Genetic Testing: Molecular Profiling Assays for Cancer Management

These services may or may not be covered by your HealthPartners plan. Please see your plan documents for your specific coverage information. If there is a difference between this general information and your plan documents, your plan documents will be used to determine your coverage.

Administrative Process
Prior authorization is required for molecular profiling assays for cancer management.

The scope of this coverage policy includes, but is not limited to, these services:

- Section 1: Cytogenetic and cytogenomic studies
- Section 2: Microsatellite instability (MSI) and mismatch repair (MMR) testing
- Section 3: Single-gene testing and targeted multiple-gene testing
- Section 4: Expanded genetic cancer marker testing
- Section 5: Testing for chimerism

Molecular profiling assays for cancer management other than as described below are also subject to a review for medical necessity, based on current clinical literature and expert recommendations.

Coverage

Indications that are covered

Section 1

Cytogenetic and cytogenomic studies

Cytogenetic and cytogenomic studies for these conditions, including, but not limited to, fluorescence in situ hybridization (FISH) and karyotype, are covered when criteria 1-2 below are met:

1. Breast cancer (except for ductal carcinoma in situ [DCIS])
2. Colorectal cancer
3. Esophageal cancer
4. Ewing sarcoma
5. Gastrointestinal stromal tumor (GIST)
6. Glioblastoma multiforme
7. Lung cancer
8. Leukemia
9. Lymphoma
10. Melanoma
11. Thyroid Carcinoma
12. Other hematological malignancies, lymphoproliferative disorders, and myelodysplastic/myeloproliferative conditions

1. The test is expected to directly impact management of the condition being evaluated.
2. A board-certified physician or advanced-practice registered nurse in pathology, endocrinology, genetics, oncology, or hematology (who is not affiliated with the commercial testing laboratory) must order the test.

Section 2

Microsatellite instability (MSI) testing and mismatch repair (MMR) testing

Microsatellite instability (MSI) and mismatch repair (MMR) testing for these conditions are covered when criteria 1-2 below are met:

1. Breast cancer (except for ductal carcinoma in situ [DCIS])
2. Colorectal cancer
3. Esophageal cancer
4. Ewing sarcoma
5. Gastrointestinal stromal tumor (GIST)
6. Glioblastoma multiforme
• Lung cancer
• Leukemia
• Lymphoma
• Melanoma
• Thyroid carcinoma
• Other hematological malignancies, lymphoproliferative disorders, and myelodysplastic/myeloproliferative conditions

The test is expected to directly impact management of the condition being evaluated.

1. The test is expected to directly impact management of the condition being evaluated.
2. A board-certified physician or advanced-practice registered nurse in pathology, endocrinology, genetics, oncology, or hematology (who is not affiliated with the commercial testing laboratory) must order the test.

Section 3

Single-gene testing and targeted multiple-gene testing

Single-gene testing and targeted multiple-gene testing for these conditions are covered when criteria 1-2 below are met:

• Breast cancer (except for ductal carcinoma in situ [DCIS])
• Colorectal cancer (BRAF, KRAS, NRAS)
• Esophageal cancer
• Ewing sarcoma
• Gastrointestinal stromal tumor (GIST) (BRAF, KIT, PDGFRA, SDH)
• Glioblastoma multiforme
• Non-small cell lung cancer (NSCLC) (ALK, EGFR, KRAS)
• Leukemia
• Lymphoma
• Melanoma (BRAF, KIT)
• Thyroid carcinoma
• Other hematological malignancies, lymphoproliferative disorders, and myelodysplastic/myeloproliferative conditions

1. The test is expected to directly impact management of the condition being evaluated.
2. A board-certified physician or advanced-practice registered nurse in pathology, endocrinology, genetics, oncology, or hematology (who is not affiliated with the commercial testing laboratory) must order the test.
3. The test does not include additional genes or analytes (genetic or molecular substances) that are not included in the list above, next to the condition being evaluated.

Section 4

Expanded genetic cancer marker testing

Afirma™ Genomic Sequencing Classifier (Veracyte, Inc.)

(Each individual nodule being tested must independently meet these criteria.) Afirma Genomic Sequencing Classifier is covered when criteria 1-3 below are met:

1. The test is expected to directly impact management of a thyroid nodule.
2. The ordering physician or healthcare provider must certify that the thyroid nodule being tested meets both of these criteria:
   A. The nodule has been labeled “indeterminate” during laboratory examination (atypia or lesion of undetermined significance), so that cancer is still considered to be a possible diagnosis.
   B. The nodule has a diameter of at least 1.0 cm.
3. The member is age 18 or older.

EndoPredict® (Myriad Genetics Laboratories, Inc.)

(Each individual tumor being tested must independently meet these criteria.) EndoPredict is covered when criteria 1-3 below are met:

1. The test is expected to directly impact management of breast cancer.
2. A board-certified physician or advanced-practice registered nurse in pathology, endocrinology, genetics, oncology, or hematology (who is not affiliated with the commercial testing laboratory) must:
   A. Order the test.
   B. Certify that the test results will be used when making a decision about adjuvant chemotherapy treatment (chemotherapy that is given after surgery).
3. Previous test results must show all of the following:
   A. The tumor is estrogen receptor (ER) positive.
The tumor is human epidermal growth factor receptor 2 (HER2) negative.

Axillary lymph nodes (located in the armpits) are free of cancer.

MammaPrint® (Agendia, Inc.)

(Each individual tumor being tested must independently meet these criteria.)

MammaPrint is covered when criteria 1-3 below are met:

1. The test is expected to directly impact management of breast cancer.
2. A board-certified physician or advanced-practice registered nurse in pathology, endocrinology, genetics, oncology, or hematology (who is not affiliated with the commercial testing laboratory) must:
   A. Order the test.
   B. Certify that the test results will be used when making a decision about adjuvant chemotherapy treatment (chemotherapy that is given after surgery).
3. Previous test results must show all of the following:
   A. The tumor is estrogen receptor (ER) positive.
   B. The tumor is human epidermal growth factor receptor 2 (HER2) negative.
   C. Axillary lymph nodes (located in the armpits) are free of cancer.
   D. The tumor has a diameter between 0.5-2.0 cm.

Oncotype DX Breast Recurrence Score® (Genomic Health, Inc.)

(Each individual tumor being tested must independently meet these criteria.)

Oncotype DX Breast Recurrence Score is covered when criteria 1-4 below are met:

1. The test is expected to directly impact management of breast cancer.
2. A board-certified physician or advanced-practice registered nurse in pathology, endocrinology, genetics, oncology, or hematology (who is not affiliated with the commercial testing laboratory) must:
   A. Order the test.
   B. Certify that the test results will be used when making a decision about treatment with hormone therapy and adjuvant chemotherapy treatment (chemotherapy that is given after surgery).
3. Previous test results must show all of the following:
   A. The tumor is estrogen receptor (ER) or progesterone receptor (PR) positive.
   B. There is no evidence that the cancer has spread to distant organs or lymph nodes (distant metastasis).
   C. There are no more than three axillary lymph nodes (located in the armpits) that have tested positive for cancer.
4. Previous test results must show one of the following:
   A. The tumor is human epidermal growth factor receptor 2 (HER2) negative, regardless of tumor size.
   B. The tumor is HER2 positive and has a diameter less than 1.0 cm.

Section 5

Testing for chimerism

Testing for chimerism, including, but not limited to, comparative analysis with short tandem repeat (STR) markers and testing single nucleotide polymorphisms (SNP), is covered when criteria 1-2 below are met:

1. The test is expected to directly impact management of a malignant disease (cancer).
2. A board-certified physician or advanced-practice registered nurse in pathology, genetics, oncology, hematology, or immunology (who is not affiliated with the commercial testing laboratory) must:
   A. Order the test.
   B. Recommend the test for one of the following indications:
      • The member has a personal history of hematopoietic cell transplantation (HCT).
      • The member has a personal history of donor lymphocyte infusion (DLI).
      • The member has a personal history of immunomodulatory cytokine therapy or other cellular therapy.
      • The member is expected to receive HCT, DLI, immunomodulatory cytokine therapy, or other cellular therapy in the immediate future.

Indications that are not covered

1. Genetic testing is considered not medically necessary when test results will not provide a diagnosis or unifying diagnosis or directly impact the treatment or management of the condition being evaluated.
2. The following services are considered not medically necessary:
   A. Comparative analysis using short tandem repeat (STR) markers that is billed separately, as it is considered to be included as part of the genetic testing, except as described in Section 5 of Indications that are Covered. One example of comparative analysis using STR markers that is not covered is the know error® DNA Specimen Provenance Assay (DSPA) (Strand Diagnostics, LLC.).
   B. Direct-to-consumer genetic testing.
Genetic testing when the cause of the member’s clinical condition, features, characteristics, or symptoms can be better explained by non-genetic factors, such as a known exposure to a toxic substance.

Genetic testing that was not ordered by a licensed healthcare provider or physician (see Definitions) who has established a direct patient care relationship with the member to be tested.

Genetic testing that is provided solely to satisfy data collection and analysis needs and that will not be used in direct clinical management.

Predictive genetic testing for asymptomatic members under 18 years of age for conditions generally accepted as having an onset in adulthood.

Repeat testing of a unique analyte (genetic or molecular substance) in a histologically-distinct tumor, whether at the same biopsy site or a different site, using the same or a similar genetic test, molecular profiling assay, or gene expression classifier.

Multiple-gene panels that include genes not associated with ruling out potential causes for the clinical condition, features, characteristics, or symptoms being evaluated or that include genes not associated with the treatment or management of the condition being evaluated.

Epi proColon® (Epigenomics Inc.)

UroVysion™ Bladder Cancer Kit (Abbott Molecular, Inc.)

The following services are considered experimental/investigational because reliable evidence does not permit conclusions concerning safety, effectiveness, or effect on health outcomes:

Expanded genetic cancer marker testing, except as described in Section 4 (also, see Definitions)

Genomic microarray testing for hematological malignancies

MicroRNA testing

Whole exome sequencing

Whole genome sequencing

Proteomic pattern testing (see Definitions), including, but not limited to:

- BDX-XL2® (Biodesix, Inc.)
- CxBladder™ Detect (Pacific Edge Diagnostics USA, Ltd.)
- CxBladder™ Monitor (Pacific Edge Diagnostics USA, Ltd.)
- VeriStrat® (Biodesix, Inc.)

Testing of liquid biopsies (see Definitions), including, but not limited to:

- GeneStrat® (Biodesix, Inc.)
- Guardant360® (Guardant Health, Inc.)
- Testing for circulating free DNA (cfDNA)
- Testing for circulating tumor DNA (ctDNA)
- SelectMDx® (MDxHealth SA)

Topographic genotyping (see Definitions), including, but not limited to:

- BarreGEN® (Interpace Diagnostics Group, LLC)
- RespriDx™ (Interpace Diagnostics Group, LLC)
- PancraGEN® (Interpace Diagnostics Group, LLC)

Testing for the following indications:

- Anal carcinoma
- Basal cell carcinoma
- Bladder cancer
- Bone cancer (except for Ewing sarcoma)
- Cancer of unknown primary site
- Cervical cancer
- Ductal carcinoma in situ (DCIS) of the breast
- Hepatocellular carcinoma
- Lung cancer (except for non-small cell lung cancer [NSCLC])
- Multiple myeloma
- Ovarian cancer
- Penile cancer
- Prostate cancer
- Renal cancer
- Soft tissue sarcomas (except for gastrointestinal stromal tumor [GIST])
- Squamous cell carcinoma of the skin
- Testicular cancer
- Tracheal cancer
**Definitions**

**Chimerism** is the presence of two genetically distinct cell lines in one person, such as cells derived from a transplant donor and a transplant recipient.

**Expanded genetic cancer marker tests** evaluate multiple genetic substances and other signs that may indicate the presence of cancer or give information about a cancer. Tests in this category could evaluate samples of blood, urine, stool, tumor tissue, or other sources. These tests could be offered before, during, or after cancer treatment.

**Healthcare provider** is any licensed non-physician (excluding naturopathic providers).

**Liquid biopsy** is a sample taken from blood, urine, or another bodily fluid to test for genetic substances and other signs that may indicate the presence of a tumor or give information about a tumor.

**Physician** is a licensed medical doctor or doctor of osteopathy.

**Proteomic pattern testing** examines the way proteins look and work in the body. The way these proteins look and work may indicate the presence of cancer or give information about a cancer.

**Topographic genotyping** (also known as molecular or integrated anatomic pathology) combines genetic testing with pathology services, such as sample preparation, genetic testing, and interpretation of the results by a pathologist.

**Codes**

*If available, codes are listed below for informational purposes only, and do not guarantee member coverage or provider reimbursement. The list may not be all-inclusive.*

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0005U</td>
<td>Oncology (prostate) gene expression profile by real-time RT-PCR of 3 genes (ERG, PCA3, and SPDEF), urine, algorithm reported as risk score</td>
</tr>
<tr>
<td>0006M</td>
<td>Oncology (hepatic), mRNA expression levels of 161 genes, utilizing fresh hepatocellular carcinoma tumor tissue, with alpha-fetoprotein level, algorithm reported as a risk classifier</td>
</tr>
<tr>
<td>0007M</td>
<td>Oncology (gastrointestinal neuroendocrine tumors), real-time PCR expression analysis of 51 genes, utilizing whole peripheral blood, algorithm reported as a nomogram of tumor disease index</td>
</tr>
<tr>
<td>0009U</td>
<td>Oncology (breast cancer), ERBB2 (HER2) copy number by FISH, tumor cells from formalin-fixed paraffin-embedded tissue isolated using image-based dielectrophoresis (DEP) sorting, reported as ERBB2 gene amplified or non-amplified</td>
</tr>
<tr>
<td>0011M</td>
<td>Oncology, prostate cancer, mRNA expression assay of 12 genes (10 content and 2 housekeeping), RT-PCR test utilizing blood plasma and/or urine, algorithms to predict high-grade prostate cancer risk</td>
</tr>
<tr>
<td>0012M</td>
<td>Oncology (urothelial), mRNA, gene expression profiling by real-time quantitative PCR of five genes (MDK, HOXA13, CDC2 [CDK1], IGFBP5, and XCR2), utilizing urine, algorithm reported as a risk score for having urothelial carcinoma</td>
</tr>
<tr>
<td>0013M</td>
<td>Oncology (urothelial), mRNA, gene expression profiling by real-time quantitative PCR of five genes (MDK, HOXA13, CDC2 [CDK1], IGFBP5, and CXCR2), utilizing urine, algorithm reported as a risk score for having recurrent urothelial carcinoma</td>
</tr>
<tr>
<td>0013U</td>
<td>Oncology (solid organ neoplasia), gene rearrangement detection by whole genome next-generation sequencing, DNA, fresh or frozen tissue or cells, report of specific gene rearrangement(s)</td>
</tr>
<tr>
<td>0014U</td>
<td>Hematology (hematolymphoid neoplasia), gene rearrangement detection by whole genome next-generation sequencing, DNA, whole blood or bone marrow, report of specific gene rearrangement(s)</td>
</tr>
<tr>
<td>0016U</td>
<td>Oncology (hematolymphoid neoplasia), RNA, BCR/ABL1 major and minor breakpoint fusion transcripts, quantitative PCR amplification, blood or bone marrow, report of fusion not detected or</td>
</tr>
</tbody>
</table>
myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; full gene sequence
ASXL1 (additional sex combs like 1, transcriptional regulator) (inhibitor resistance), gene analysis, variants in the kinase domain
ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase) (R172M)
IDH2 (isocitrate dehydrogenase 2 [NADP+], mitochondrial) (IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (embedded tissue, algorithm reported as risk of metastasis)
Oncology (uveal melanoma), mRNA, gene-expression profiling by real-time RT-PCR of
buccal DNA, for specimen identity verification
Comparative DNA analysis using multiple selected single-nucleotide polymorphisms (SNPs), urine and
Oncology (colorectal), microRNA, RT-PCR expression profiling of miR-31-3p, formalin-fixed paraffin
normalized percentile rank
analysis of
Oncology (solid organ neoplasia), mRNA, gene expression profiling by massively parallel sequencing for
Hematology (acute myelogenous leukemia), DNA, whole genome next-generation sequencing to detect
biopsy specimen, algorithm reported as probability of higher tumor grade
Oncology (prostate cancer), FISH analysis of 4 genes (ASAP1, HDAC9, CHD1 and PTEN), needle
interrogation for sequence variants, copy number variants or rearrangements
Targeted genomic sequence analysis panel, non-small cell lung neoplasia. DNA and RNA analysis, 23 genes, interrogation for sequence variants and rearrangements, reported as presence/absence of variants and associated therapy(ies) to consider
Oncology (acute myelogenous leukemia), DNA, genotyping of internal tandem duplication, p.D835, p.I836, using mononuclear cells, reported as detection or nondetection of FLT3 mutation and indication for or against the use of midostaurin
Oncology (thyroid), DNA and mRNA of 112 genes, next-generation sequencing, fine needle aspirate of thyroid nodule, algorithmic analysis reported as a categorical result (“Positive, high probability of malignancy” or “Negative, low probability of malignancy”)
JAK2 (Janus kinase 2) (eg. myeloproliferative disorder) gene analysis, targeted sequence analysis exons 12-15
Exome (ie, somatic mutations), paired formalin-fixed paraffin-embedded tumor tissue and normal
specimen, sequence analyses
Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden
BCR/ABL1 (t(9;22)) (eg. chronic myelogenous leukemia) translocation analysis, major breakpoint, quantitative
Oncology (breast ductal carcinoma in situ), mRNA, gene expression profiling by real-time RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence score
FLT3 (fms-related tyrosine kinase 3) (eg. acute myeloid leukemia) internal tandem duplication (ITD) variants, quantitative
Oncology (prostate), mRNA, gene expression profiling by real-time RT-PCR of 17 genes (12 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a risk score
Oncology (solid organ neoplasm), DNA, targeted sequencing of protein-coding exons of 468 cancer- associated genes, including interrogation for somatic mutations and microsatellite instability, matched with normal specimens, utilizing formalin-fixed paraffin-embedded tumor tissue, report of clinically significant mutation(s)
NPM1 (nucleophosmin) (eg. acute myeloid leukemia) gene analysis, quantitative
Targeted genomic sequence analysis panel, acute myelogenous leukemia, DNA analysis, 194 genes, interrogation for sequence variants, copy number variants or rearrangements
Oncology (prostate cancer), FISH analysis of 4 genes (ASAP1, HDAC9, CHD1 and PTEN), needle biopsy specimen, algorithm reported as probability of higher tumor grade
Hematology (acute myelogenous leukemia), DNA, whole genome next-generation sequencing to detect gene rearrangement(s), blood or bone marrow, report of specific gene rearrangement(s)
Oncology (solid organ neoplasm), mRNA, gene expression profiling by massively parallel sequencing for analysis of 51 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a normalized percentile rank
Oncology (colorectal), microRNA, RT-PCR expression profiling of miR-31-3p, formalin-fixed paraffin- embedded tissue, algorithm reported as an expression score
Comparative DNA analysis using multiple selected single-nucleotide polymorphisms (SNPs), urine and buccal DNA, for specimen identity verification
Oncology (uveal melanoma), mRNA, gene-expression profiling by real-time RT-PCR of 15 genes (12 content and 3 housekeeping genes), utilizing fine needle aspirate or formalin-fixed paraffin-embedded tissue, algorithm reported as risk of metastasis
IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (eg, glioma), common variants (eg. R132H, R132C)
IDH2 (isocitrate dehydrogenase 2 [NADP+], mitochondrial) (eg, glioma), common variants (eg, R140W, R172M)
ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase) (eg. acquired imatinib tyrosine kinase inhibitor resistance), gene analysis, variants in the kinase domain
ASXL1 (additional sex combs like 1, transcriptional regulator) (eg. myelodyplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; full gene sequence
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>81272</td>
<td>ASXL1 (additional sex combs like 1, transcriptional regulator) (eg, myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; targeted sequence analysis (eg, exon 12)</td>
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<tr>
<td>81270</td>
<td>APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; full gene sequence</td>
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<tr>
<td>81268</td>
<td>APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; duplication/deletion variants</td>
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<tr>
<td>81266</td>
<td>BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; major breakpoint, qualitative or quantitative</td>
</tr>
<tr>
<td>81264</td>
<td>BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; minor breakpoint, qualitative or quantitative</td>
</tr>
<tr>
<td>81262</td>
<td>BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; other breakpoint, qualitative or quantitative</td>
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<tr>
<td>81260</td>
<td>BRAF (v-raf murine sarcoma viral oncogene homolog B1) (eg, colon cancer), gene analysis, V600E variant</td>
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<tr>
<td>81258</td>
<td>CEBPA (CCAAT/enhancer binding protein [C/EBP], alpha) (eg, acute myeloid leukemia), gene analysis, full gene sequence</td>
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<tr>
<td>81256</td>
<td>CALR (calreticulin) (eg, myeloproliferative disorders), gene analysis, common variants in exon 9</td>
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<tr>
<td>81254</td>
<td>Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (eg, bacterial artificial chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis)</td>
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<tr>
<td>81252</td>
<td>Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities</td>
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<tr>
<td>81250</td>
<td>BTK (Bruton's tyrosine kinase) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, C481S, C481R, C481F)</td>
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<tr>
<td>81248</td>
<td>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)</td>
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<tr>
<td>81246</td>
<td>EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, myelodysplastic syndrome, myeloproliferative neoplasms) gene analysis, full gene sequence</td>
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<tr>
<td>81244</td>
<td>FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia), gene analysis; internal tandem duplication (ITD) variants (ie, exons 14, 15)</td>
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<tr>
<td>81242</td>
<td>FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia), gene analysis; tyrosine kinase domain (TKD) variants (eg, D835, I836)</td>
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<tr>
<td>81240</td>
<td>IGH@ (Immunoglobulin heavy chain locus) (eg, leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); amplified methodology (eg, polymerase chain reaction)</td>
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<tr>
<td>81238</td>
<td>IGH@ (Immunoglobulin heavy chain locus) (eg, leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); direct probe methodology (eg, Southern blot)</td>
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<tr>
<td>81236</td>
<td>ASXL1 (additional sex combs like 1, transcriptional regulator) (eg, myelodysplastic syndrome, acute myeloid leukemia), gene analysis; tyrosine kinase domain (TKD) variants (eg, D835, I836)</td>
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<tr>
<td>81234</td>
<td>Comparative analysis using Short Tandem Repeat (STR) markers; patient and comparative specimen (eg, pre-transplant recipient and donor germline testing, post-transplant non-hematopoietic recipient germline [eg, buccal swab or other germline tissue sample] and donor testing, twin zygosity testing, or maternal cell contamination of fetal cells)</td>
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<tr>
<td>81232</td>
<td>Comparative analysis using Short Tandem Repeat (STR) markers; each additional specimen (eg, 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)</td>
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<tr>
<td>81230</td>
<td>Chimerism (engraftment) analysis, post transplantation specimen (eg, hematopoietic stem cell), includes comparison to previously performed baseline analyses; without cell selection</td>
</tr>
<tr>
<td>81228</td>
<td>Chimerism (engraftment) analysis, post transplantation specimen (eg, hematopoietic stem cell), includes comparison to previously performed baseline analyses; with cell selection (eg, CD3, CD33), each cell type</td>
</tr>
<tr>
<td>81226</td>
<td>JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) gene analysis, p.Val617Phe (V617F) variant</td>
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<tr>
<td>81224</td>
<td>KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (eg, gastrointestinal stromal tumor [GIST], acute myeloid leukemia, melanoma), gene analysis, targeted sequence analysis (eg, exons 8, 11, 13, 17, 18)</td>
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<tr>
<td>81222</td>
<td>KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (eg, mastocytosis), gene analysis, D816 variant(s)</td>
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<td>Code</td>
<td>Description</td>
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<tr>
<td>81275</td>
<td>KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (eg, carcinoma) gene analysis, variants in codons 12 and 13</td>
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<tr>
<td>81276</td>
<td>KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; additional variant(s) (eg, codon 61, codon 146)</td>
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<td>81277</td>
<td>MGMT (O-6-methylguanine-DNA methyltransferase) (eg, glioblastoma multiforme), methylation analysis</td>
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<tr>
<td>81278</td>
<td>MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis</td>
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<tr>
<td>81279</td>
<td>MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis</td>
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<tr>
<td>81280</td>
<td>MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants</td>
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<tr>
<td>81281</td>
<td>MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis</td>
</tr>
<tr>
<td>81282</td>
<td>MSH6 (mutS homolog 6 (E. coli)) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants</td>
</tr>
<tr>
<td>81300</td>
<td>MSH6 (mutS homolog 6 (E. coli)) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis</td>
</tr>
<tr>
<td>81301</td>
<td>Microsatellite instability analysis (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) markers for mismatch repair deficiency (eg, BAT25, BAT26), includes comparison of neoplastic and normal tissue, if performed</td>
</tr>
<tr>
<td>81302</td>
<td>MYD88 (myeloid differentiation primary response 88) (eg, Waldenstrom's macroglobulinemia, lymphoplasmacytic leukemia) gene analysis, p.Leu265Pro (L265P) variant</td>
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<tr>
<td>81310</td>
<td>NPM1 (nucleophosmin) (eg, acute myeloid leukemia) gene analysis, exon 12 variants</td>
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<tr>
<td>81311</td>
<td>NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (eg, colorectal carcinoma), gene analysis, variants in exon 2 (eg, codons 12 and 13) and exon 3 (eg)</td>
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<tr>
<td>81313</td>
<td>PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kalikrein-related peptidase 3 [prostate specific antigen]) ratio (eg, prostate cancer)</td>
</tr>
<tr>
<td>81314</td>
<td>PDGFRA (platelet-derived growth factor receptor, alpha polypeptide) (eg, gastrointestinal stromal tumor [GIST]) gene analysis, targeted sequence analysis (eg, exons 12, 18)</td>
</tr>
<tr>
<td>81315</td>
<td>PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative</td>
</tr>
<tr>
<td>81316</td>
<td>PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; single breakpoint (eg, intron 3, intron 6 or exon 6), qualitative or quantitative</td>
</tr>
<tr>
<td>81317</td>
<td>PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis</td>
</tr>
<tr>
<td>81319</td>
<td>PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants</td>
</tr>
<tr>
<td>81320</td>
<td>PLCG2 (phospholipase C gamma 2) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, R665W, S707F, L845F)</td>
</tr>
<tr>
<td>81321</td>
<td>PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis</td>
</tr>
<tr>
<td>81323</td>
<td>PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; duplication/deletion variant</td>
</tr>
<tr>
<td>81327</td>
<td>SEPT9 (Septin9) (eg, colorectal cancer) methylation analysis</td>
</tr>
<tr>
<td>81334</td>
<td>RUNX1 (run related transcription factor 1) (eg, acute myeloid leukemia, familial platelet disorder with associated myeloid malignancy), gene analysis, targeted sequence analysis (eg, exons 3-8)</td>
</tr>
<tr>
<td>81340</td>
<td>TRB@ (T cell antigen receptor, beta) (eg, leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using amplification methodology (eg, polymerase chain reaction)</td>
</tr>
<tr>
<td>81341</td>
<td>TRB@ (T cell antigen receptor, beta) (eg, leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using direct probe methodology (eg, Southern blot)</td>
</tr>
<tr>
<td>81342</td>
<td>TRG@ (T cell antigen receptor, gamma) (eg, leukemia and lymphoma), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)</td>
</tr>
<tr>
<td>81345</td>
<td>TERT (telomerase reverse transcriptase) (eg, thyroid carcinoma, glioblastoma multiforme) gene analysis, targeted sequence analysis (eg, promoter region)</td>
</tr>
<tr>
<td>81400</td>
<td>MOLECULAR PATHOLOGY PROCEDURE LEVEL 1</td>
</tr>
<tr>
<td>81401</td>
<td>MOLECULAR PATHOLOGY PROCEDURE LEVEL 2</td>
</tr>
<tr>
<td>81402</td>
<td>MOLECULAR PATHOLOGY PROCEDURE LEVEL 3</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>81403</td>
<td>MOLECULAR PATHOLOGY PROCEDURE LEVEL 4</td>
</tr>
<tr>
<td>81404</td>
<td>MOLECULAR PATHOLOGY PROCEDURE LEVEL 5</td>
</tr>
<tr>
<td>81405</td>
<td>MOLECULAR PATHOLOGY PROCEDURE LEVEL 6</td>
</tr>
<tr>
<td>81406</td>
<td>MOLECULAR PATHOLOGY PROCEDURE LEVEL 7</td>
</tr>
<tr>
<td>81407</td>
<td>MOLECULAR PATHOLOGY PROCEDURE LEVEL 8</td>
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<tr>
<td>81408</td>
<td>MOLECULAR PATHOLOGY PROCEDURE LEVEL 9</td>
</tr>
<tr>
<td>81445</td>
<td>Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed</td>
</tr>
<tr>
<td>81450</td>
<td>Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KRAS, KIT, MLL, NRAS, NPM1, NOTCH1), interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed</td>
</tr>
<tr>
<td>81455</td>
<td>Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed</td>
</tr>
<tr>
<td>81504</td>
<td>Oncology (tissue of origin), microarray gene expression profiling of &gt; 2000 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as tissue similarity scores</td>
</tr>
<tr>
<td>81518</td>
<td>Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 11 genes (7 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithms reported as percentage risk for metastatic recurrence and likelihood of benefit from extended endocrine therapy</td>
</tr>
<tr>
<td>81519</td>
<td>Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence score</td>
</tr>
<tr>
<td>81520</td>
<td>Oncology (breast), mRNA gene expression profiling by hybrid capture of 58 genes (50 content and 8 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence risk score</td>
</tr>
<tr>
<td>81521</td>
<td>Oncology (colon), mRNA, microarray gene expression profiling of 70 content genes and 465 housekeeping genes, utilizing fresh frozen or formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk of distant metastasis</td>
</tr>
<tr>
<td>81525</td>
<td>Oncology (colon), mRNA, gene expression profiling by real-time RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence score</td>
</tr>
<tr>
<td>81540</td>
<td>Oncology (tumor of unknown origin), mRNA, gene expression profiling by real-time RT-PCR of 92 genes (87 content and 5 housekeeping) to classify tumor into main cancer type and subtype, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a probability of a predicted main cancer type and subtype</td>
</tr>
<tr>
<td>81541</td>
<td>Oncology (prostate), mRNA gene expression profiling by real-time RT-PCR of 46 genes (31 content and 15 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a disease-specific mortality risk score</td>
</tr>
<tr>
<td>81545</td>
<td>Oncology (thyroid), gene expression analysis of 142 genes, utilizing fine needle aspirate, algorithm reported as a categorical result (eg, benign or suspicious)</td>
</tr>
<tr>
<td>81551</td>
<td>Oncology (prostate), promoter methylation profiling by real-time RT-PCR of 3 genes (GSTP1, APC, RASSF1), utilizing formalin-fixed, paraffin-embedded tissue, algorithm reported as a likelihood of prostate cancer detection on repeat biopsy</td>
</tr>
<tr>
<td>81599</td>
<td>Unlisted multianalyte assay with algorithmic analysis</td>
</tr>
<tr>
<td>88120</td>
<td>Cytopathology, in situ hybridization (eg, FISH), urinary tract specimen with morphometric analysis, 3-5 molecular probes, each specimen; manual</td>
</tr>
<tr>
<td>88121</td>
<td>Cytopathology, in situ hybridization (eg, FISH), urinary tract specimen with morphometric analysis, 3-5 molecular probes, each specimen; using computer-assisted technology</td>
</tr>
<tr>
<td>88182</td>
<td>Flow cytometry, cell cycle or DNA analysis</td>
</tr>
<tr>
<td>88245</td>
<td>Chromosome analysis for breakage syndrome; baseline Sister Chromatic Exchange (SCE), 20-25 cells</td>
</tr>
<tr>
<td>88248</td>
<td>Chromosome analysis for breakage syndromes; baseline breakage, score 50-100 cells, count 20 cells, 2 karyotypes (eg, for ataxia telangiectasia, Fanconi anemia, fragile X)</td>
</tr>
<tr>
<td>88249</td>
<td>Chromosome analysis for breakage syndromes; score 100 cells, clastogen stress (eg, diepoxybutane, mitomycin C, ionizing radiation, UV radiation</td>
</tr>
<tr>
<td>88261</td>
<td>Chromosome analysis; count 5 cells, 1 karyotype, with banding</td>
</tr>
<tr>
<td>88262</td>
<td>Chromosome analysis; count 15-20 cells, 2 karyotypes, with banding</td>
</tr>
<tr>
<td>88263</td>
<td>Chromosome analysis; count 45 cells for mosaicism, 2 karyotypes, with banding</td>
</tr>
</tbody>
</table>
Chromosome analysis, analyze 20-25 cells

Molecular cytogenetics; DNA probe, each (eg, FISH)

Molecular cytogenetics; chromosomal in situ hybridization, analyze 3-5 cells (eg, for derivatives and markers)

Molecular cytogenetics; chromosomal in situ hybridization, analyze 10-30 cells (eg, for microdeletions)

Molecular cytogenetics; interphase in situ hybridization, analyze 25-99 cells

Molecular cytogenetics; chromosomal in situ hybridization, analyze 10-30 cells (eg, for microdeletions)

Molecular cytogenetics; interphase in situ hybridization, analyze 100-300 cells

Chromosome analysis; additional karyotypes, each study

Molecular cytogenetics; additional specialized banding technique (eg, NOR, C-banding)

Molecular cytogenetics; chromosomal in situ hybridization, analyze 3-5 cells (eg, for derivatives and markers)

Molecular cytogenetics; interphase in situ hybridization, analyze 25-99 cells

Chromosome analysis; additional high resolution study

Morphometric analysis; tumor (eg, DNA ploidy)

In situ hybridization (eg, FISH), per specimen; each additional single probe stain procedure (List separately in addition to code for primary procedure)

In situ hybridization (eg, FISH), per specimen; initial single probe stain procedure

In situ hybridization (eg, FISH), per specimen; each multiplex probe stain procedure

Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), using computer-assisted technology, per specimen; initial single probe stain procedure

Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), manual, per specimen; initial single probe stain procedure

Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), using computer-assisted technology, per specimen; each additional single probe stain procedure (List separately in addition to code for primary procedure)

Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), manual, per specimen; each additional single probe stain procedure (List separately in addition to code for primary procedure)

Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), using computer-assisted technology, per specimen; each multiplex probe stain procedure

Morphometric analysis, in situ hybridization (quantitative or semi-quantitative), manual, per specimen; each multiplex probe stain procedure

RAS (KRAS and NRAS) gene mutation testing performed before initiation of anti-EGFR MoAb

Gene expression profiling panel for use in the management of breast cancer treatment

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Approved Medical Director Committee 10/13/15; Revised 3/1/16, 10/1/16, 1/5/17, 4/5/17, 7/1/18, 7/19/18, 1/4/19, 3/18/19; Annual Review 10/16, 4/17, 4/18

References


classifier in radical prostatectomy patients with lymph node metastasis. Research and Reports in Urology, 8, 77-84.


