-approved Humanitarian Use Device for use only as an adjunct to the endomyocardial biopsy to detect grade 3 heart transplant rejection in patients who have had a heart transplant within the last year and an endomyocardial biopsy within the prior month. The test involves collecting breath samples from the patient and analysis of the samples performed in a laboratory. These test results are then compared to endomyocardial biopsy findings and the results are provided to the clinician shortly thereafter.

(See section Heartsbreath under the coverage guideline section for specific coverage guidelines)

Molecular Pathology/Molecular Diagnostics/Genetic Testing

(See NCD 260.10)

ChemoFx

ChemoFx® is a drug response marker. It's a test that quantifies an individual cancer patient's probable tumor response to various chemotherapeutic and biologic agents—providing both sensitivity and resistance information. As such, ChemoFx® provides valuable insights that help guide physicians' treatment decisions and give both physicians and patients an edge against cancer.

In vitro, also referred to as ex vivo, chemoresponse (chemotherapy sensitivity and chemotherapy resistance) assays have been proposed as a means of predicting tumor response to various chemotherapy agents. Chemoresponse assays are intended to assist with the selection of chemotherapy agents for the treatment of cancer in individual patients.

Assay-guided therapy has been proposed as an alternative to empiric therapy. In assay-guided therapy, tumor cells from the individual patient are exposed to chemotherapeutic agents in vitro. Empiric therapy refers to the selection of chemotherapy agents based on the critical evaluation of outcome evidence from well-designed clinical trials.

(InVitro Chemo Response Assay, Chemo Response Assay, Chemo FX Response Assay, InVitro Chemo FX Culture, Chemo FX Resistance, Chemo FX Sensitivity are all addressed in this section)

(See section ChemoFx under the coverage guideline section for specific coverage guidelines)

Sweat Test

The sweat test is an important diagnostic tool in cystic fibrosis and may be covered when used for that purpose. Usage of the sweat test as a predictor of efficacy of sympathectomy in peripheral vascular disease is unproven and, therefore, is not covered. (NCD 190.5)

AlloMap

AlloMap Molecular Expression Testing is a non-invasive gene expression test used to aid in the identification of heart transplant recipients with stable allograft function who have a low probability of moderate/severe acute cellular rejection at the time of testing in conjunction with standard clinical assessment. AlloMap testing measures the expression levels of 20 genes from a blood sample. The combined expression of these genes is represented as an AlloMap test score. AlloMap is performed in the XDx CLIA-certified laboratory and has been commercially available since 2005. AlloMap was cleared by the U.S. Food and Drug Administration in 2008 and was CE marked for the European Union in April 2011. Use of AlloMap is also included in the International Society of Heart and Lung Transplant (ISHLT) Practice Guidelines, published in August 2010, the worldwide standard for the care of heart transplant patients. Approximately 66% of the United States heart transplant population is covered for AlloMap. (See section Allomap under the coverage guideline section for specific coverage guidelines)

Reimbursement Guidelines

Title XVIII of the Social Security Act, Section 1862(a) (1) (A) states *"...no Medicare payment shall be made for items or services which are not reasonable and necessary for the diagnosis and treatment of illness or injury..."*. Furthermore, it has been a longstanding CMS policy that "tests that are performed in the absence of signs, symptoms, complaints, or personal history of disease or injury are not covered unless explicitly authorized by statute". **Screening services**, such as pre-symptomatic genetic tests and services, are those used to detect an undiagnosed disease or disease predisposition, and as such are not a Medicare benefit and not covered by Medicare. Similarly, Medicare may not reimburse the costs of tests/examinations that assess the risk for and/or of a condition unless the risk assessment clearly and directly effects the management of the patient.

Testing of unaffected family members or other individuals is considered by Medicare to be screening and is not payable by UHC.

For the above syndromes, those individuals who are determined not to be carriers may be prevented from undergoing unnecessary prophylactic surgery such as total versus partial colectomy, mastectomy, hysterectomy, and oophorectomy. Frequency of surveillance procedures (mammography, colonoscopy, etc.) may be affected depending on the presence or absence of a mutation.

1. Genetic tests for cancer are only a covered benefit for a **member with a personal history** of an illness, injury, or signs/symptoms thereof (i.e. clinically affected). A person with a personal history of a relevant cancer is a clinically affected person, even if the cancer is considered cured. Genetic testing is considered a non-covered screening test for patients unaffected by a relevant illness, injury, or signs/symptoms thereof.

2. Predictive or pre-symptomatic genetic tests and services, in the absence of past or present illness in the member, are not covered under national Medicare rules. For example, UHC does not cover genetic tests based on family history alone.
3. A covered genetic test must be used to manage a patient. UHC does not cover a genetic test for a clinically affected individual for purposes of family planning, disease risk assessment of other family members, when the treatment and surveillance of the member will not be affected, or in any other circumstance that does not directly affect the diagnosis or treatment of the member.
4. The results of the genetic test must potentially affect at least one of the management options considered by the referring physician in accordance with accepted standards of medical care (e.g. surgery, the extent of surgery, a change in surveillance, hormonal manipulation, or a change from standard therapeutic or adjuvant chemotherapy).
5. Pre-test genetic counseling must be provided by a qualified and appropriately trained practitioner.
6. An informed consent form signed by the patient prior to testing which includes a statement that he/she agree to post-test counseling is required. This consent form must be available on request by Medicare.
7. Genetic analysis must be provided through a laboratory which meets the American Society of Clinical Oncology (ASCO) recommended requirements:
    a. The lab must meet appropriate Clinical Laboratory Improvement Amendment (CLIA) 1988 regulations;
    b. Successful participation in the American College of Medical Genetics (ACMG)/College of American Pathologists (CAP) inspection and survey program;
    c. appropriate state licensing; and
    d. credentialing of laboratory directors and staff by the American Board of Medical Genetics (ABMG).

Hereditary Breast and Ovarian Cancer Syndromes

BRCA1 and BRCA2 genetic testing is covered only for the following individuals: For the purpose of this policy, only genetic relations are relevant (i.e. "blood relatives"). Non-genetic relations, such as through marriage or adoption are not relevant to coverage. A close relative means a first degree (parents, full siblings, offspring), second degree (grandparents, grandchildren, aunts, uncles, nephews, nieces, half-siblings), or third degree (great-grandparents, great-aunts, great-uncles, first cousins) relatives.) Also, for this policy, invasive and ductal carcinoma in situ (DCIS) breast cancers should be included. If the individual is of Ashkenazi Jewish descent, test the three common mutations first. Then if negative, consider full sequence ("Reflex") testing based on assessment of individual and family history as if the individual is of non-Ashkenazi Jewish descent.

1. Personal history of breast cancer + one or more of the following:
    - Diagnosed age ≤45 y, with or without family history
    - Diagnosed age ≤50 y or two breast primaries, with ≥1 close blood relative(s) with breast cancer ≤50 y and/or ≥1 close blood relative(s) with epithelial ovarian/fallopian tube/primary peritoneal cancer
    - Two breast primaries when first breast cancer diagnosis occurred prior to age 50
    - Diagnosed at any age, with ≥2 close blood relatives with breast and/or epithelial ovarian/fallopian tube/primary peritoneal cancer, at any age
    - Close male blood relative with breast cancer
    - Personal history of epithelial ovarian/fallopian tube/primary peritoneal cancer
    - If of certain ethnicity associated with higher mutation frequency, (e.g., founder populations of Ashkenazi Jewish, Icelandic, Swedish, Hungarian or other) no additional family history required
    - a close relative with a known BRCA1 or BRCA2 gene mutation
2. Personal history of epithelial ovarian/fallopian tube/primary peritoneal cancer.
3. Personal history of male breast cancer.

Oncotype Diagnostic Test for Breast Cancer Prognosis

The Oncotype DX test is covered for patients with estrogen-receptor positive, node-negative carcinoma of the breast, for patients with estrogen receptor positive micro metastases of carcinoma of the breast, and for patients with estrogen positive breast carcinoma with 1-3 positive nodes.

Medical tests are covered only when ordered by the treating physician, when necessary for diagnosis or treatment decisions, and when used in patient care. Documentation on file with the treating physician should

indicate that results of the Oncotype DX test are expected to play a significant role in management of the patient. For example, a patient with a large, high grade carcinoma who, in agreement with the oncologist and patient, has decided to have adjuvant chemotherapy regardless of the results of the test would not be an appropriate candidate for this test. In certain circumstances the lymph nodes are indeterminable or unknown at diagnosis. Examples include: a patient having undergone a previous surgery removing the lymph nodes or where treatment decisions are needed prior to the initial surgery. Palmetto will consider payment for patients where the lymph node status is unknown or indeterminable when all other criteria for ordering Oncotype Dx are met (i.e. timeliness of the test and when used by the physician to guide a treatment decision).
A key output of the Oncotype DX test is its use in decision-making for adjuvant chemotherapy of non-metastatic breast carcinoma or for patients with micro metastases and/or 1-3 positive nodes. Usually chemotherapies have been studied for effectiveness based on initiation within 3 months of diagnosis. Oncotype DX test is not considered reasonable and necessary for care when more than six months have elapsed since diagnosis, since the value of the test for highly delayed chemotherapy is not established.
Breast cancer that is ER negative or has 4 or more positive lymph nodes is not covered for this test because clinical test show the test cannot be used for prognosis or determination of clinical course.

Mammaprint Test – Breast Cancer Prognosis

The test is covered for breast cancer that is estrogen receptor positive or negative and non-invasive (node negative) or invasive stage I or 2. In addition, more recent clinical data supports its use for nodal micro metastases and for patients with 1-3 positive lymph nodes. As is true for other clinical laboratory tests, controls, estrogen receptor and confirmatory results are considered part of the initial payment for the test.

Typically one would not perform this test more than once in a lifetime; but there are rare conditions where breast cancer can occur in a contralateral breast that is of a different cell type or different gene expression. In these cases a second test will be covered. Chart documentation should support the second test.

Based on analysis of peer-reviewed publications, FDA approval, local guidance by practicing oncologists, review by knowledgeable pathologists, and guidance from our Contractor Advisory Committee oncologists, Palmetto GBA has determined that the MammaPrint genetic expression profiling test is considered safe and effective and reasonable and necessary to contribute to breast cancer prognoses with the following limitations:

1. Characteristics of the Disease
   The MammaPrint test is covered for patients with breast cancer with the following criteria:
   - Tumor size <5.0 cm
   - Lymph node negative
   - Stage 1 and Stage 2 invasive breast cancer
   - ER+ or ER-
   - Tamoxifen independent
   - Nodal micro metastases (< 2.0 mm)
   - No more than three positive lymph nodes
2. Medical Necessity of the Test
   Medical tests are covered only when ordered by the treating physician, when necessary for diagnosis or treatment decisions, and when used in patient care. Documentation on file with the treating physician should indicate that results of the MammaPrint test are expected to play a significant role (along with other clinical findings) in the prognosis of the patient. For example, a patient with a large, high grade stage 3 invasive carcinoma who in agreement with the oncologist and patient, has decided to have adjuvant chemotherapy regardless of the results of the test would not be an appropriate candidate for this test.
3. Timeliness of the Test
   MammaPrint is FDA approved for assisting in the prognosis of patients with breast cancer of non-metastatic or stage 1 and 2 invasive breast carcinoma. In addition, more recent clinical data supports its use for micro metastases and for 1-3 positive lymph nodes. Usual chemotherapies have been studied for effectiveness based on initiation within 3 months of diagnosis. MammaPrint test is not considered reasonable and necessary for care when more than six months have elapsed since diagnosis, or if chemotherapy has been initiated, since the value of the test for highly delayed chemotherapy is not established.

Hereditary Colorectal Cancer Syndromes

hMLH1, hMSH2, hMSH6 and PMS2 gene tests are covered to diagnose Lynch syndrome. hMLH1, hMSH2 and

hMSH6 gene testing must be negative before a test for the less common PMS2gene mutations is considered reasonable and necessary. The tests are covered for a member who has or has had colorectal or endometrial cancer and meets one of the following criteria:

1. Amsterdam II Criteria for Lynch syndrome genetic testing

   At least two close relatives of the affected member must have or have had a cancer associated with Lynch syndrome; and all of the following criteria must be present:

   - One must be a first-degree relative of the other two;
   - At least two successive generations must be affected;
   - At least one of the relatives or the member with cancer associated with hereditary non-polyposis colorectal cancer should be diagnosed before the age 50 years;
   - Familial adenomatous polyposis (FAP) should be excluded in the colorectal cancer case(s) (if any);
   - Histologic diagnosis of tumors should be verified whenever possible.

2. Revised Bethesda guidelines
   - Colorectal cancer diagnosed in a member at less than 50 years of age
   - Presence of synchronous or metachronous Lynch syndrome-associated cancers*, regardless of age
   - Colorectal cancer with the MSI-H histology diagnosed in a member who is less than 60 years of age
   - Colorectal cancer with one or more first-degree relatives with a Lynch syndrome-associated cancer*, with one of the cancers being diagnosed under age 50 years
   - Colorectal cancer with two or more first- or second-degree relatives with Lynch syndrome-associated cancers*, regardless of age

   * Lynch syndrome-associated cancers include endometrial, ovarian, gastric, pancreas, ureter and renal pelvis, biliary tract, brain (usually glioblastoma), and small intestine cancers, as well as sebaceous gland adenomas/carcinomas and keratoacanthomas.
3. Has a blood relative with a known Lynch syndrome related gene mutation
4. Endometrial cancer diagnosed in a member at less than 50 years of age

   5. If any of the Bethesda guidelines are met, microsatellite instability (MSI) and/or immunohistochemistry (IHC) testing on the colon cancer tissue may be clinically appropriate. If the tumor is MSI positive or mutation of one of the mismatch repair genes is indicated by failure of IHC staining, then genetic testing should be undertaken. Further unnecessary testing can often be avoided by performance of IHC prior to any MSI testing. NAS leaves to the provider's judgment and the individual clinical situation in determining the order of performance of any of these two test protocols. This does not apply to MSI or IHC testing of non-GI primary tumors since the sensitivity and specificity of MSI/IHC testing in these tumors is poorly documented at this time.

   APC and MYH gene testing for Familial Adenomatous Polyposis (FAP), Attenuated FAP (AFAP), or MYH-associated polyposis (MAP) is covered for the following individuals;

   - A member with ≥ 20 cumulative colorectal adenomas over a lifetime.
   - Testing for APC gene mutations should precede testing for the less common MYH mutation.

HLA-B*5701 Testing

The Department of Health and Human Services (DHHS) Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) is a working group of the Office of AIDS Research Advisory Council (OARAC). The Panel recommends HLA-B*5701 testing prior to initiating abacavir therapy to reduce the risk of hypersensitivity reaction. HLA-B*5701-positive patients should not be prescribed abacavir, and the positive status should be recorded as an abacavir allergy in the patient's medical record.

Therapy-Directing testing

Coverage for KRAS testing is limited to use in patients with metastatic colorectal cancer for whom either cetuximab (Erbitux) or panitumumab (Vectibix) therapy is contemplated as being appropriate. Although there remain some unanswered questions concerning the role of "personalized medicine," it appears that there is sufficient sensitivity and specificity in the K-RAS testing to allow the decision to be made that use of either of the two drugs noted above would be inappropriate if the KRAS mutation is identified.

Coverage for JAK2 testing is appropriate in patients with signs or symptoms suggesting an underlying chronic myeloproliferative disorder, including increased red-cell mass, increased platelets, unexplained persistent peripheral cytopenia to cytosis, unexplained peripheral or hepatic vein thrombosis (Budd-Chiari Syndrome) or

bone marrow examination showing features of a chronic myeloproliferative disorder. Documentation must also indicate that the provider anticipates that the test result is likely to be of use in management of the condition. The *BCR/ABL fusion* gene is the classic mutation seen in Chronic Myelogenous Leukemia (CML) and is also seen in Acute Lymphocytic Leukemia (ALL) and certain other hematologic diseases. Major factors influencing consideration of testing for this gene include some that are too non-specific to support coverage.

Multiple Myeloma Gene Expression Profile

Should the criteria not be met, denial will occur.
This test will not be used to make the diagnosis of multiple myeloma or as a 'rule/out' event. This test will not be for monitoring therapy on a routine basis. It is expected this test will be needed no more than three times during the clinical history of a myeloma patient and not to exceed twice in one year. Edits to monitor use have been made, and denials after exceeding the above limits will be reviewed in the appeals process for potential coverage.

Loss-of-Heterozygosity Based Topographic Genotyping with PathfinderTG®

PathfinderTG® Technology will be covered as a "reasonable and necessary" service specifically and only for the indications of pancreatic cyst/mass where diagnostic evaluations are inconclusive under "Coverage with Appropriateness Development," in keeping with the Social Security Act Section 1862(a)(1)(A) allowance for "Coverage with Appropriateness Development."

Heartsbreath

Effective for services performed on or after December 8, 2008, the Centers for Medicare & Medicaid Services has determined that the evidence does not adequately define the technical characteristics of the test nor demonstrate that Heartsbreath testing to predict heart transplant rejection improves health outcomes in Medicare beneficiaries. Thus, we conclude that the Heartsbreath test is not reasonable and necessary under section 1862(a) (1) (A) of the Social Security Act and is non-covered.

ChemoFx

For states with no LCDs or Articles, refer to the UHC Medical Policy for Chemosensitivity and Chemoresistance Assay in Cancer for coverage guidelines.

- *Chemoresistance assays and chemosensitivity assays (including, but not limited to, the ChemoFX® assay) are unproven for predicting response to chemotherapy.* Results of the available studies fail to provide convincing evidence that information obtained with chemoresistance and chemosensitivity testing is beneficial for health outcomes in patients with cancer. Although numerous studies have been conducted, the evidence does not demonstrate that there is an improved survival among patients in whom chemosensitivity and chemoresistance assays were used to select chemotherapy regimens. Well-designed prospective, randomized controlled clinical trials are needed to determine the impact of chemosensitivity and chemoresistance assays on tumor response and patient survival. Medicare does not cover human tumor drug sensitivity assays as they are considered experimental.

Sweat Test

The sweat test is an important diagnostic tool in cystic fibrosis and may be covered when used for that purpose. Usage of the sweat test as a predictor of efficacy of sympathectomy in peripheral vascular disease is unproven and, therefore, is *not covered*. (NCD 190.5)

AlloMap

No coverage information could be found.

Documentation Guidelines

The medical record must contain documentation that the testing is expected to influence treatment of the condition toward which the testing is directed.

The documentation is not required at the time of the initial claim, but may be requested for post-payment review. Documentation must be adequate to verify that coverage guidelines listed above have been met. The documentation, which must be made available upon request from the laboratory or billing provider, must include personal and family history information consistent with this policy, and a *signed informed consent* indicating that the patient was informed of the following issues and information:

- cancer risks associated with each possible test result
- likelihood of carrying a gene mutation given the patient's personal and family history (e.g. pedigree analysis)

- implication for family members
- potential adverse effects, benefits, and limitations of testing
- relevant management options such as surveillance, prophylactic surgery, and medical preventive or therapeutic measures if available and risks associated with them.

For these tests, the billing provider must provide to the laboratory copies of the signed informed consent documentation.
The laboratory or billing provider must have on file the physician requisition which sets forth the diagnosis or condition (ICD-9-CM code) that warrants the test.
The documentation must be made available from the billing provider (i.e. the laboratory) upon request.
The HCPCS/CPT code(s) may be subject to Correct Coding Initiative (CCI) edits. This policy does not take precedence over CCI edits. Please refer to the CCI for correct coding guidelines and specific applicable code combinations prior to billing Medicare.
When the documentation does not meet the criteria for the service rendered or the documentation does not establish the medical necessity for the services, such services will be denied as not reasonable and necessary under Section 1862(a)(1) of the Social Security Act.

Oncotype Diagnostic Test for Breast Cancer Prognosis

Available documentation with the laboratory and/or the ordering physician should indicate that the patient has carcinoma of the breast which is hormone-receptor positive and node-negative and:

- Node-negative
- Micro metastases present
- Three or less positive nodes.

In addition, documentation of the ordering physician prior to ordering the test should indicate that the intention to treat or not treat with adjuvant chemotherapy would be contingent, at least in part, on the results of the test for the individual patient in question.
Negotiated rulemaking for laboratories indicate that upon medical review and determinations of the contractor, payment to the billing laboratory may be denied based on inadequate or nonsupportive documentation of a referring physician.
Genomic Health public documents filed with the SEC note that Oncotype DX is not currently regulated by the FDA (neither approved nor disapproved), but this status could be subject to change.

Mammaprint Test – Breast Cancer Prognosis

Available documentation with the laboratory and/or the ordering physician should indicate that the patient has carcinoma of the breast which is either estrogen-receptor positive or negative and:

- Non-invasive Node-negative
- Invasive stage 1 or 2
- Invasive with nodal micro metastases
- Invasive with no more than three positive lymph nodes

In addition, documentation of the ordering physician prior to ordering the test should indicate that the prognostic results of the test (along with other testing and discussions with the patients) will be used by the physician in the overall decision making for the patient.
Agendia, the company that manufactures and performs the MammaPrint test has established clearance with the FDA for the test.

Multiple Myeloma Gene Expression Profile

1. Documentation supporting the medical necessity should be legible, maintained in the patient's medical record and made available to Medicare upon request.
2. 'MyPRS' should be entered in box 19, or electronic equivalent, on the claim with a diagnosis of 203.00 for initial testing after diagnosis, and 203.02 for those beneficiaries in relapse.
3. As most of the claims will be generated by a reference laboratory, intake information should be adequate for any reviews by any Medicare contractors who may ask for documentation to support the testing.

Loss-of-Heterozygosity Based Topographic Genotyping with PathfinderTG®

1. All documentation must be maintained in the patient's medical record and available to the contractor upon

request.

2. Every page of the record must be legible and include appropriate patient identification information (e.g., complete name, dates of service(s)). The record must include the physician or non-physician practitioner responsible for and providing the care of the patient.
3. The submitted medical record should support the use of the selected ICD-9-CM code(s). The submitted CPT/HCPCS code should describe the service performed.
4. The date of service for laboratory specimens.

According to the Medicare Internet Only Manual; 100-04 Claims Processing; Chapter 16, Section 40.8 and 42 CFR §414.510, the date of service for laboratory tests is as follows:

General Rule
The date of service (DOS) of the test shall be the date the specimen was collected.
Variation
If a specimen is collected over a period that spans two calendar days, then the DOS shall be the date the collection ended.
Exceptions
DOS for tests performed on stored specimens

In the case of a test performed on a stored specimen, if a specimen was stored for less than or equal to 30 calendar days from the date it was collected, the DOS of the test must be the date the test was performed **only if**:

- The test is ordered by the patient's physician 14 days following the date of the patient's discharge from hospital;
- The specimen was collected while the patient was undergoing a hospital surgical procedure;
- It would be medically inappropriate to have collected the sample other than during the hospital procedure for which the patient was admitted;
- The results of the test do not guide treatment provided during the hospital stay; **AND**
- The test was reasonable and medically necessary for the treatment of illness.

If the specimen was stored for more than 30 calendar days before testing, the specimen was considered to have been archived and the DOS of the test must be the date the specimen was obtained from storage.

Cytogenetic Studies

The term cytogenetic study is used to describe the microscopic examination of the physical appearance of human chromosomes.

Medicare covers these tests when they are reasonable and necessary for the diagnosis or treatment of the following conditions:

1. Genetic disorders (e.g., mongolism) in a fetus
2. Failure of sexual development
3. Chronic myelogenous leukemia
4. Acute leukemias lymphoid (FAB L1-L3), myeloid (FAB M0-M7), and unclassified
5. Myelodysplasia

CPT / HCPCS Codes

Code	Description
0279T	Cell enumeration using immunologic selection and identification in fluid specimen (eg, circulating tumor cells in blood). Deleted 01/01/2013 and replaced with 86152
0280T	Cell enumeration using immunologic selection and identification in fluid specimen (eg, circulating tumor cells in blood); interpretation and report. Deleted 01/01/2013 and replaced with 86153
81161	DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed
81200	ASPA (aspartoacylase) (e.g., Canavan disease) gene analysis, common variants (e.g., E285A, Y231X)

Molecular Pathology/Molecular Diagnostics/Genetic Testing

81201	APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; full gene sequence
81202	APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; known familial variants
81203	APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; duplication/deletion variants
81205	BCKDHB (branched-chain keto acid dehydrogenase E1, beta polypeptide) (e.g., Maple syrup urine disease) gene analysis, common variants (e.g., R183P, G278S, E422X)
81206	BCR/ABL1 (t(9;22)) (e.g., chronic myelogenous leukemia) translocation analysis; major breakpoint, qualitative or quantitative
81207	BCR/ABL1 (t(9;22)) (e.g., chronic myelogenous leukemia) translocation analysis; minor breakpoint, qualitative or quantitative
81208	BCR/ABL1 (t(9;22)) (e.g., chronic myelogenous leukemia) translocation analysis; other breakpoint, qualitative or quantitative
81209	BLM (Bloom syndrome, RecQ helicase-like) (e.g., Bloom syndrome) gene analysis, 2281del6ins7 variant
81210	BRAF (v-raf murine sarcoma viral oncogene homolog B1) (e.g., colon cancer), gene analysis, V600E variant
81211	BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants in BRCA1 (i.e., exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)
81212	BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants
81213	BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; uncommon duplication/deletion variants
81214	BRCA1 (breast cancer 1) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants (i.e., exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)
81215	BRCA1 (breast cancer 1) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant
81216	BRCA2 (breast cancer 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81217	BRCA2 (breast cancer 2) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; common variants (e.g., ACMG/ACOG guidelines)
81221	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; known familial variants
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; duplication/deletion variants
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; full gene sequence
81224	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; intron 8 poly-T analysis (e.g., male infertility)
81225	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *4, *8, *17)

Molecular Pathology/Molecular Diagnostics/Genetic Testing

81226	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN)
81227	CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *5, *6)
81228	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (e.g., Bacterial Artificial Chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis)
81229	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities
81235	EGFR (epidermal growth factor receptor) (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)
81240	F2 (prothrombin, coagulation factor II) (e.g., hereditary hypercoagulability) gene analysis, 20210G>A variant
81241	F5 (coagulation Factor V) (e.g., hereditary hypercoagulability) gene analysis, Leiden variant
81242	FANCC (Fanconi anemia, complementation group C) (e.g., Fanconi anemia, type C) gene analysis, common variant (e.g., IVS4+4A>T)
81243	FMR1 (Fragile X mental retardation 1) (e.g., fragile X mental retardation) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles
81244	FMR1 (Fragile X mental retardation 1) (e.g., fragile X mental retardation) gene analysis; characterization of alleles (e.g., expanded size and methylation status)
81245	FLT3 (fms-related tyrosine kinase 3) (e.g., acute myeloid leukemia), gene analysis, internal tandem duplication (ITD) variants (i.e., exons 14, 15)
81250	G6PC (glucose-6-phosphatase, catalytic subunit) (e.g., Glycogen storage disease, Type 1a, von Gierke disease) gene analysis, common variants (e.g., R83C, Q347X)
81251	GBA (glucosidase, beta, acid) (e.g., Gaucher disease) gene analysis, common variants (e.g., N370S, 84GG, L444P, IVS2+1G>A)
81252	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; full gene sequence
81253	GJB2 (gap junction protein, beta 2, 26kDa; connexin 26) (eg, nonsyndromic hearing loss) gene analysis; known familial variants
81254	GJB6 (gap junction protein, beta 6, 30kDa, connexin 30) (eg, nonsyndromic hearing loss) gene analysis, common variants (eg, 309kb [del(GJB6-D13S1830)] and 232kb [del(GJB6-D13S1854)])
81255	HEXA (hexosaminidase A [alpha polypeptide]) (e.g., Tay-Sachs disease) gene analysis, common variants (e.g., 1278insTATC, 1421+1G>C, G269S)
81256	HFE (hemochromatosis) (e.g., hereditary hemochromatosis) gene analysis, common variants (e.g., C282Y, H63D)
81257	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis, for common deletions or variant (e.g., Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, alpha4.2, alpha20.5, and Constant Spring)
81260	IKBKAP (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein) (e.g., familial dysautonomia) gene analysis, common variants (e.g., 2507+6T>C, R696P)

Molecular Pathology/Molecular Diagnostics/Genetic Testing

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	IGH@ (Immunoglobulin heavy chain locus) (e.g., leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); 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)
81265	Comparative analysis using Short Tandem Repeat (STR) markers; patient and comparative specimen (e.g., pre-transplant recipient and donor germline testing, post-transplant non-hematopoietic recipient germline [e.g., buccal swab or other germline tissue sample] and donor testing, twin zygosity testing, or maternal cell contamination of fetal cells)
81266	Comparative analysis using Short Tandem Repeat (STR) markers; each additional specimen (e.g., additional cord blood donor, additional fetal samples from different cultures, or additional zygosity in multiple birth pregnancies) (List separately in addition to code for primary procedure)
81267	Chimerism (engraftment) analysis, post transplantation specimen (e.g., hematopoietic stem cell), includes comparison to previously performed baseline analyses; without cell selection
81268	Chimerism (engraftment) analysis, post transplantation specimen (e.g., hematopoietic stem cell), includes comparison to previously performed baseline analyses; with cell selection (e.g., CD3, CD33), each cell type
81270	JAK2 (Janus kinase 2) (e.g., myeloproliferative disorder) gene analysis, p.Val617Phe (V617F) variant
81275	KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (e.g., carcinoma) gene analysis, variants in codons 12 and 13
81280	Long QT syndrome gene analyses (e.g., KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); full sequence analysis
81281	Long QT syndrome gene analyses (e.g., KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); known familial sequence variant
81282	Long QT syndrome gene analyses (e.g., KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); duplication/deletion variants
81287	MGMT (O-6-methylguanine-DNA methyltransferase) (eg, glioblastoma multiforme), methylation analysis. (New Code for 2014)
81290	MCOLN1 (mucolipin 1) (e.g., Mucolipidosis, type IV) gene analysis, common variants (e.g., IVS3-2A>G, del6.4kb)
81291	MTHFR (5,10-methylenetetrahydrofolate reductase) (e.g., hereditary hypercoagulability) gene analysis, common variants (e.g., 677T, 1298C)
81292	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81293	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81294	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81295	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis

Molecular Pathology/Molecular Diagnostics/Genetic Testing

81296	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81297	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81298	MSH6 (mutS homolog 6 [E. coli]) (e.g. hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81299	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81300	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81301	Microsatellite instability analysis (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) of markers for mismatch repair deficiency (e.g., BAT25, BAT26), includes comparison of neoplastic and normal tissue, if performed
81302	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; full sequence analysis
81303	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; known familial variant
81304	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; duplication/deletion variants
81310	NPM1 (nucleophosmin) (e.g., acute myeloid leukemia) gene analysis, exon 12 variants
81315	PML/RARalpha, (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	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (e.g., promyelocytic leukemia) translocation analysis; single breakpoint (e.g., intron 3, intron 6 or exon 6), qualitative or quantitative
81317	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81318	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81319	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81321	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis
81322	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; known familial variant
81323	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; duplication/deletion variant
81324	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; duplication/deletion analysis
81325	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; full sequence analysis
81326	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; known familial variant
81330	SMPD1(sphingomyelin phosphodiesterase 1, acid lysosomal) (e.g., Niemann-Pick disease, Type A) gene analysis, common variants (e.g., R496L, L302P, fsP330)

Molecular Pathology/Molecular Diagnostics/Genetic Testing

81331	SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (e.g., Prader-Willi syndrome and/or Angelman syndrome), methylation analysis
81332	SERPINA1 (serpin peptidase inhibitor, clade A, alpha-1 antiproteinase, antitrypsin, member 1) (e.g., alpha-1-antitrypsin deficiency), gene analysis, common variants (e.g., *S and *Z)
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	TRB@ (T cell antigen receptor, beta) (e.g., leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); 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)
81355	VKORC1 (vitamin K epoxide reductase complex, subunit 1) (e.g., warfarin metabolism), gene analysis, common variants (e.g., -1639/3673)
81370	HLA Class I and II typing, low resolution (e.g., antigen equivalents); HLA-A, -B, -C, -DRB1/3/4/5, and -DQB1
81371	HLA Class I and II typing, low resolution (e.g., antigen equivalents); HLA-A, -B, and -DRB1/3/4/5 (e.g., verification typing)
81372	HLA Class I typing, low resolution (e.g., antigen equivalents); complete (i.e., HLA-A, -B, and -C)
81373	HLA Class I typing, low resolution (e.g., antigen equivalents); one locus (e.g., HLA-A, -B, or -C), each
81374	HLA Class I typing, low resolution (e.g., antigen equivalents); one antigen equivalent (e.g., B*27), each
81375	HLA Class II typing, low resolution (e.g., antigen equivalents); HLA-DRB1/3/4/5 and -DQB1
81376	HLA Class II typing, low resolution (e.g., antigen equivalents); one locus (e.g., HLA-DRB1/3/4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each
81377	HLA Class II typing, low resolution (e.g., antigen equivalents); one antigen equivalent, each
81378	HLA Class I typing, high resolution (i.e., alleles or allele groups); complete (i.e., HLA-A, -B, and -C)
81379	HLA Class I typing, high resolution (i.e., alleles or allele groups); complete (i.e., HLA-A, -B, and -C)
81380	HLA Class I typing, high resolution (i.e., alleles or allele groups); one locus (e.g., HLA-A, -B, or -C), each
81381	HLA Class I typing, high resolution (i.e., alleles or allele groups); one allele or allele group (e.g., B*57:01P), each
81382	HLA Class II typing, high resolution (i.e., alleles or allele groups); one locus (e.g., HLA-DRB1, -DRB3, -DRB4, -DRB5, -DQB1, -DQA1, -DPB1, or -DPA1), each
81383	HLA Class II typing, high resolution (i.e., alleles or allele groups); one allele or allele group (e.g., HLA-DQB1*06:02P), each
81400	Molecular pathology procedure, Level 1 analysis)(eg, identification of single germline variant [eg, SNP] by techniques such as restriction enzyme digestion or melt curve analysis) ACADM (acyl-CoA dehydrogenase, C-4 to C-12 straight chain, MCAD) (e.g., medium chain acyl dehydrogenase deficiency), K304E variant ACE (angiotensin converting enzyme) (e.g., hereditary blood pressure regulation), insertion/deletion variant AGTR1 (angiotensin II

	receptor, type 1) (e.g., essential hypertension), 1166A>C variant CCR5 (chemokine C-C motif receptor 5) (e.g., HIV resistance), 32-bp deletion mutation/794 825del32 deletion DPYD (dihydropyrimidine dehydrogenase) (e.g., 5-fluorouracil/5-FU and capecitabine drug metabolism), IVS14+1G>A variant F2 (coagulation factor 2) (e.g., hereditary hypercoagulability), 1199G>A variant F5 (coagulation factor V) (e.g., hereditary hypercoagulability), HR2 variant F7 (coagulation factor VII [serum prothrombin conversion accelerator]) (e.g., hereditary hypercoagulability), R353Q variant F13B (coagulation factor XIII, B polypeptide) (e.g., hereditary hypercoagulability), V34L variant FGB (fibrinogen beta chain) (e.g., hereditary ischemic heart disease), -455G>A variant Human Platelet Antigen 1 genotyping (HPA-1), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa], antigen CD61 [GPIIIa]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), HPA-1a/b (L33P) Human Platelet Antigen 2 genotyping (HPA-2), GP1BA (glycoprotein Ib [platelet], alpha polypeptide [GPIba]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), HPA-2a/b (T145M) Human Platelet Antigen 3 genotyping (HPA-3), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex], antigen CD41 [GPIIb]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), HPA-3a/b (I843S) Human Platelet Antigen 4 genotyping (HPA-4), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa], antigen CD61 [GPIIIa]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), HPA-4a/b (R143Q) Human Platelet Antigen 5 genotyping (HPA-5), ITGA2 (integrin, alpha 2 [CD49B, alpha 2 subunit of VLA-2 receptor] [GPIa]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), HPA-5a/b (K505E) Human Platelet Antigen 6 genotyping (HPA-6w), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa, antigen CD61] [GPIIIa]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), HPA-6a/b (R489Q) Human Platelet Antigen 9 genotyping (HPA-9w), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex, antigen CD41] [GPIIb]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), HPA-9a/b (V837M) Human Platelet Antigen 15 genotyping (HPA-15), CD109 (CD109 molecule) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), HPA-15a/b(S682Y) SERPINE1 (serpine peptidase inhibitor clade E, member 1, plasminogen activator inhibitor -1, PAI-1) (e.g., thrombophilia), 4G variant
81401	Molecular pathology procedure, Level 2 (e.g., 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat) ABL (c-abl oncogene 1, receptor tyrosine kinase) (e.g., acquired imatinib resistance), T315I variant ACADM (acyl-CoA dehydrogenase, C-4 to C-12 straight chain, MCAD) (e.g., medium chain acyl dehydrogenase deficiency), common variants (e.g., K304E, Y42H) ADRB2 (adrenergic beta-2 receptor surface) (e.g., drug metabolism), common variants (e.g., G16R, Q27E) APOE (apolipoprotein E) (e.g., hyperlipoproteinemia type III, cardiovascular disease, Alzheimer disease), common variants (e.g., *2, *3, *4) CBFB/MYH11 (inv(16)) (e.g., acute myeloid leukemia), qualitative, and quantitative, if performed CCND1/IGH (BCL1/IgH, t(11;14)) (e.g., mantle cell lymphoma) translocation analysis, major breakpoint, qualitative, and quantitative, if performed CFH/ARMS2 (complement factor H/age-related maculopathy susceptibility 2) (e.g., macular degeneration), common variants (e.g., Y402H [CFH], A69S [ARMS2]) CYP3A4 (cytochrome P450, family 3, subfamily A, polypeptide 4) (e.g., drug metabolism), common variants (e.g., *2, *3, *4, *5, *6) CYP3A5 (cytochrome P450, family 3, subfamily A, polypeptide 5) (e.g., drug metabolism), common variants (e.g., *2, *3, *4, *5, *6) DMPK (dystrophia myotonica-protein kinase) (e.g., myotonic dystrophy, type 1), evaluation to detect abnormal (e.g., expanded) alleles F11 (coagulation factor XI) (e.g., coagulation disorder), common variants (e.g., E117X [Type II], F283L [Type III], IVS14del14, and IVS14+1G>A [Type I]) FGFR3 (fibroblast growth factor receptor 3) (e.g., achondroplasia), common variants (e.g., 1138G>A, 1138G>C) FIP1L1/PDGFRA (del[4q12]) (e.g., imatinib-sensitive chronic eosinophilic leukemia), qualitative, and quantitative, if performed GALT (galactose-1-phosphate uridylyltransferase) (e.g., galactosemia), common variants (e.g., Q188R, S135L, K285N, T138M, L195P, Y209C, IVS2-2A>G, P171S, del5kb, N314D, L218L/N314D) HBB (hemoglobin, beta) (e.g., sickle cell anemia, hemoglobin C, hemoglobin E), common variants (e.g., HbS, HbC, HbE) HTT

	(huntingtin) (e.g., Huntington disease), evaluation to detect abnormal (e.g., expanded) alleles RUNX1/RUNX1T1 (t(8;21)) (e.g., acute myeloid leukemia) translocation analysis, qualitative, and quantitative, if performed SEPT9 (Septin 9) (e.g., colon cancer), methylation analysis TPMT (thiopurine S-methyltransferase) (e.g., drug metabolism), common variants (e.g., *2, *3) VWF (von Willebrand factor) (e.g., von Willebrand disease type 2N), common variants (e.g., T791M, R816W, R854Q)
81402	Molecular pathology procedure, Level 3 (e.g., >10 SNPs, 2-10 methylated variants, or 2-10 somatic variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants 1 exon) CYP21A2 (cytochrome P450, family 21, subfamily A, polypeptide 2) (e.g., congenital adrenal hyperplasia, 21-hydroxylase deficiency), common variants (e.g., IVS2-13G, P30L, I172N, exon 6 mutation cluster [I235N, V236E, M238K], V281L, L307FfsX6, Q318X, R356W, P453S, G110VfsX21, 30-kb deletion variant) ESR1/PGR (receptor 1/progesterone receptor) ratio (e.g., breast cancer) KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (e.g., mastocytosis), common variants (e.g., D816V, D816Y, D816F) MEFV (Mediterranean fever) (e.g., familial Mediterranean fever), common variants (e.g., E148Q, P369S, F479L, M680I, I692del, M694V, M694I, K695R, V726A, A744S, R761H) MPL (myeloproliferative leukemia virus oncogene, thrombopoietin receptor, TPOR) (e.g., myeloproliferative disorder), common variants (e.g., W515A, W515K, W515L, W515R) TRD@ (T cell antigen receptor, delta) (e.g., leukemia and lymphoma), gene rearrangement analysis, evaluation to detect abnormal clonal population
81403	Molecular pathology procedure, Level 4 (e.g., analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons) ABL1 (c-abl oncogene 1, receptor tyrosine kinase) (e.g., acquired imatinib tyrosine kinase inhibitor resistance), variants in the kinase domain DAZ/SRY (deleted in azoospermia and sex determining region Y) (e.g., male infertility), common deletions (e.g., AZFa, AZFb, AZFc, AZFd) GJB1 (gap junction protein, beta 1) (e.g., Charcot-Marie-Tooth X-linked), full gene sequence JAK2 (Janus kinase 2) (e.g., myeloproliferative disorder), exon 12 sequence and exon 13 sequence, if performed KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (e.g., carcinoma), gene analysis, variant(s) in exon 2 MPL (myeloproliferative leukemia virus oncogene, thrombopoietin receptor, TPOR) (e.g., myeloproliferative disorder), exon 10 sequence VHL (von Hippel-Lindau tumor suppressor) (e.g., von Hippel-Lindau familial cancer syndrome), deletion/duplication analysis VWF (von Willebrand factor) (e.g., von Willebrand disease types 2A, 2B, 2M), targeted sequence analysis (e.g., exon 28)
81404	Molecular pathology procedure, Level 5 (e.g., analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis) BTD (biotinidase) (e.g., biotinidase deficiency), full gene sequence CYP1B1 (cytochrome P450, family 1, subfamily B, polypeptide 1) (e.g., primary congenital glaucoma), full gene sequence DMPK (dystrophia myotonica-protein kinase) (e.g., myotonic dystrophy type 1), characterization of abnormal (e.g., expanded) alleles EGR2 (early growth response 2) (e.g., Charcot-Marie-Tooth), full gene sequence FKRP (Fukutin related protein) (e.g., congenital muscular dystrophy type 1C [MDC1C], limb-girdle muscular dystrophy [LGMD] type 2I), full gene sequence FOXG1 (forkhead box G1) (e.g., Rett syndrome), full gene sequence FSHMD1A (facioscapulohumeral muscular dystrophy 1A) (e.g., facioscapulohumeral muscular dystrophy), evaluation to detect abnormal (e.g., deleted) alleles FSHMD1A (facioscapulohumeral muscular dystrophy 1A) (e.g., facioscapulohumeral muscular dystrophy), characterization of haplotype(s) (i.e., chromosome 4A and 4B haplotypes) HBB (hemoglobin, beta, Beta-Globin) (e.g., thalassemia), full gene sequence KIT (C-kit) (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (e.g., GIST, acute myeloid leukemia, melanoma), targeted gene analysis (e.g., exons 8, 11, 13, 17, 18) LITAF (lipopolysaccharide-induced TNF factor) (e.g., Charcot-Marie-Tooth), full gene sequence MEFV (Mediterranean fever) (e.g., familial Mediterranean fever), full gene sequence NRAS

	(neuroblastoma RAS viral oncogene homolog) (e.g., colorectal carcinoma), exon 1 and exon 2 sequences PDGFRA (platelet-derived growth factor receptor alpha polypeptide) (e.g., gastrointestinal stromal tumor), targeted sequence analysis (e.g., exons 12, 18) RET (ret proto-oncogene) (e.g., multiple endocrine neoplasia, type 2B and familial medullary thyroid carcinoma), common variants (e.g., M918T, 2647_2648delinsTT, A883F) SDHD (succinate dehydrogenase complex, subunit D, integral membrane protein) (e.g., hereditary paraganglioma), full gene sequence VHL (von Hippel-Lindau tumor suppressor) (e.g., von Hippel-Lindau familial cancer syndrome), full gene sequence VWF (von Willebrand factor) (e.g., von Willebrand disease type 1C), targeted sequence analysis (e.g., exons 26, 27, 37)
81405	Molecular pathology procedure, Level 6 (e.g., analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons) CYP21A2 (cytochrome P450, family 21, subfamily A, polypeptide2) (e.g., steroid 21-hydroxylase isoform, congenital adrenal hyperplasia), full gene sequence FKTN (fukutin) (e.g., limb-girdle muscular dystrophy [LGMD] type 2M or 2L), full gene sequence MPZ (myelin protein zero) (e.g., Charcot-Marie-Tooth), full gene sequence NEFL (neurofilament, light polypeptide) (e.g., Charcot-Marie-Tooth), full gene sequence RET (ret proto-oncogene) (e.g., multiple endocrine neoplasia, type 2A and familial medullary thyroid carcinoma), targeted sequence analysis (e.g., exons 10, 11, 13-16) SDHB (succinate dehydrogenase complex, subunit B, iron sulfur) (e.g., hereditary paraganglioma), full gene sequence TGFBR1 (transforming growth factor, beta receptor 1) (e.g., Marfan syndrome), full gene sequence TGFBR2 (transforming growth factor, beta receptor 2) (e.g., Marfan syndrome), full gene sequence THRB (thyroid hormone receptor, beta) (e.g., thyroid hormone resistance, thyroid hormone beta receptor deficiency), full gene sequence or targeted sequence analysis of >5 exons TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome, tumor samples), full gene sequence or targeted sequence analysis of >5 exons VWF (von Willebrand factor) (e.g., von Willebrand disease type 2N), targeted sequence analysis (e.g., exons 18-20, 23-25)
81406	Molecular pathology procedure, Level 7 (e.g., analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia) CAPN3 (Calpain 3) (e.g., limb-girdle muscular dystrophy [LGMD] type 2A, calpainopathy), full gene sequence Cytogenomic microarray analysis, neoplasia (e.g., interrogation of copy number, and loss-of-heterozygosity via single nucleotide polymorphism [SNP]-based comparative genomic hybridization [CGH] microarray analysis) GALT (galactose-1-phosphate uridylyltransferase) (e.g., galactosemia), full gene sequence HEXA (hexosaminidase A, alpha polypeptide) (e.g., Tay-Sachs disease), full gene sequence LMNA (lamin A/C) (e.g., Emery-Dreifuss muscular dystrophy [EDMD1, 2 and 3] limb-girdle muscular dystrophy [LGMD] type 1B, dilated cardiomyopathy [CMD1A], familial partial lipodystrophy [FPLD2]), full gene sequence PAH (phenylalanine hydroxylase) (e.g., phenylketonuria), full gene sequence POLG (polymerase [DNA directed], gamma) (e.g., Alpers-Huttenlocher syndrome, autosomal dominant progressive external ophthalmoplegia), full gene sequence POMGNT1 (protein O-linked mannose beta1,2-N acetylglucosaminyltransferase) (e.g., muscle-eye-brain disease, Walker-Warburg syndrome), full gene sequence POMT1 (protein-O-mannosyltransferase 1) (e.g., limb-girdle muscular dystrophy [LGMD] type 2K, Walker-Warburg syndrome), full gene sequence POMT2 (protein-O-mannosyltransferase 2) (e.g., limb-girdle muscular dystrophy [LGMD] type 2N, Walker-Warburg syndrome), full gene sequence RYR1 (ryanodine receptor 1, skeletal) (e.g., malignant hyperthermia), targeted sequence analysis of exons with functionally confirmed mutations VWF (von Willebrand factor) (von Willebrand disease type 2A), extended targeted sequence analysis (e.g., exons 11-16, 24-26, 51, 52)
81407	Molecular pathology procedure, Level 8 (e.g., analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform) SCN1A (sodium channel, voltage-gated, type 1, alpha subunit) (e.g., generalized epilepsy with febrile seizures), full gene sequence
81408	Molecular pathology procedure, Level 9 (e.g., analysis of >50 exons in a single gene by DNA sequence analysis) FBN1 (fibrillin 1) (e.g., Marfan syndrome), full gene sequence NF1

	(neurofibromin 1) (e.g., neurofibromatosis, type 1), full gene sequence RYR1 (ryanodine receptor 1, skeletal) (e.g., malignant hyperthermia), full gene sequence VWF (von Willebrand factor) (e.g., von Willebrand disease types 1 and 3), full gene sequence
81479	Unlisted molecular pathology procedure
83890	Molecular diagnostics; molecular isolation or extraction, each nucleic acid type (i.e., DNA or RNA) Deleted 01/01/2013; See 81200-81479
83891	Molecular diagnostics; isolation or extraction of highly purified nucleic acid, each nucleic acid type (i.e., DNA or RNA). Deleted 01/01/2013; See 81200-81479
83892	Molecular diagnostics; enzymatic digestion, each enzyme treatment. Deleted 01/01/2013; See 81200-81479
83893	Molecular diagnostics; dot/slot blot production, each nucleic acid preparation. Deleted 01/01/2013; See 81200-81479
83894	Molecular diagnostics; separation by gel electrophoresis (e.g., agarose, polyacrylamide), each nucleic acid preparation. Deleted 01/01/2013; See 81200-81479
83896	Molecular diagnostics; nucleic acid probe, each. Deleted 01/01/2013; See 81200-81479
83898	Molecular diagnostics; amplification, target, each nucleic acid sequence. Deleted 01/01/2013; See 81200-81479
83900	Molecular diagnostics; amplification, target, multiplex, first 2 nucleic acid sequences. Deleted 01/01/2013; See 81200-81479
83904	Molecular diagnostics; mutation identification by sequencing, single segment, each segment. Deleted 01/01/2013; See 81200-81479
83909	Molecular diagnostics; separation and identification by high resolution technique (e.g., capillary electrophoresis), each nucleic acid preparation. Deleted 01/01/2013; See 81200-81479
83912	Molecular diagnostics; interpretation and report. Deleted 01/01/2013; See 81200-81479
84999	Unlisted chemistry procedure
85999	Unlisted hematology and coagulation procedure
86152	Cell enumeration using immunologic selection and identification in fluid specimen (eg, circulating tumor cells in blood)
86153	Cell enumeration using immunologic selection and identification in fluid specimen (eg, circulating tumor cells in blood); physician interpretation and report, when required
86849	Unlisted immunology procedure
87999	Unlisted microbiology procedure
88120	Cytopathology, in situ hybridization (eg, FISH), urinary tract specimen with morphometric analysis, 3-5 molecular probes, each specimen; manual
88121	Cytopathology, in situ hybridization (eg, FISH), urinary tract specimen with morphometric analysis, 3-5 molecular probes, each specimen; using computer-assisted technology
88199	Unlisted cytopathology procedure
88230	Tissue culture for non-neoplastic disorders; lymphocyte
88233	Tissue culture for non-neoplastic disorders; skin or other solid tissue biopsy
88235	Tissue culture for non-neoplastic disorders; amniotic fluid or chorionic villus cells
88237	Tissue culture for neoplastic disorders; bone marrow, blood cells
88239	Tissue culture for neoplastic disorders; solid tumor
88240	Cryopreservation, freezing and storage of cells, each cell line
88241	Thawing and expansion of frozen cells, each aliquot

Molecular Pathology/Molecular Diagnostics/Genetic Testing

88245	Chromosome analysis for breakage syndromes; baseline Sister Chromatid Exchange (SCE), 20-25 cells
88248	Chromosome analysis for breakage syndromes; baseline breakage, score 50-100 cells, count 20 cells, 2 karyotypes (eg, for ataxia telangiectasia, Fanconi anemia, fragile X)
88249	Chromosome analysis for breakage syndromes; score 100 cells, clastogen stress (eg, diepoxybutane, mitomycin C, ionizing radiation, UV radiation)
88261	Chromosome analysis; count 5 cells, 1 karyotype, with banding
88262	Chromosome analysis; count 15-20 cells, 2 karyotypes, with banding
88263	Chromosome analysis; count 45 cells for mosaicism, 2 karyotypes, with banding
88264	Chromosome analysis; analyze 20-25 cells
88267	Chromosome analysis, amniotic fluid or chorionic villus, count 15 cells, 1 karyotype, with banding
88269	Chromosome analysis, in situ for amniotic fluid cells, count cells from 6-12 colonies, 1 karyotype, with banding
88271	Molecular cytogenetics; DNA probe, each (eg, FISH)
88272	Molecular cytogenetics; chromosomal in situ hybridization, analyze 3-5 cells (eg, for derivatives and markers)
88273	Molecular cytogenetics; chromosomal in situ hybridization, analyze 10-30 cells (eg, for microdeletions)
88274	Molecular cytogenetics; interphase in situ hybridization, analyze 25-99 cells
88275	Molecular cytogenetics; interphase in situ hybridization, analyze 100-300 cells
88280	Chromosome analysis; additional karyotypes, each study
88283	Chromosome analysis; additional specialized banding technique (eg, NOR, C-banding)
88285	Chromosome analysis; additional cells counted, each study
88289	Chromosome analysis; additional high resolution study
88291	Cytogenetics and molecular cytogenetics, interpretation and report
88299	Unlisted cytogenetic study
88365	In situ hybridization (eg, FISH), each probe
88367	Morphometric analysis, in situ hybridization (quantitative or semi-quantitative) each probe; using computer-assisted technology
88368	Morphometric analysis, in situ hybridization (quantitative or semi-quantitative) each probe; manual
88399	Unlisted surgical pathology procedure
89240	Unlisted miscellaneous pathology test
89398	Unlisted reproductive medicine laboratory procedure
G0452	Molecular pathology procedure; physician interpretation and report
S0265	Genetic counseling, under physician supervision, each 15 minutes
S3800	Genetic testing for amyotrophic lateral sclerosis (ALS)
S3841	Genetic testing for retinoblastoma
S3842	Genetic testing for Von Hippel-Lindau disease
S3845	Genetic testing for alpha-thalassemia
S3846	Genetic testing for hemoglobin E beta-thalassemia
S3849	Genetic testing for Niemann-Pick disease

Molecular Pathology/Molecular Diagnostics/Genetic Testing

S3850	Genetic testing for sickle cell anemia
S3852	DNA analysis for APOE epsilon 4 allele for susceptibility to Alzheimer's disease
S3853	Genetic testing for myotonic muscular dystrophy
S3854	Gene expression profiling panel for use in the management of breast cancer treatment
S3855	Genetic testing for detection of mutations in the presenilin - 1 gene
S3861	Genetic testing, sodium channel, voltage-gated, type V, alpha subunit (SCN5A) and variants for suspected Brugada Syndrome
S3866	Genetic analysis for a specific gene mutation for hypertrophic cardiomyopathy (HCM) in an individual with a known HCM mutation in the family
S3870	Comparative genomic hybrization (CGH) microarray testing for developmental delay, autism spectrum disorder and/or mental retardation

Modifiers

Code	Description
0A	BRCA1 (hereditary breast/ovarian cancer) (Expired 12/31/2012)
0B	BRCA2 (hereditary breast cancer) (Expired 12/31/2012)
0C	Neurofibromin (neurofibromatosis, type 1) (Expired 12/31/2012)
0D	Merlin (neurofibromatosis, type 2) (Expired 12/31/2012)
0E	c-RET (multiple endocrine neoplasia, types 2A/B, familial medullary thyroid carcinoma) (Expired 12/31/2012)
0F	VHL (Von Hippel Lindau disease, renal carcinoma) (Expired 12/31/2012)
0G	SDHD (hereditary paraganglioma) (Expired 12/31/2012)
0H	SDHB (hereditary paraganglioma) (Expired 12/31/2012)
0I	ERRB2, commonly called Her-2/neu (Expired 12/31/2012)
0J	MLH1 (HNPCC, mismatch repair genes) (Expired 12/31/2012)
0K	MSH2, MSH6, or PMS2 (HNPCC, mismatch repair genes) (Expired 12/31/2012)
0L	APC (hereditary polyposis coli) (Expired 12/31/2012)
0M	Rb (retinoblastoma) (Expired 12/31/2012)
1Z	Sarcoma gene, not otherwise specified (Expired 12/31/2012)
26	Professional Component
2A	RUNX1 or CBFA2T1, commonly called AML1 or ETO, genes associated with t(8;21) AML1 - also ETO (acute myelogenous leukemia) (Expired 12/31/2012)
2B	BCR or ABL1, genes associated with t(9;22) (chronic myelogenous or acute leukemia) BCR-also ABL (chronic myeloid, acute lymphoid leukemia) (Expired 12/31/2012)
2C	PBX1 or TCF3, genes associated with t(1;19) (acute lymphoblastic leukemia) CGF1 (Expired 12/31/2012)
2D	CBFB or MYH11, genes associated with inv 16 (acute myelogenous leukemia) CBF beta (leukemia) (Expired 12/31/2012)
2E	MLL (acute leukemia) (Expired 12/31/2012)
2F	PML or RARA, genes associated with t(15;17) (acute promyelocytic leukemia) PML/RAR alpha (promyelocytic leukemia) (Expired 12/31/2012)
2G	ETV6, commonly called TEL, gene associated with t(12;21) (acute leukemia) TEL (Leukemia) (Expired 12/31/2012)
2H	BCL2 (B cell lymphoma, follicle center cell origin) BCL-2 (Lymphoma) (Expired 12/31/2012)

Molecular Pathology/Molecular Diagnostics/Genetic Testing

2I	CCND1, commonly called BCL1, cyclin D1 (Mantle cell lymphoma, myeloma) BCL-1 (lymphoma) (Expired 12/31/2012)
2J	Myc (Burkitt lymphoma) c-Myc (lymphoma) (Expired 12/31/2012)
2K	IgH (lymphoma/leukemia) (Expired 12/31/2012)
2Z	Lymphoid/hematopoetic neoplasia, not otherwise specified (Expired 12/31/2012)
3A	F5, commonly called Factor V (Leiden, others) (hypercoagulable state) (Expired 12/31/2012)
3B	FACC (Fanconi anemia) (Expired 12/31/2012)
3C	FACD (Fanconi anemia) (Expired 12/31/2012)
3D	HBB, beta globin (thalassemia, sickle cell anemia, other hemoglobinopathies) (Expired 12/31/2012)
3E	HBA, commonly called alpha globin (thalassemia) (Expired 12/31/2012)
3F	MTHFR (Elevated homocysteine) (Expired 12/31/2012)
3G	F2, commonly called prothrombin (20210, others) (hypercoagulable state) prothrombin (factor II, 20210A) (hypercoagulable state) (Expired 12/31/2012)
3H	F8, commonly called factor VIII (hemophilia A/VWF) (Expired 12/31/2012)
3I	F9, commonly called factor IX (hemophilia B) (Expired 12/31/2012)
3Z	Non-neoplastic hematology/coagulation, not otherwise specified (Expired 12/31/2012)
4A	HLA-A (Expired 12/31/2012)
4B	HLA-B* (Expired 12/31/2012)
4C	HLA-CI (Expired 12/31/2012)
4E	HLA-DR (Expired 12/31/2012)
4F	HLA-DQ* (Expired 12/31/2012)
4G	HLA-DP (Expired 12/31/2012)
4H	Kell (Expired 12/31/2012)
4Z	Histocompatibility/typing, not otherwise specified (Expired 12/31/2012)
52	Reduced Services
59	Distinct Procedural Service
5A	ASPA, commonly called Aspartoacylase A (Canavan disease) (Expired 12/31/2012)
5B	FMR-1 (fragile X, FRAXA, syndrome) (Expired 12/31/2012)
5C	FRDA, commonly called Frataxin (Freidreich ataxia) (Expired 12/31/2012)
5D	HD, commonly called Huntington (Huntington's disease) (Expired 12/31/2012)
5E	GABRA5, NIPA1, UBE3A, or ANCR GABRA (Prader Willi-Angelman syndrome) (Expired 12/31/2012)
5F	GJB2, commonly called Connexin-26 (hereditary hearing loss) Connexin-32 (GJB2) (hereditary deafness) (Expired 12/31/2012)
5G	GJB1, commonly called Connexin-32 (X-linked Charcot-Marie-Tooth disease) (Expired 12/31/2012)
5H	SNRPN (Prader Willi-Angelman syndrome) (Expired 12/31/2012)
5I	SCA1, commonly called Ataxin-1 (spinocerebellar ataxia, type 1) (Expired 12/31/2012)
5J	SCA2, commonly called Ataxin-2 (spinocerebellar ataxia, type 2) (Expired 12/31/2012)
5K	MJD, commonly called Ataxin-3 (spinocerebellar ataxia, type 3, Machado-Joseph disease) (Expired 12/31/2012)

Molecular Pathology/Molecular Diagnostics/Genetic Testing

5L	CACNA1A (spinocerebellar ataxia, type 6) (Expired 12/31/2012)
5M	ATXN7 Ataxin-7 (spinocerebellar ataxia, type 7) (Expired 12/31/2012)
5N	PMP-22 (Charcot-Marie-Tooth disease, type 1A) (Expired 12/31/2012)
5O	MECP2 (Rett syndrome) (Expired 12/31/2012)
5Z	Neurologic, non-neoplastic, not otherwise specified (Expired 12/31/2012)
6A	DMD, commonly called dystrophin (Duchenne/Becker muscular dystrophy) (Expired 12/31/2012)
6B	DMPK (myotonic dystrophy, type 1) (Expired 12/31/2012)
6C	ZNF-9 (myotonic dystrophy, type 2) (Expired 12/31/2012)
6D	SMN1/SMN2 (autosomal recessive spinal muscular atrophy) (Expired 12/31/2012)
6Z	Muscular, not otherwise specified (Expired 12/31/2012)
7A	APOE, commonly called apolipoprotein E (cardiovascular disease or Alzheimer's disease) (Expired 12/31/2012)
7B	NPC1 or NPC2, commonly called sphingomyelin phosphodiesterase (Nieman-Pick disease) (Expired 12/31/2012)
7C	GBA, commonly called acid beta glucosidase (Gaucher disease) (Expired 12/31/2012)
7D	HFE (hemochromatosis) (Expired 12/31/2012)
7E	HEXA, commonly called hexosaminidase A (Tay-Sachs disease) (Expired 12/31/2012)
7Z	Metabolic, other, not otherwise specified (Expired 12/31/2012)
8A	CFTR (cystic fibrosis) (Expired 12/31/2012)
8Z	Metabolic, transport, not otherwise specified (Expired 12/31/2012)
90	Reference (Outside) Laboratory
91	Repeat Clinical Diagnostic Laboratory Test
99	Multiple Modifiers
9A	TPMT, commonly called (thiopurine methyltransferase) (patients on antimetabolite therapy) (Expired 12/31/2012)
9L	Metabolic-pharmacogenetics, not otherwise specified (Expired 12/31/2012)
9M	FGFR1 (Pfeiffer and Kallmann syndromes) (Expired 12/31/2012)
9N	FGFR2 (Crouzon, Jackson-Weiss, Apert, Saethre-Chotzen syndromes) (Expired 12/31/2012)
9O	FGFR3 (achondroplasia, hypochondroplasia, thanatophoric dysplasia, types I and II, Crouzon syndrome with acanthosis nigricans, Muencke syndromes) (Expired 12/31/2012)
9P	TWIST (Saethre-Chotzen syndrome) (Expired 12/31/2012)
9Q	DGCR, commonly called CATCH-22 (DiGeorge and 22q11 deletion syndromes) (Expired 12/31/2012)
9Z	Dysmorphology, not otherwise specified (Expired 12/31/2012)
AQ	Physician providing a service in an unlisted health professional shortage area (HPSA)
AR	Physician provider services in a physician scarcity area
CR	Catastrophe/Disaster related
ET	Emergency services
GA	Waiver of liability statement issued as required by payer policy, individual case
GC	This service has been performed in part by a resident under the direction of a teaching physician

GY	Item or service statutorily excluded, does not meet the definition of any Medicare benefit or for non-Medicare insurers, is not a contract benefit
GZ	Item or service expected to be denied as not reasonable and necessary
KX	Requirements specified in the medical policy have been met
QP	Documentation is on file showing that the laboratory test(s) was ordered individually or ordered as a CPT-recognized panel other than automated profile codes 80002-80019, G0058, G0059, and G0060
CLIA	Clinical Laboratory Improvement Amendments

References Included (but not limited to):

CMS NCD(s)

NCD 190.3 Cytogenetic Studies

NCD 190.5 Sweat Test

NCD 190.7 Human Tumor Stem Cell Drug Sensitivity Assays

CMS LCD(s)

CMS Articles

Numerous Articles

CMS Benefit Policy Manual

Chapter 15; § 80.1–80.1.3 Clinical Laboratory Services

CMS Claims Processing Manual

Chapter 3; § 90.3.1-90.3.3 Allogeneic Stem Cell Transplantation/Billing for Stem Cell Transplantation

Chapter 4; § 231.11 Billing for Allogeneic Stem Cell Transplants

Chapter 12; § 60 Payment for Pathology Services

Chapter 16; § 10 Laboratory Services – General Explanation of Payment; § 40 & 40.7 Billing for Clinical Laboratory Tests/Billing for Noncovered Clinical Laboratory Tests

CMS Transmittals

Transmittal 2365, Change Request 7654, Dated 12/09/2011 (Calendar Year (CY) 2012 Annual Update for Clinical Laboratory Fee Schedule and Laboratory Services Subject to Reasonable Charge Payment)

UnitedHealthcare Medicare Advantage Coverage Summaries

Genetic Testing

Laboratory Tests and Services

Maternity and Newborn Care

UnitedHealthcare Reimbursement Policies

Preventive Lab Services

UnitedHealthcare Medical Policies

Chemosensitivity and Chemoresistance Assays in Cancer

Gene Expression Tests

Genetic Testing for Hereditary Breast and/or Ovarian Cancer Syndrome (HBOC)

MLN Matters

Article MM7137, Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Myelodysplastic Syndrome (MDS)

Others

Medicare National Coverage Determinations (NCD)Coding Policy Manual and Change Report January 2013

History

Date	Revisions
08/28/2014	Policy content modified to remove reference to the Advance Beneficiary Notice of Noncoverage (ABN)
04/23/2014	Merged NCD 190.3 Cytogenetic Studies into this policy; NCD 190.3 to be archived

Molecular Pathology/Molecular Diagnostics/Genetic Testing

01/22/2014	• Adding CPT Code 81287; New Code for 2014 • Submit Edit Recommendations to NICE, BCCI, CES
05/01/2013	Adding additional new 2013 CPT Codes to list above
04/24/2013	The Unlisted Codes (81479, 84999, 85999, 86849, 87999, 88199, 88299, 88399, 89240 and 89398) will hit the UNL flag (from testing with Roy) so will not be included in the Custom Rule CSLB3 of additional codes being added from above
04/08/2013	• Added a new LCD (L32288) and CPT coding information above • Add CPT/HCPCS Codes to the iCES Edit above
02/27/2013	Annual Review for MRP Committee presentation and approval
02/26/2013	Per discussion in pre-meeting, remove covered ICD-9 Codes and put the Non-covered Screening diagnosis codes in document
08/15/2012	Custom Rule CSLB3 was implemented on 08/15/2012
12/09/2012	Updated list of modifiers with Expiration date of 12/31/2012
04/11/2012	Updates approved by Committee
04/02/2012	Updated policy with ChemoFx, Heartsbreath coverage information
01/25/2012	Policy Approved
12/15/2011	Policy Created

