Local Coverage Determination (LCD)

# Molecular Pathology Procedures

L35000

## Contractor Information

| Contractor Name | Contract Type | Contract Number | Jurisdiction | States |
|---|---|---|---|---|
| National Government Services, Inc. | MAC - Part A | 06101 - MAC A | J - 06 | Illinois |
| National Government Services, Inc. | MAC - Part B | 06102 - MAC B | J - 06 | Illinois |
| National Government Services, Inc. | MAC - Part A | 06201 - MAC A | J - 06 | Minnesota |
| National Government Services, Inc. | MAC - Part B | 06202 - MAC B | J - 06 | Minnesota |
| National Government Services, Inc. | MAC - Part A | 06301 - MAC A | J - 06 | Wisconsin |
| National Government Services, Inc. | MAC - Part B | 06302 - MAC B | J - 06 | Wisconsin |
| National Government Services, Inc. | A and B and HHH MAC | 13101 - MAC A | J - K | Connecticut |
| National Government Services, Inc. | A and B and HHH MAC | 13102 - MAC B | J - K | Connecticut |
| National Government Services, Inc. | A and B and HHH MAC | 13201 - MAC A | J - K | New York - Entire State |
| National Government Services, Inc. | A and B and HHH MAC | 13202 - MAC B | J - K | New York - Downstate |
| National Government Services, Inc. | A and B and HHH MAC | 13282 - MAC B | J - K | New York - Upstate |
| National Government Services, Inc. | A and B and HHH MAC | 13292 - MAC B | J - K | New York - Queens |
| National Government Services, Inc. | A and B and HHH MAC | 14111 - MAC A | J - K | Maine |
| National Government Services, Inc. | A and B and HHH MAC | 14112 - MAC B | J - K | Maine |

| Contractor Name | Contract Type | Contract Number | Jurisdiction | States |
|---|---|---|---|---|
| National Government Services, Inc. | A and B and HHH MAC | 14211 - MAC A | J - K | Massachusetts |
| National Government Services, Inc. | A and B and HHH MAC | 14212 - MAC B | J - K | Massachusetts |
| National Government Services, Inc. | A and B and HHH MAC | 14311 - MAC A | J - K | New Hampshire |
| National Government Services, Inc. | A and B and HHH MAC | 14312 - MAC B | J - K | New Hampshire |
| National Government Services, Inc. | A and B and HHH MAC | 14411 - MAC A | J - K | Rhode Island |
| National Government Services, Inc. | A and B and HHH MAC | 14412 - MAC B | J - K | Rhode Island |
| National Government Services, Inc. | A and B and HHH MAC | 14511 - MAC A | J - K | Vermont |
| National Government Services, Inc. | A and B and HHH MAC | 14512 - MAC B | J - K | Vermont |

## LCD Information

### Document Information

**LCD ID**
L35000

**LCD Title**
Molecular Pathology Procedures

**Proposed LCD in Comment Period**
N/A

**Source Proposed LCD**
DL35000

**Original Effective Date**
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**Revision Effective Date**
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**Revision Ending Date**
N/A

**Retirement Date**
N/A

**Notice Period Start Date**
05/29/2025

### Notice Period End Date
07/12/2025



## Issue

### Issue Description
Based on a New LCD Request, the specific genes (CYP2C19,CYP2C9 and CYP2D6), related to Pharmacogenomic Testing, have been transitioned to the new Pharmacogenomic Testing LCD. Please refer to L39995. The new LCD and related Billing and Coding Article provide clarification regarding Pharmacogenomic Testing coverage.

## CMS National Coverage Policy

N/A

## Coverage Guidance

### Coverage Indications, Limitations, and/or Medical Necessity
Molecular pathology procedures have broad clinical and research applications. The following examples of applications may not be relevant to a Medicare beneficiary or may not meet a Medicare benefit category and/or reasonable and necessary threshold for coverage. Such examples include Genetic Testing and Genetic Counseling (when applicable) for:

- Disease Risk,
- Carrier Screening,
- Hereditary Cancer Syndromes,
- Gene Expression Profiling for certain cancers,
- Prenatal Diagnostic testing, and
- Diagnosis and Monitoring Non-Cancer Indications

This Local Coverage Determination (LCD) addresses the circumstances under which the item or service may be reasonable and necessary. For laboratory services, a service may be reasonable and necessary if the service is safe and effective; and appropriate, including the duration and frequency that is considered appropriate for the item or service, in terms of whether it is furnished in accordance with accepted standards of medical practice for the diagnosis of the patient's condition; furnished in a setting appropriate to the patient's medical needs and condition; ordered and furnished by qualified personnel; one that meets, but does not exceed, the patient's medical need; and is at least as beneficial as an existing and available medically appropriate alternative.

Many applications of the molecular pathology procedures are not covered services given lack of benefit category (e.g., preventive service or screening for a genetic abnormality in the absence of a suspicion of disease) and/or failure to the reasonable and necessary threshold for coverage (e.g., based on quality of clinical evidence and strength of recommendation or when the results would not reasonably be used in the management of a beneficiary). Furthermore, payment of claims in the past (based on stacking codes) or in the future (based on the new code series) is not a statement of coverage since the service may not have been audited for compliance with program requirements and documentation supporting the reasonable and necessary testing for the beneficiary. Certain molecular pathology procedures may be subject to prepayment medical

review (records requested) and paid claims must be supportable, if selected, for post payment audit by the MAC or other contractors. Molecular pathology tests for diseases or conditions that manifest severe signs or symptoms in newborns and in early childhood or that result in early death (e.g., Canavan disease) could be subject to automatic denials since these tests are not usually relevant to a Medicare beneficiary.

This LCD gives general guidance to the medically reasonable and necessary applications of the Molecular Pathology Procedures and Genomic Sequencing Procedures, described in Current Procedural Terminology (CPT). Coding guidance is provided in Molecular Pathology Procedures Article A56199, attached below.

Indications:
Molecular pathology procedures (Tier1 and Tier 2) may be eligible for coverage when ALL of the following criteria are met:

- Alternative laboratory or clinical tests to definitively diagnose the disorder/identify the condition are unavailable or results are clearly equivocal; AND
- Availability of a clinically valid test, based on published peer reviewed medical literature; AND
- Testing assay(s) are Food and Drug Administration (FDA) approved/cleared or if LDT (lab developed test) or LDT protocol or FDA modified test(s) the laboratory documentation should support assay(s) of analytical validity and clinical utility; AND
- Results of the testing must directly impact treatment or management of the Medicare beneficiary; AND
- For testing panels, including but not limited to, multiple genes or multiple conditions, and in cases where a tiered approach/method is clinically available, testing would be covered ONLY for the number of genes or test that are reasonable and necessary to obtain necessary information for therapeutic decision making; AND
- Individual has not previously received genetic testing for the disease/condition. (In general, diagnostic genetic testing for a disease should be performed once in a lifetime.) Exceptions include clinical scenarios whereby repeat testing of somatically-acquired mutations (for example, pre- and post- therapy) may be required to inform appropriate therapeutic decision-making.

Limitations:

- Any procedures required prior to cell lysis should be reported separately and utilization must be clearly supported based on the application and clinical utility. Such claims may be subject to prepayment medical review.
- The medically necessary interpretation and report of a molecular pathology test, written by a pathologist, which is above and beyond the report of standard laboratory results may not be reported by Non- physician practitioners (e.g., PhD, scientists etc.); only physicians are eligible to report this service.
- Testing for quality assurance component of the service is not separately billable.

Indications and Limitations of Coverage

ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase) (eg, acquired imatinib tyrosine kinase inhibitor resistance), gene analysis, variants in the kinase domain is considered medically necessary in patients with acute lymphoblasic leukemia (ALL) and chronic myeloid leukemia (CML) to guide therapeutic decision making.

ATP7B is considered medically necessary in patients with symptoms of Wilson's disease to guide therapeutic decision making.

BCR/ABL is indicated in patients with suspected CML with either persistent, unexplained leukocytosis or thrombocytosis. BCR/ABL is considered medically necessary in the evaluation of individuals with chronic myelogenous leukemia or BCR-ABL positive acute lymphoblastic leukemia to evaluate treated individuals who manifest suboptimal response to initial tyrosine kinase inhibitor therapy or loss of response to tyrosine kinase inhibitor therapy.

BLM (Bloom syndrome, RecQ helicase-like)(e.g. Bloom syndrome) gene analysis, 2281 del6ins7 variant is considered medically necessary for a beneficiary who may have Bloom syndrome to confirm diagnosis and guide medical decision-making.

BRAF gene analysis is considered medically necessary for patients who have malignant melanoma, non-small cell lung cancer, hairy cell leukemia, or metastatic colorectal cancer when needed to determine if a Medicare covered therapy is a reasonable option given the individual's specific clinical presentation.

BRCA1 and BRCA2 genetic testing is considered medically necessary for a beneficiary with a current diagnosis or a personal history of a cancer associated with the BRCA mutation who meets one or more of the criteria found in the most recent version of the NCCN guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian or other evidence based guideline addressing genetic testing, and the results will be used to benefit the individual tested in terms of potential to guide therapeutic decision making.

**Cardiology (heart transplant), mRNA**, gene expression profiling by real-time quantitative PCR of 20 genes (11 content and 9 housekeeping), utilizing subtraction of peripheral blood, algorithm reported as rejection risk score is considered medically necessary for heart transplant patients to guide therapeutic decision-making.

**CEBPA** (CCAAT/enhancer binding protein [C/EBP], alpha) (eg, acute myeloid leukemia), full gene sequence is considered medically necessary in patients with acute myelogenous leukemia (AML) to guide therapeutic decision making.

**CALR** (calreticulin) (eg, myeloproliferative disorders), gene analysis, common variants in exon 9 is considered medically necessary in the initial diagnostic work-up of BCR-ABL negative, JAK2-negative adults with clinical, laboratory, or pathological findings suggesting polycythemia vera (PV), essential thrombocythemia (ET) or primary myelofibrosis (PMF).

**CCND1/IGH** (BCL1/IgH, t)(eg, mantle cell lymphoma) translocation analysis, major breakpoint, qualitative and quantitative, if performed is considered medical necessary for patients who have non- Hodgkin's lymphoma to guide therapeutic decision-making.

**Ceramides Risk Score** (Ceramides by liquid chromatography-tandem mass spectrometry, plasma, quantitative report with risk score for major cardiac events) is considered not medically necessary.

**CFTR** (cystic fibrosis transmembrane conductance regulator) (e.g.cystic fibrosis) gene analysis, common variants (e.g. ACMG/ACOG guidelines) is considered medically necessary for a beneficiary who has or may have cystic fibrosis to guide therapeutic decision-making**.**

**Chimerism analysis** to identify appropriate donors and monitor engraftment success or disease reoccurrence is considered medically necessary.

**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) [when specified as EGFR mutation analysis testing] EGFR testing is considered medically necessary as a technique to predict treatment response for individuals with non-small cell lung cancer undergoing treatment with EGFR tyrosine kinase inhibitor (TKI) therapy (for example, erlotinib [Tarceva® ], gefitinib [Iressa® ], or afatinib [Gilotrif® ]).

**F2** gene (prothrombin coagulation factor II) and **F5** gene (coagulation factor V) The F2 and F5 genetic tests are not considered to be clinically efficacious; therefore, testing is not medically necessary.

**FLT3** is considered medically necessary in patients with acute myeloid leukemia (AML) to guide therapeutic decision making.

**Gene Testing for Warfarin Response** Pharmacogenomic Testing for Warfarin Response, gene testing on **CYP2C9 and/or VKORC1** see NCD 90.1 for coverage information.

**HFE** (hemochromatosis)(hereditary hemochrosis) gene analysis, common variants (e.g. C282Y, H63D) is considered medically necessary in patients with iron overload of uncertain etiology (e.g. when the test is used to avoid liver biopsy in someone when the ferritin and the transferrin saturation are elevated greater than 45%). The genotyping of patients with iron overload of uncertain etiology is allowed only once per lifetime.

**HLA** Class I or II typing is considered medically necessary when one of the following indications is met:

- Transplantation:
    - Standard of care determination of HLA matching for solid organ transplant (donor/recipient). – Solid organ transplant registries include both serological HLA testing (e.g., crossmatch) and genomic molecular DNA typing. Family members, or unrelated living donors or cadaveric donors who donate bone marrow or a solid organ are HLA tested pre-transplant to determine compatibility with the potential recipients.
    - Standard of care determination of HLA matching for solid organ transplant (donor/recipient). – Solid organ transplant registries include both serological HLA testing (e.g., crossmatch) and genomic molecular DNA typing. Family members, or unrelated living donors or cadaveric donors who donate bone marrow or a solid organ are HLA tested pre-transplant to determine compatibility with the potential recipients.
    - Standard of care identification of determination of HLA matching for hematopoietic stem cell/bone marrow transplantation -allele-level typing will provide clinical guidance for the HLA-A,B,C Class I and DRB1, DQB1,DPB1, and DQA1 Class II loci in the average transplant program because it is well established that mismatches at certain HLA loci between donor-recipients are closely linked to the risk of graft versus host disease. Potential marrow donors may enroll with a national registry such as the United States National Marrow Donor Program or the Canadian Blood Services registry.
- Disease Association:
    - Standard of care testing to diagnose certain HLA related diseases/conditions when the testing is supported by the clinical literature and is informative for the direct management of a patient bearing a certain allele(s). It is not expected that more than one test would be required in a given beneficiary's lifetime. Possible covered indications when standard laboratory testing (tissue typing) not adequate:
        - HLA-B*27 for the diagnosis of certain cases of symptomatic patients with presumed ankylosing spondylitis or related inflammatory disease. HLA-B*27 is covered for ankylosing spondylitis in cases where other methods of diagnosis would not be appropriate or have yielded inconclusive results (NCD 190.1).

    - In the work-up of certain patients with an unclear diagnosis of celiac disease and gluten hypersensitivity usually related to ambiguous standard laboratory results and/or inconsistent biopsy results (e.g., HLA-DQ2 by HLA-DQB1*02 and of DQ8 by HLA-DQB1*0302).
- Pharmacogenetics: Refer to Pharmacogenomic Testing LCD L39995

HUMAN PLATELET ANTIGEN 1-15 as genotyping for human platelet antigens is important for identifying woman at risk for neonatal alloimmune thrombocytopenia (NAIT). Post-transfusion purpura is an immune reaction against human platelet antigens, often occurring when a woman is sensitized during pregnancy, then subsequently receives a transfusion. There are few Medicare beneficiaries for whom this testing will be clinically actionable.

IGH@ (Immunoglobulin heavy chain locus) is considered medically necessary for acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), and lymphoma, B-cell to guide therapeutic decision making.

JAK2 V617F genotyping is considered medically necessary in the initial diagnostic work-up of BCR-ABL negative, adults with clinical, laboratory, or pathological findings suggesting myeloproliferative neoplasm (MPN) (polycythemia vera (PV), essential thrombocythemia (ET) or primary myelofibrosis (PMF)) or a myelodysplastic syndrome (MDS).

JAK2 (Janus kinase 2) (eg, myeloproliferative disorder), exon 12 sequence and exon 13 sequence is considered medically necessary in the initial work-up of BCR-ABL and JAK2 (V617F variant) negative adults with clinical, laboratory, or pathological findings suggesting polycythemia vera.

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) is considered medically necessary in patients who have GIST, acute myeloid leukemia (AML) or melanoma to guide therapeutic decision making.

KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (eg, mastocytosis), gene analysis, D816 variant(s) is considered medically necessary in patients who have mastocytosis to guide therapeutic decision making.

KRAS gene analysis, variants in codons 12 and 13, is considered medically necessary in patients with colorectal cancer or non-small cell lung cancer when needed to determine if a Medicare covered therapy is a reasonable option given the individual's specific clinical presentation.

KRAS (Kirsten rat sarcoma viral oncogene homolog) (e.g., carcinoma) gene analysis; additional variant(s) (e.g., codon 61, codon 146) is considered medically necessary in patients with colorectal cancer or non-small cell lung cancer when needed to determine if a Medicare covered therapy is a reasonable option given the individual's specific clinical presentation.

MEN1 (multiple endocrine neoplasia 1) (eg, multiple endocrine neoplasia type 1, Wermer syndrome), duplication/deletion and CPT code 81405 MEN1 (multiple endocrine neoplasia 1) e.g. multiple endocrine neoplasia type 1, Wermer syndrome), duplication/deletion analysis) are considered medically necessary in patients with multiple endocrine neoplasia to guide therapeutic decision-making.

MET proto-oncogene, receptor tyrosine kinase, is considered medically necessary in patients with non-small cell lung cancer when needed to determine if a Medicare covered therapy is a reasonable option given the individuals specific clinical presentation.

MGMT (O-6-methylguanine-DNA methyltransferase) (e.g., glioblastoma multiforme), methylation analysis) is considered medically necessary in patients with malignant brain neoplasm to guide therapeutic decision making.

MPL (myeloproliferative leukemia virus oncogene, thrombopoietin receptor, TPOR) (eg, myeloproliferative disorder), common variants (eg, W515A, W515K, W515L, W515R) is considered medically necessary in the initial work-up of BCR-ABL negative, JAK2 negative, and CALR negative adults with clinical, laboratory, or pathological findings suggesting thrombocytosis, essential thrombocythemia (ET), or primary myelofibrosis (PMF).

MPL (myeloproliferative leukemia virus oncogene, thrombopoietin receptor, TPOR) (eg, myeloproliferative disorder), exon 10 sequence is considered medically necessary in the initial work-up of BCR-ABL negative, JAK2 negative, and CALR negative adults with clinical, laboratory, or pathological findings suggesting thrombocytosis, essential thrombocythemia (ET), or primary myelofibrosis (PMF).

MTHFR (5,10-methyenetetrahydrofolate reductase) (e.g. hereditary hypercoaguability), gene analysis, common variants(e.g., EG, 677T, 1298C) is not considered to be clinically efficacious; therefore, testing is not medically necessary.

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 and is considered medically necessary in individuals who have colorectal cancer (CRC) diagnosed at less than or equal to 70 years of age, and those greater than 70 years who meet the revised Bethesda Lynch Syndrome (LS) guidelines to guide therapeutic decision-making. Despite the high penetrance of CRC and endometrial cancer and recommendations of consideration for screening unaffected first-degree relatives following diagnosis of an LS proband, testing of genetic carriers who are unaffected with a Lynch-related cancer is not a Medicare benefit, and is statutorily excluded from coverage.

MSI testing is also required by FDA for the clinical use of Keytruda (pembrolizumab) in a restricted population of patients. These are patients who have unresectable or metastatic solid tumors who have progressed following prior treatment and have no satisfactory alternative options. When Keytruda (pembrolizumab) is a potential clinically appropriate therapeutic choice, MSI testing is medically necessary in these patients. Because this is a wide-ranging population of advanced cancer patients, ICD-10 specificity is impractical, therefore use an ICD-10 appropriate for the tumor type and location.

MYD88 genetic test is considered medically necessary in patients with Marginal Zone Lymphoma (MZL), Waldenstrom's Macroglobulinemia (WM) and Lymphoplasmacytic Lymphoma (LPL) to guide therapeutic decision-making.

NPM1 (nucleophosmin) is considered medically necessary in patients with acute myeloid leukemia (AML) to guide therapeutic decision making.

NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (e.g., colorectal carcinoma), gene analysis, variants in exon 2 (e.g., codons 12 and 13) and exon 3 (e.g., codon 61) is considered medically necessary in patients with colorectal cancer when needed to determine if a Medicare covered therapy is a reasonable option given the individual's specific clinical presentation.

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 is considered medically necessary to guide therapeutic decision-making in patients with the following findings:

- estrogen-receptor positive, node-negative carcinoma of the breast
- estrogen-receptor positive micrometastases of carcinoma of the breast, and
- estrogen-receptor positive breast carcinoma with 1-3 positive nodes.

PDGFRA (platelet-derived growth factor receptor, alpha polypeptide) (e.g., gastrointestinal stromal tumor [GIST]), gene analysis, targeted sequence analysis (eg, exons 12, 18) is considered medically necessary in patients with PDGFRA-associated chronic eosinophilic leukemia or GIST caused by mutations in the PDGFRA gene to guide therapeutic decision making.

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 is considered medically necessary in patients with promyelocytic leukemia.

Prosigna® Breast Cancer Prognostic Gene Signature Assay is considered medically necessary in patients who have undergone surgery in conjunction with locoregional treatment consistent with standard of care, either as:

- A prognostic indicator for distant recurrence-free survival at 10 years in post- menopausal women with Hormone Receptor-Positive (HR+), lymph node-negative, Stage I or II breast cancer to be treated with adjuvant endocrine therapy alone, when used in conjunction with other clinicopathological factors.
- A prognostic indicator for distant recurrence-free survival at 10 years in post- menopausal women with Hormone Receptor-Positive (HR+), lymph node-positive (1-3 positive nodes}, Stage II breast cancer to be treated with adjuvant endocrine therapy alone, when used in conjunction with other clinicopathological factors. The device is not intended for patients with 4 or more positive nodes

RARS (SF3B1 mutation) is considered medically necessary in patients with Myelodysplastic Syndrome to guide therapeutic decision-making.

RET (ret-proto-oncogene) is considered medically necessary in patients with medullary CA of thyroid, multiple endocrine neoplasia, pheochromocytoma, and parathyroid tumors) to guide therapeutic decision making.

ROS proto-oncogene 1, receptor tyrosine kinase, is considered medically necessary in patients with non-small cell lung cancer when needed to determine if a Medicare covered therapy is a reasonable option given the individuals specific clinical presentation.

SERPINA1 (serpin peptidase inhibitor, clade A, alpha-1- antiproteinase, antitrypsin, member 1) (e.g., antitrypsin deficiency), gene analysis, common variants (e.g. *S and *Z) is considered medically necessary for patients who have antitrypsin deficiency to guide therapeutic decision-making.

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 is considered not medically necessary except when used to guide treatment decision making in individuals with non-small cell lung cancer (please refer to LCD L37810).

TP53 (tumor protein 53) (e.g. tumor samples), targeted sequence analysis of 2-5 exons, and CPT code 81405 TP53 (tumor protein 53) (e.g. Li-Fraumeni syndrome, tumor samples), full gene sequence or targeted sequence analysis of >5 exons are considered medically necessary in individuals who have Acute Myelogenous Leukemia, chronic lymphocytic leukemia (CLL), or Myelodysplastic Disease to guide therapeutic decision-making.

TRB@ (T CELL antigen receptor, BETA) (e.g., leukemia and lymphoma), gene rearrangement analysis to detect abnormal cloning population(s); using amplification methodology is considered necessary to guide therapeutic decision-making for individuals with acute lymphoid leukemia, aplastic anemia, and T cell prolymphocytic leukemia.

TRG@ (T CELL antigen receptor, GAMMA ) (e.g., leukemia and lymphoma), gene rearrangement analysis , evaluation to detect abnormal cloning population(s) are considered medically necessary to guide therapeutic decision-making for individuals with acute lymphoid leukemia, aplastic anemia, and T cell prolymphocytic leukemia and mastocytosis.

Tier 2 Covered Gene/Gene Combinations

Limited coverage may be provided for specific genes reported below:

ACE
ATP7B (ATPase, Cu++ transporting, beta polypeptide)
CCND1/IGH
CBFB-MYH11
CDKN2A (cyclin-dependent kinase inhibitor 2A)
E2A/PBX1
EML4-ALK
ETV6-RUNX1
EWSR1/ERG
EWSR1/FLI1
EWSR1/WT1
F11coagulation factor XI
F13B
F5
F7
F8 (coagulation factor VIII)
FGB
FIP1L1-PDGFR
FOXO1/PAX3
FOXO1/PAX7
MEN1 (multiple endocrine neoplasia 1) (eg, multiple endocrine neoplasia type 1, Wermer syndrome), duplication/deletion
MEN1 (multiple endocrine neoplasia 1) (eg, multiple endocrine neoplasia type 1, Wermer syndrome), full gene sequence
MUTYH (mutY homolog [E.coli])
NPM/ALK
PAX8/PPARG
PRSS1 (protease, serine, 1 [trypsin 1])
RARS (SF3B1
RUNX1/RUNX1T1
TP53 (tumor protein 53) (e.g. tumor samples), targeted sequence analysis of 2-5 exons
TP53 (tumor protein 53) (e.g. Li-Fraumeni syndrome, tumor samples), full gene sequence or targeted sequence analysis of >5 exons
VHL (von Hippel-Lindau tumor suppressor)

Tier 2 Individual Review Codes/Gene Combinations

Any genetic test reported with a Tier 2 CPT code, not listed above or below, is subject to individual review.

Tier 2 Non-covered Codes/Gene Combinations

The following individual Tier 2 genetic tests are unlikely to impact therapeutic decision-making, directly impact treatment, outcome and/or clinical management in the care of the beneficiary and will be denied as not medically necessary (Please note that this list of non-covered genes is not exhaustive, and the fact that a specific gene is not mentioned does not mean it is covered. In addition, many genes have several names that are used. The most common names have been used in this policy):

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| ABCC8 |
| ACADM |
| ACADS (acyl-CoA dehydrogenase) |

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| ACADVL (acyl-CoA dehydrogenase, very long chain) |
| ADRB2 |
| AGTR1 |
| AIRE (APSI) |
| AKT1 |
| ANG (angiogenin, ribonuclease, RNase A family, 5) |
| APOE |
| AQP2 (aquaporin 2 [collecting duct]) |
| AR (androgen receptor) |
| ARX (aristaless related homeobox) |
| ATN1 |
| BTD (biotinidase) |
| C9orf72 |
| CASR (CAR, EIG8, extracellular calcium-sensing receptor, FHH, FIH, GPRC2A, HHC, HHC1, NSHPT, PCAR1) |
| CAV3 (caveolin 3) (eg, CAV3-related distal myopathy, limb-girdle muscular dystrophy type 1C), full gene sequence |
| CBS (cystathionine-beta-synthase) |
| CCR5 |
| CDKL5 (cyclin-dependent kinase-like 5) |
| CFH/ARMS2 |
| Chromosome 18q- |
| CLRN1 |
| CLRN1 (clarin 1) |
| CYP1B1 (cytochrome P450, family 1, subfamily B, polypeptide 1) |
| CYP21A2 (cytochrome P450, family 21, subfamily A, polypeptide2) |
| CYP21A2 |
| DEK/NUP214 |
| DLAT (dihydrolipoamide S-acetyltransferase) |
| DLD (dihydrolipoamide dehydrogenase) |
| DMPK (dystrophia myotonica-protein kinase (DM gene and DM1) |
| DMPK (dystrophia myotonica-protein kinase) |
| DYT1 (TOR1A) |
| EGR2 (early growth response 2) (eg, Charcot-Marie-Tooth) |
| F8 (coagulation factor VIII) |
| F8 (coagulation factor VIII) |

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| FGFR2 (fibroblast growth factor receptor 2) (2 EXONS) |
| FGFR3 |
| FGFR3 |
| FGFR3 (fibroblast growth factor receptor 3) (4 EXONS) |
| FGFR3 (fibroblast growth factor receptor 3) one exon |
| FKRP (Fukutin related protein) |
| FOXG1 (forkhead box G1) |
| FSHMD1A (facioscapulohumeral muscular dystrophy 1A) |
| FSHMD1A (facioscapulohumeral muscular dystrophy 1A) |
| FXN (frataxin) |
| GALT (galactose-1-phosphate uridylyltransferase) |
| GALT (galactose-1-phosphate uridylyltransferase) |
| GJB1 (gap junction protein, beta 1) (eg, Charcot-Marie-Tooth X-linked), full gene sequence |
| H19 |
| HADHA (hydroxyacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase [trifunctional protein] alpha subunit) |
| HAX1 (HAX1_HUMAN, HCLS1- associated protein X-1, HCLSBP1, HS1-associating protein X-1, HS1 binding protein, HS1-binding protein 1, HS1BP1, HSP1BP-1) |
| HEXA (hexosaminidase A, alpha polypeptide) |
| HNF1B (HNF1 homeobox B) |
| HRAS (v-Ha-ras Harvey rat sarcoma viral oncogene homolog Costello syndrome) |
| HRAS (v-Ha-ras Harvey rat sarcoma viral oncogene homolog) |
| HTT (huntingtin) |
| IL28B |
| IVD |
| KCNJ10 (potassium inwardly-rectifying channel, subfamily J, member 10) |
| KCNQ10T1 (KCNQ1 overlapping transcript 1) |
| KIF6 |

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| Level 8 Molecular Pathology Procedures |
| Level 9 Molecular Pathology Procedures |
| LMNA (lamin A/C) |
| LPA intron 25 genotype |
| MEFV (Mediterranean fever) (eg, familial Mediterranean fever) |
| MEG3/DLK1 |
| MEK1 |
| MLL/AFF |
| MPZ (myelin protein zero) |
| MT-ATP6 |
| MT-ND4, MT-ND6 |
| MT-ND5 mitochondrially encoded tRNA leucine 1 [UUA/G] mitochondrially encoded NADH dehydrogenase 5) |
| MT-RNR1 (mitochondrially encoded 12S RNA) |
| MT-RNR1 (mitochondrially encoded 12S RNA) |
| MT-TK (mitochondrially encoded tRNA lysine) |
| MT-TL1 |
| MT-TS1 |
| MT-TS1 (mitochondrially encoded tRNA serine 1) |
| MUTYH (mutY homolog [E. coli]) |
| NF2 (neurofibromin 2 [merlin]) |
| NSD1 (nuclear receptor binding SET domain protein 1) |
| PAH (phenylalanine hydroxylase) |
| PAX2 (paired box 2) |
| PDHA1 (pyruvate dehydrogenase [lipoamide] alpha1) |
| PIK3C, PI3Ks, PI(3)Ks, PI-3Ks |
| POLG (polymerase [DNA directed], gamma) |
| PRKAG2 (protein kinase, AMP-activated, gamma 2 non-catalytic subunit) |
| PRSS1 (protease, serine, 1 [trypsin 1]) |
| PTPN11 (protein tyrosine phosphatase, non-receptor type 11) |
| RET (ret-proto-oncogene) (eg, Hirschsprung disease), full gene sequence |
| SCA1 |
| SDA2 |

| |
|---|
| SLC25A4 (solute carrier family 25 [mitochondrial carrier; adenine nucleotide translocation] |
| SLC9A6 (solute carrier family 9 [sodium/hydrogen exchanger] member 6) |
| SMN1 |
| SMN1 (survival of motor neuron 1, telomeric) |
| SMN1/SMN2 (survival of motor neuron 1, telomeric/survival of motor neuron 2, centromeric) |
| SOS1 (son of sevenless homolog 1) |
| SPG4 |
| TAZ (tafazzin) |
| TOR1A |
| TRD |
| TSC1 (tuberous sclerosis 1) |
| TSC2 (tuberous sclerosis 2) |
| UBE3A (ubiquitin protein ligase) |
| UPD (Uniparental disomy) |
| VEGFR2 (CD309, FLK1, VEGFR) |
| VWF (von Willebrand factor) |

## Summary of Evidence

### HUMAN PLATELET ANTIGEN 1-15

Coverage of (HUMAN PLATELET ANTIGEN 1-15) as genotyping for human platelet antigens is important for identifying woman at risk for neonatal alloimmune thrombocytopenia (NAIT). Post-transfusion purpura is an immune reaction against human platelet antigens, often occurring when a woman is sensitized during pregnancy, then subsequently receives a transfusion. There are few Medicare beneficiaries for whom this testing will be clinically actionable.

### *IFNL3* (IL28B)

Newer treatment regimens are replacing PEG-interferon therapies. Per UpToDate: “Several clinical features that were predictors of response to interferon-based regimens are no longer relevant to combination direct-acting antiviral (DAA) regimens…Polymorphisms in the IL28B gene, which encodes interferon lambda 3, effectively predicted responses to treatment with interferon-based therapies and accounted for a significant proportion of the differential response observed in patients of certain races, such as patients of African descent. In contrast, neither non-CC IL28 genotype nor race has consistently been associated with lower sustained virologic response (SVR) rates in multiple trials and cohort studies of contemporary DAA combination regimens. Although some studies have suggested a limited impact of IL28 genotype or race on SVR rates with DAA regimens, the magnitude of the impact is small when appropriate regimens are used and not sufficient enough to recommend IL28B genotype testing in routine clinical practice."

### *G6PD*

The WHO recommends testing of drugs to predict for risk of hemolysis in G6PD deficient individuals if the drugs are to be prescribed in areas of high prevalence of G6PD deficiency.

Reconsideration Request- October 2022

### IGH and TP53

NCCN Category 2A designation supports coverage of IGH and TP53 gene testing for Chronic Lymphocytic Leukemia (CLL) patients.

New LCD Request October 2022

Ceramides Risk Score

Mantovani et al (2020) evaluated the association between previously identified high-risk ceramides [Cer(d18:1/16:0), Cer(d18:1/18:0), Cer(d18:1/22:0), Cer(d18:1/24:0) and Cer(d18:1/24:1)] and risk of major adverse cardiovascular events in adult population. The authors concluded that higher plasma levels of Ceramides were associated with major adverse cardiovascular events, and lower plasma levels of Ceramides were not. However, the authors indicated that additional research is required to elucidate the different role of ceramides on pathways involved in cardiovascular disease.

UpToDate (Accessed 04/04/2022) review stated, “Overview of possible risk factors for cardiovascular disease” (Wilson, 2019) states that “Serum ceramides (the combination of sphingosine and a fatty acid) are being investigated as potential cardiovascular risk factors due to their role in atherosclerosis, diabetes, and inflammation. Greater plasma ceramide levels are associated with an increased risk of cardiovascular death and major adverse cardiac events in patients with stable coronary artery disease, independent of traditional risk factors including lipid and C-reactive protein levels. Simvastatin has been reported to lower ceramide concentrations by approximately 25 %. However, measurement of serum ceramides is not widely available outside of research settings”.

Park et al (2022) explored the evidence regarding the relationship between ceramides and left ventricular dysfunction and heart failure and found that overall cardiovascular disease (CVD) mortality and all-cause mortality were associated with higher ceramides. The authors stated that high levels of total ceramides are noted in heart failure and may be a valuable biomarker of preclinical left ventricular dysfunction, remodeling, heart failure and mortality. However, continued exploration of the mechanisms underlying these profound relationships are necessary to develop specific lipid modulators.

Hilvo et al (2020) stated that “A direct cause-effect relationship between CVD and ceramide has not been established to date” and that the ceramide risk score may have a unique utility as a motivational tool to increase patient's adherence to medical therapy and lifestyle changes; however, future prospective studies should be done.

Laaksonen et al studied the prognostic value of plasma ceramides (Cer) as cardiovascular death (CV death) markers in three independent coronary artery disease (CAD) cohorts. The authors concluded that distinct plasma ceramide ratios are significant predictors of CV death both in patients with stable CAD and ACS, over and above currently used lipid markers and noted that the value of Cer may improve the identification of high-risk patients in need of more aggressive therapeutic interventions.

Havulinna et al examined whether ceramides are associated with major adverse cardiovascular events (MACEs) among apparently healthy individuals. The authors concluded that distinct serum ceramides are associated with the risk of incident MACE in apparently healthy individuals. However, remarked that the results should encourage more detailed analyses of ceramides in cardiovascular pathobiology and suggest new biomarkers of MACE risk.

Havulinna et al examined whether ceramides are associated with major adverse cardiovascular events (MACEs) among apparently healthy individuals. The authors concluded that distinct serum ceramides are associated with the risk of incident MACE in apparently healthy individuals. However, remarked that the results should encourage more detailed analyses of ceramides in cardiovascular pathobiology and suggest new biomarkers of MACE risk.

Meeusen et al (2018) measured plasma ceramides in 495 participants before nonurgent coronary angiography. Coronary artery disease, defined as >50% stenosis in >/=1 coronary artery, was identified in 265 (54%) cases. Ceramides were not significantly associated with coronary artery disease. However, the authors concluded that Elevated plasma concentrations of ceramides are independently associated with major adverse cardiovascular events in patients with and without coronary artery disease.

Hilvo et al (2020) found that a direct cause-effect relationship between CVD and ceramide had not been established to date. As ceramide-specific medications are being developed, conventional strategies such as lipid lowering agents and lifestyle interventions can be used to reduce overall risk. Ceramides can identify a very high-risk coronary heart disease category of patients in need for more intense medical attention, specifically those patients at higher risk as highlighted in the 2019 European Society of Cardiology guidelines for stable chronic coronary syndrome patients. In addition, the ceramide risk score may be used as a decision-making tool in primary prevention patients with moderate CVD risk. Finally, the ceramide risk score may have a unique utility as a motivational tool to increase patient's adherence to medical therapy and lifestyle changes.

Mantovani et al (2020) studied data from eligible studies and meta-analysis was performed using random-effects modeling. Seven cohort studies with aggregate data on 29,818 individuals (2736 new cases of cardiovascular events over a median follow-up of 6 years) were included. Higher plasma levels of Cer(d18:1/16:0) (random effects hazard ratio [HR] per standard deviation 1.21, 95% confidence interval [CI] 1.11-1.32, I(2) = 88%), Cer(d18:1/18:0) (HR 1.19, 95% CI 1.10-1.27, I(2) = 68%), and Cer(d18:1/24:1) (HR 1.17, 95% CI 1.08-1.27, I(2) = 83%) were associated with major adverse cardiovascular events.

Conversely, no association with plasma levels of Cer(d18:1/22:0) (HR 1.14 95% CI 0.88-1.47, I(2) = 88%) and Cer(d18:1/24:0) (HR 0.97, 95% CI 0.89-1.05, I(2) = 73%) was found. Subgroup analyses did not substantially modify the findings. The authors concluded that higher plasma levels of Cer(d18:1/16:0), Cer(d18:1/18:0) and Cer(d18:1/24:1) were associated with major adverse cardiovascular events, whereas plasma levels of Cer(d18:1/22:0) and Cer(d18:1/24:0) were not. It was determined that additional research is required to elucidate the different role of ceramides on pathways involved in cardiovascular disease.

Meeusen et al (2020) found that elevated plasma concentrations of ceramides are associated with multiple risk factors of atherosclerotic cardiovascular diseases and comorbidities including obesity, insulin resistance and diabetes mellitus. Also, atherosclerotic plaques have been shown to be highly enriched with ceramides. Increases in ceramide content may accelerate atherosclerosis development by promoting LDL infiltration to the endothelium and aggregation within the intima of artery walls. Recently published data have shown that ceramides are not only of scientific interest but may also have diagnostic value. Their independent prognostic value for future cardiovascular outcomes over and above LDL cholesterol and other traditional risk factors have consistently been shown in numerous clinical studies. Thus, ceramide testing with a mass spectrometer offers a simple, reproducible and cost-effective blood test for risk stratification in atherosclerotic cardiovascular diseases.

Vasile et al (2021) found that the CERT2 test appears to be particularly robust in the risk stratification of patients with type 2 diabetes. The authors mentioned that it would be interesting to probe CERT2 in other community populations and compare the test with other established risk calculators used in clinical practice to stratify atherosclerotic risk. However, they determined that more validation studies were warranted before considering implementing CERT2 into routine clinical practice for primary prevention.

Vasile et al (2021) investigated the role of ceramide scores in a cohort of subjects from the community with average burden of CAD. This investigation identified the ceramide risk score as a biomarker that could be used for primary prevention, and could be applied particularly in patients at intermediate risk. The finding was thought to be important for risk stratification and therapeutic intensity options, as well as a reasonable tool to assess response to intervention. The authors thought that specific subgroups of ceramides may identify patients at higher risk who may be overlooked and conversely, a particular category of high risk patients defined by the ASCVD score may be treated too aggressively; however, it was determined that further studies were warranted.

Akhiyat et al (2022) examined the role of plasma ceramides in early coronary atherosclerosis characterized by coronary endothelial dysfunction. Participants presenting with chest pain and nonobstructive epicardial coronary artery disease underwent coronary endothelial function. The current study demonstrated an association between increased circulating ceramide levels and coronary endothelial dysfunction in the absence of epicardial coronary artery disease. This study supports the role of plasma ceramides as a potential biomarker or a therapeutic target for early coronary atherosclerosis in humans.

## Analysis of Evidence (Rationale for Determination)

HUMAN PLATELET ANTIGEN 1-15

There are too few Medicare beneficiaries that would both be pregnant and at risk for neonatal alloimmune thrombocytopenia to warrant coverage outside of appeal.

*IFNL3* (IL28B)

Given that PEG interferon treatment of HCV is becoming obsolete, so is related companion genetic testing. In addition, when used and IL28 testing is negative, there is little evidence that clinicians still do not use the PEG-interferon-alpha-containing regimens despite the unfavorable response genotype. The testing is, therefore, considered not medically necessary.

*G6PD*

While initial and even confirmatory testing for G6PD deficiency when certain high-risk drugs are used is appropriate, the use of molecular/genetic/DNA methods is not established. General screening, not to be confused with testing immediately before prescription of high-risk drugs, is not a Medicare benefit.

**IGH and TP53**

Coverage is provided for IGH and TP53 genes to facilitate decision-making in the medical management of Chronic Lymphocytic Leukemia (CLL) patients. NCCN Category 2A designation supports coverage of IGH and TP53 gene testing for Chronic Lymphocytic Leukemia (CLL) patients.

Ceramides Risk Score

Although the ceramide risk score may have promise as an indicator of potential major cardiovascular events, additional research is required to fully understand the value of the risk score in the therapeutic medical management of the patient's condition. The testing is, therefore, not considered medically necessary.

## General Information

### Associated Information

N/A

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## Revision History Information

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| 07/13/2025 | R24 | Under Coverage Indications and Limitations section, the indication was corrected to read "**JAK2 V617F** genotyping is considered medically necessary in the initial diagnostic work-up of BCR-ABL negative, adults with clinical, laboratory, or pathological findings suggesting myeloproliferative neoplasm (MPN) (polycythemia vera (PV), essential thrombocythemia (ET) or primary myelofibrosis (PMF)) or a myelodysplastic syndrome (MDS)." | • Provider Education/Guidance |
| 08/01/2024 | R23 | The following language was added to the Indication and Limitations Section: **Ceramides Risk Score** (Ceramides by liquid chromatography-tandem mass spectrometry, plasma, quantitative report with risk score for major cardiac events) is considered not medically necessary.<br><br>The Summary Of Evidence, Analysis of Evidence and Bibliography sections were updated. | • Provider Education/Guidance |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| 08/06/2023 | R22 | Due to an inadvertent typographical error, the MLH1 gene has been removed from the Coverage Indications, Limitations and/or Medical Necessity section-Tier 2 Non-covered Codes/Gene Combinations, effective for services rendered on or after 8/6/2023. | • Provider Education/Guidance |
| 08/06/2023 | R21 | Based upon the two Reconsideration Requests received, chronic lymphocytic leukemia was added to the following Indications of Coverage:<br><br>TP53 (tumor protein 53) (e.g. tumor samples), targeted sequence analysis of 2-5 exons, and CPT code 81405 TP53 (tumor protein 53) (e.g. Li-Fraumeni syndrome, tumor samples), full gene sequence or targeted sequence analysis of >5 exons are considered medically necessary in individuals who have Acute Myelogenous Leukemia, chronic lymphocytic leukemia (CLL), or Myelodysplastic Disease to guide therapeutic decision-making.<br><br>IGH@ (Immunoglobulin heavy chain locus) is considered medically necessary for acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), and lymphoma, B-cell to guide therapeutic decision making.<br><br>Corrected the LCD number referenced in the following paragraph from L36376 to L37810:<br><br>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 is considered not medically necessary except when used to guide treatment decision making in individuals with non-small cell lung cancer (please refer to LCD L37810). | • Provider Education/Guidance |
| 07/01/2020 | R20 | Based on a Reconsideration Request, added CYP2C9 testing which is indicated for the treatment of relapsing forms of multiple sclerosis and requires CYP2C9 genotyping for dosing in accordance with the FDA prescribing information. CYP2C9 testing must include the *1, *2, and *3 alleles that are necessary to safely dose the FDA-approved drug Mayzent, effective for services rendered on or after July, 1, 2020. | • Reconsideration Request<br>• Other (FDA Label) |
| 10/03/2019 | R19 | This LCD was converted to the new "no-codes" format. There has been no change in coverage with this LCD revision. | • Revisions Due To Code Removal |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| 01/01/2019 | R18 | Based on CR10901 and the annual CPT/HCPCS update, coding guidance has been transitioned to the Molecular Pathology Procedures Article A56199.<br><br>*DATE (01/01/2019): At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.* | • Provider Education/Guidance<br>• Revisions Due To CPT/HCPCS Code Changes<br>• Other (CR10901) |
| 10/01/2018 | R17 | Due to the annual ICD-10-CM update, diagnosis codes C43.11, C43.12, D03.11, and D03.12 were deleted from code ranges C43.0 - C43.9 and D03.0 - D03.9, and the following codes were added to code ranges C43.0 - C43.9 and D03.0 - D03.9 in the "ICD-10 Codes that Support Medical Necessity" section, Group 4 and Group 15: C43.111, C43.112, C43.121, C43.122, D03.111, D03.112, D03.121, D03.122.<br><br>*DATE (10/01/2018): At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.* | • Revisions Due To ICD-10-CM Code Changes |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| 09/01/2018 | R16 | ICD-10-CM Groups 30-34 were established for CPT codes 81120, 81121 (Group 33); 81335 (Group 30); 81175, 81176 (Group 32); 81334 (Group 31); 81479- MYD88 (Group 34).<br><br>**CPT codes 81105-81112 (HUMAN PLATELET ANTIGEN 1-15), 81283 (IFNL3/IL28B) and 81247-81249 (G6PD)-** Added language to "Summary of Evidence" and "Analysis of Evidence (Rationale for Determination)".<br><br>**CPT code 81170**- Added ICD-10-CM 0codes C91.00-C91.02 to the "ICD-10 Codes that Support Medical Necessity" section- Group 2.<br><br>**Code 81401-**Removed MEN from Non-Covered listing in the "Indications and Limitations of Coverage" section.<br><br>**CPT codes 81218 (CEBPA), 81245- 81246 (FLT3), 81272 (KIT), 81310 (NPM1) -**Added ICD-10-CM codes C92.90, C92.92, C93.00, C93.02, C94.80, C94.82, C95.00, C95.02, C95.90, C95.92, R16.1, R16.2 to the "ICD-10 Codes that Support Medical Necessity" section- Groups 5, 11, 15, 28.<br><br>**CPT codes-81270 (JAK2), 81402 (MPL), 81403 (MPL), 81403 (JAK2, exons 12 and 13), and 81219 (CALR)-** Corrected ICD-10-CM diagnosis codes by removing D45, D46.0, D46.1, D46.20, D46.21, D46.22, D46.A, D46.B, D46.C, D46.4, D46.Z, and D46.9 from the "ICD-10 Codes that Support Medical Necessity" section and added C88.8, C92.20, C92.22, C93.10, C93.12, C93.90, C93.92, C93.Z0, C93.Z2, C94.40, C94.41, C94.42, C95.10, C95.12, C96.Z, D47.1, D47.3, D47.4, D47.9, D47.Z9, D72.821, D72.828, D72.829, D72.89, D72.9, D75.9, D77, R16.1, R16.2- Group14<br><br>**CPT code 81314-**Added ICD-10-CM codes C49.A0-C49.A9 to "ICD-10 Codes that Support Medical Necessity" section- Group 20.<br><br>**CPT codes 81261-81264-**Added ICD-10-CM codes C91.00-C91.02 to the "ICD-10 Codes that Support Medical Necessity" section- Group 13 and corrected the Indication of Coverage criteria by replacing acute lymphoblastic leukemia (AML) with acute lymphoblastic leukemia (ALL). The AML ICD-10-CM codes were removed to correct- Group 13.<br><br>**CPT codes 81206-81208-**Added ICD-10-CM codes C91.00-C91.02 to the "ICD-10 Codes that Support Medical Necessity" section- Group 3 and added the following language to the "Indications and Limitations of Coverage" section: "BCR/ABL is indicated in patients with suspected CML with either persistent, unexplained leukocytosis or thrombocytosis."<br><br>**CPT code 81301-**Added the following language to the "Indications and Limitations of Coverage" section: "MSI testing is also required by FDA for the clinical use of | • Provider Education/Guidance<br>• Reconsideration Request |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| | | Keytruda (pembrolizumab) in a restricted population of patients. These are patients who have unresectable or metastatic solid tumors who have progressed following prior treatment and have no satisfactory alternative options. When Keytruda (pembrolizumab) is a potential clinically appropriate therapeutic choice, MSI testing is medically necessary in these patients. Because this is a wide-ranging population of advanced cancer patients, ICD-10 specificity is impractical, therefore use an ICD-10 appropriate for the tumor type and location."<br><br>CPT Codes 81404-81405 (TP53), Added ICD-10-CM codes C88.8, C92.20, C92.22, C92.90, C92.92, C93.00, C93.02, C93.10, C93.12, C93.90, C93.92, C93.Z0, C93.Z2, C94.40, C94.41, C94.42, C94.80, C94.82, C95.00, C95.02, C95.10, C95.12, C95.90, C95.92, C96.9, C96.Z, D45, D47.1, D47.3, D47.4, D47.9, D47.Z9, D61.818, D69.49, D69.6, D69.8, D69.9, D70.8, D70.9, D72.810, D72.818, D72.819, D72.821, D72.828, D72.829, D72.89, D72.9, D75.81, D75.89, D75.9, D77, R16.1, R16.2 to the "ICD-10 Codes that Support Medical Necessity" section- Groups 29.<br><br>Added "Mesa R, Jamieson C, Bhatia R, et al. Myeloproliferative Neoplasms. NCCN Clinical Practice Guidelines in Oncology. 2017;Version 2.2018." to Sources of Information section.<br><br>Added sources of information to the Bibliography. | |
| 01/01/2018 | R15 | Added CPT code 81232 which was inadvertently omitted from CPT/HCPCS Code section- Group 3. | • Typographical Error |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| 01/01/2018 | R14 | Added the following ICD-10-CM diagnosis codes to the "ICD-10-CM That Supports Medical Necessity section"- Group 1, effective for services rendered on or after January 1, 2018: C25.0, C25.1, C25.2, C25.3, C25.4, C25.7, C25.8, C25.9, C48.1, C50.011, C50.012, C50.019, C50.021, C50.022, C50.029, C50.111, C50.112, C50.119, C50.121, C50.122, C50.129, C50.211, C50.212, C50.219, C50.221, C50.222, C50.229, C50.311, C50.312, C50.319, C50.321, C50.322, C50.329, C50.411, C50.412, C50.419, C50.421, C50.422, C50.429, C50.511, C50.512, C50.519, C50.521, C50.522, C50.529, C50.611, C50.612, C50.619, C50.621, C50.622, C50.629, C50.811, C50.812, C50.819, C50.821, C50.822, C50.829, C50.911, C50.912, C50.919, C50.921, C50.922, C50.929, C56.1, C56.2, C56.9, C57.00, C57.01, C57.02, C61, D05.11, D05.12.<br><br>Based on a reconsideration request to provide coverage for CPT code 0007M received in March 2017, sources reviewed were added to the Bibliography section. No changes in coverage were made.<br><br>*DATE (01/01/2018): At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.* | • Request for Coverage by a Practitioner (Part B) |
| 01/01/2018 | R13 | Added ICD-10-CM codes Z85.07 and Z85.46 to the “ICD-10-CM that Supports Medical Necessity” section- Group 1, effective for services rendered on or after 01/01/2018.<br><br>Based on a reconsideration request to provide coverage for CPT code 0007M received in July 2017, sources reviewed were added to the Bibliography section. No changes in coverage were made.<br><br>*DATE (01/01/2018): At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.* | • Request for Coverage by a Practitioner (Part B) |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| 01/01/2018 | R12 | Due to the annual HCPCS update, the following Tier 1 CPT codes were added to CPT/HCPCS section- Group 2: 81105-81112; 81120, 81121, 81175, 81176, 81238; 81247-81249; 81283, 81334, 81335, 81346, 81448, 81521, 81541, 81551.<br><br>The following Tier 1 CPT codes replaced existing Tier 2 codes and were added to CPT /HCPCS section- Group 3: 81232 replaced 81400-DPYD; 81258, 81259, 81269 replaced 81404-HBA1/HBA2; 81230-81231 replaced 81401-CYP3A4-CYP3A5; 81327 replaced 81401-SEPT9; 81328 replaced 81479-SLCO1B1; 81361-81364 replaced 81404-HBB.<br><br>ICD-10-CM Diagnosis Code Z85.43 was added to the ICD-10-CM Diagnosis Code section that supports medical necessity-Group 1.<br><br>Tier 1 CPT code 81520 replaced 0008M and was added to CPT/HCPCS section-Group 1 and to the ICD-10-CM Diagnosis Code section that supports medical necessity-Group 26.<br><br>*DATE (01/01/2018): At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.* | • Revisions Due To CPT/HCPCS Code Changes |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| 10/01/2017 | R11 | Due to the annual ICD-10-CM update, the following ICD-10 codes were deleted from the ICD-10 Codes that Support Medical Necessity section: C96.2 was deleted from Group 15 and was replaced by C96.20-C96.22, and C06.29; D47.0 was deleted from Group 15 and was replaced D47.01-D47.02, and D47.09; C96.2 was deleted from Group 22 and was replaced C96.20-C96.22, and C06.29.<br><br>Due to the annual ICD-10-CM update, the following ICD-10 code description was changed in the ICD-10 Codes that DO NOT Support Medical Necessity section: Z31.5 descriptor was changed from “Encounter for genetic counseling” to “Encounter for procreative genetic counseling”.<br><br>Due to the annual ICD-10-CM update, ICD-10 code, Z36, was deleted from the ICD-10 Codes that DO NOT Support Medical Necessity section and was replaced by Z36.0.<br><br>Added the following ICD-10-CM code range to the ICD-10 Codes that Support Medical Necessity section for CPT codes 81261-81264, Group 13: C85.10-C85.99, effective for services rendered on or after 4/1/2016.<br><br>*DATE (10/01/2017): At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.* | • Revisions Due To ICD-10-CM Code Changes |
| 08/01/2017 | R10 | Added the following screening codes to ICD-10 Codes that DO NOT Support Medical Necessity- Group1: Z13.71, Z13.79, and Z36.<br><br>*DATE (08/01/2017): At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy.* | • Provider Education/Guidance |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| 06/01/2017 | R9 | **CPT Codes 81162, 81211, 81212, 81213, 81214, 81215, 81216, 81217**<br>Added the following clarifying language to the Indications of Coverage section: " and the results will be used to benefit the individual tested in terms of potential to guide therapeutic decision making." -no change in coverage.<br><br>**CPT Code 81270**<br>Clarified the language in the Indications of Coverage section and deleted "in JAK2 V617F negative individuals"<br><br>**CPT code 81404, and 81405**<br>Added the following clarifying wording in the Indications of Coverage section: CPT code 81404 MEN1 (multiple endocrine neoplasia 1) (eg, multiple endocrine neoplasia type 1, Wermer syndrome), duplication/deletion and CPT code 81405 MEN1 (multiple endocrine neoplasia 1) (e.g. multiple endoctine neoplasia type 1, Wermer syndrome, duplication/deletion analysis) are considered medically necessary in patients with multiple endocrine neoplasia to guide therapeutic decision-making.<br><br>CPT code 81404 TP53 (tumor protein 53) (e.g. tumor samples), targeted sequence analysis of 2-5 exons, and CPT code 81405 TP53 (tumor protein 53) (e.g. Li-Fraumeni syndrome, tumor samples), full gene sequence or targeted sequence analysis of >5 exons are considered medically necessary for individuals who have Acute Myelogenous Leukemia or Myeloplastic Disease to guide therapeutic decision-making.<br><br>Added the complete narratives of the following genes to the COVERED MOLECULAR PATHOLOGY PROCEDURES section-:<br>81404 MEN1 (multiple endocrine neoplasia 1) (eg, multiple endocrine neoplasia type 1, Wermer syndrome), duplication/deletion<br><br>81404 TP53 (tumor protein 53) (e.g. tumor samples), targeted sequence analysis of 2-5 exons<br><br>81405 TP53 (tumor protein 53) (e.g. Li-Fraumeni syndrome, tumor samples), full gene sequence or targeted sequence analysis of >5 exons<br><br>81405 MEN1 (multiple endocrine neoplasia 1) (eg, multiple endocrine neoplasia type 1, Wermer syndrome), full gene sequence<br><br>Added the complete narrative to the following gene in the NON-COVERED MOLECULAR PATHOLOGY PROCEDURES section- no change in coverage: 81406 RET (ret-proto-oncogene) (eg, Hirschsprung disease), full gene sequence | • Provider Education/Guidance |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| | | Added CPT codes 81270 (JAK2), and 81219 (CALR) previously Group 6 to Group 14 ICD10CM Codes that support Medical Necessity section.<br><br>Added CPT codes 81404 and 81405 (RET- MEN Types 2B (81404) and 2A (81405)) to the narrative in Group 24 in the ICD10CM Codes that support Medical Necessity section paragraph and corrected the typographical error by deleting Diagnosis code E83.01.<br><br>Added the following language to the Indications of Coverage section: CPT codes 81404 TP53 (tumor protein 53) (e.g. tumor samples), targeted sequence analysis of 2-5 exons, and CPT code 81405 TP53 (tumor protein 53) (e.g. Li-Fraumeni syndrome, tumor samples), full gene sequence or targeted sequence analysis of >5 exons are considered medically necessary for individuals who have Acute Myelogenous Leukemia or Myelodysplastic Disease to guide therapeutic decision-making.<br><br>Added the following ICD-10-CM codes to Group 29 in the ICD-10-CM Codes that support Medical Necessity section: C92.00, C92.02, C92.30, C92.32, C92.40, C92.42, C92.50, C92.52, C92.60, C92.62, C92.A0, C92.A2, C92.Z0, C92.Z2, C94.00, C94.02, C94.6, D46.0, D46.1, D46.20, D46.21, D46.22, D46.A, D46.B, D46.C, D46.4, D46.Z, D46.9.<br><br>CPT code 81479<br>Added the following language to the Indications of Coverage section: RARS (SF3B1 mutation) is considered medically necessary in patients with Myelodysplastic Syndrome to guide therapeutic decision-making. | |
| 02/01/2017 | R8 | CPT code 81450 was removed from CPT/HCPCS NON-COVERED MOLECULAR PATHOLOGY PROCEDURES - Group 3. Refer to LCD L36926 Genomic Sequence Analysis Panels in the Treatment of Acute Myelogenous Leukemia (AML), effective for services rendered on or after 2/1/2017. | • Provider Education/Guidance |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| 01/01/2017 | R7 | The following revisions are effective for services rendered on or after 1/1/2017:<br>CPT codes 81280, 81281, 81282, 81413, and 81414<br>CPT codes 81280, 81281, and 81282 will be deleted as of 12/31/2016. The genes addressed by CPT codes 81280-81282 are now included in new CPT codes 81413 and 81414. CPT codes 81413 and 81314 also include genes which would have been reported with Tier 2 molecular CPT codes or CPT code 81479 which were considered not medically necessary. Codes 81413 and 81314 will be added to Group 3- NON-COVERED MOLECULAR PATHOLOGY PROCEDURES, effective for services rendered on or after 1/1/2017. No change in coverage.<br><br>CPT Code 81422<br>Added new CPT code 81422 to Group 3- NON-COVERED MOLECULAR PATHOLOGY PROCEDURES, effective 1/1/2017. For dates of service prior to 12/31/2016, Tier 2 molecular CPT codes or CPT code 81479 would have been used to report the genes included in this code which were considered not medically necessary. No change in coverage.<br><br>CPT Code 81439<br>Added new CPT code 81439 to Group 3- NON-COVERED MOLECULAR PATHOLOGY PROCEDURES. For dates of service prior to 12/31/2016, Tier 2 molecular CPT codes or CPT code 81479 would have been used to report the genes included in this code which were considered not medically necessary. No change in coverage.<br><br>CPT Code 81218<br>Added the following additional ICD-10-CM codes to the ICD-10 Codes that Support Medical Necessity section, Group 5: C92.00, C92.30, C92.02, C92.32, C92.40, C92.42, C92.50, C92.52, C92.A0, C92.A2, C92.Z0, C94.00, C94.02, C92.Z2. Removed ICD-10-CM codes C91.00-C91.02 that had been added previously in error. The ICD-10-CM diagnosis codes now align with the Indications of Coverage for Acute Myelogenous Leukemia (AML).<br><br>CPT Codes 81245, 81246<br>Added the following additional ICD-10-CM codes to the ICD-10 Codes that Support Medical Necessity section, Group 12: C92.30, C92.32, C94.00, C94.02, C92.Z0, C92.Z2, C92.A0, C92.A2. Removed the following ICD-10-CM codes to the ICD-10 Codes that Support Medical Necessity section, Group 12: C92.01, C92.41, C92.51, C92.61.<br><br>CPT Codes 81261-81264<br>Corrected the ICD-10 Codes that Support Medical Necessity section, Group 14 to align with the Indications of Coverage by removing the incorrect ranges (C91.00-C91.32, C91.50- C91.62, C91.A0-C93.92) and adding the | • Revisions Due To CPT/HCPCS Code Changes |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| | | following specific ICD-10-CM codes to Group 14 : C92.00, C92.02, C92.30, C92.32, C92.40, C92.42, C92.50, C92.52, C92.60, C92.62, C92.A0, C92.A2, C92.Z0, C92.Z2, C94.00, and C94.02.<br><br>CPT Code 81272<br>Added the following additional ICD-10-CM codes to the ICD-10 Codes that Support Medical Necessity section, Group 16: C92.30, C92.32, C92.Z0, C92.Z2, C92.60, C92.62, C92.A0, C92.A2, and C94.00, C94.02<br><br>CPT Code 81310<br>Added a new ICD-10-CM to CPT code Group 29 to align with the Indications of Coverage for Acute Myelogenous Leukemia (AML). Added the following additional ICD-10-CM codes to the ICD-10 Codes that Support Medical Necessity section, Group 29: C92.00, C92.02, C92.30, C92.32, C92.40, C92.42, C92.50, C92.52, C92.60, C92.62, C92.A0, C92.A2, C92.Z0, C92.Z2, C94.00, and C94.02.<br><br>The following revisions, not listed in prior Revision History # 6, are effective for services rendered on or after 12/1/2016:<br>CPT Code 81210<br>Added the following additional ICD-10-CM codes to the ICD-10 Codes that Support Medical Necessity section, Group 4: C17.0-C17.9, C18.0-C19, C20, C21.1-C21.8, C78.4, C78.5, Z85.038, Z85.048<br><br>CPT 81219<br>Removed CPT code 81219 (CALR) in the ICD-10 Codes that Support Medical Necessity section, Group 15.<br><br>CPT 81287<br>Added the following ICD-10-CM codes to the ICD-10 Codes that Support Medical Necessity section, Group 18: C71.0 - C71.9<br><br>CPT code 81301<br>Added the following ICD-10-CM codes to theICD-10 Codes that Support Medical Necessity section Group 19: C17.0 -C17.9, C18.0-C18.9, C19, C20, C21.1-C21.8, C33, C34.00-C34.12, C34.2, C34.30-C34.32, C34.80-C34.82, C34.90-C34.92, Z85.038, Z85.048<br><br>CPT 81332<br>Added the following ICD-10-CM code to the ICD-10 Codes that Support Medical Necessity section Group 22: E88.01<br><br>CPT code 81340, 81341, 81342<br>Added the following ICD-10-CM codes to the ICD-10 Codes that Support Medical Necessity section Group 23: C91.00-C91.02, C95.90-C95.92, D60.0, D60.1, D60.8, D61.01, D61.09, D61.1-D61.3, D61.89, D61.9 | |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
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| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| 12/01/2016 | R6 | Consolidated Molecular Pathology Procedures into three (3) separate CPT/HCPCS section Groups: Group 1- COVERED MOLECULAR PATHOLOGY PROCEDURES, GROUP-2 MOLECULAR PATHOLOGY PROCEDURES THAT REQUIRE INDIVIDUAL REVIEW, and GROUP 3- NON-COVERED MOLECULAR PATHOLOGY PROCEDURES<br><br>CPT Codes 81162, 81211, 81212, 81213, 81214, 81215, 81216, 81217 (BRCA1 and BRCA2)<br>Removed CPT/HCPCS Codes from Group 2, TIER 1 AND TIER 2 MOLECULAR PATHOLOGY PROCEDURES THAT REQUIRE INDIVIDUAL REVIEW and added to CPT/HCPCS Codes section, GROUP 1- COVERED MOLECULAR PATHOLOGY PROCEDURES. Added ICD-10-CM diagnosis codes Z86.000 and Z85.3 as payable for these CPT codes.<br><br>CPT code 81170 (ABL1)<br>Revised the Indications of Coverage section by removing the typographical error “chronic lymphoblastic leukemia (CLL)” and replacing with “chronic myeloid leukemia (CML)”. Revised the ICD-10 Codes that Support Medical Necessity section, Group 2, by removing the typographical error and replacing ICD-10-CM diagnosis code ranges C91.00-C91.02 and C91.10-C91.12 with ICD-10-CM diagnosis code ranges C92.10-C92.12 and C92.20-C92.22.<br><br>CPT code 81209 (BLM (Bloom syndrome, RecQ helicase-like)<br>Removed CPT code from TIER 1 NON-COVERED MOLECULAR PATHOLOGY PROCEDURES, Group 3, and added to CPT/HCPCS Codes section, GROUP 1- COVERED MOLECULAR PATHOLOGY PROCEDURES, Group1. Added criteria to the Indications and Limitations of Coverage section.<br><br>CPT Codes 81220, 81221, 81222, 81223, 81224 (CFTR)<br>Removed CPT codes from CPT/HCPCS Codes section, TIER 1 NON-COVERED MOLECULAR PATHOLOGY PROCEDURES, Group 3, and added to CPT/HCPCS Codes section, GROUP 1- COVERED MOLECULAR PATHOLOGY PROCEDURES. Added criteria to Indications and Limitations of Coverage section.<br><br>CPT code 81272 (KIT)<br>Added 2017 ICD-10-CM diagnosis code range C49.A0-C49.A9 to the ICD-10 Codes that Support Medical Necessity section, Group 16.<br><br>CPT code 81313 (PCA3)<br>Removed 81313 from CPT/HCPCS Codes section, Group 2, TIER 1 AND TIER 2 MOLECULAR PATHOLOGY PROCEDURES THAT REQUIRE INDIVIDUAL REVIEW and added to CPT/HCPCS Codes section, GROUP 1- COVERED | • Provider Education/Guidance |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| | | MOLECULAR PATHOLOGY PROCEDURES. Added ICD-10-CM diagnosis code R97.2 to ICD-10 Codes that Support Medical Necessity section, Group 7.<br><br>CPT Codes 81315, 81316 (PML/RARALPHA, (T(15;17)))<br>Removed CPT codes from CPT/HCPCS Codes section, Group 2, TIER 1 AND TIER 2 MOLECULAR PATHOLOGY PROCEDURES THAT REQUIRE INDIVIDUAL REVIEW, and added to CPT/HCPCS Codes section, GROUP 1-COVERED MOLECULAR PATHOLOGY PROCEDURES. Added ICD-10 Code range C92.40-C92.42 Acute promyelocytic leukemia to ICD-10 Codes that Support Medical Necessity section, Group 8.<br><br>CPT code 81401 (CBFB-MYH11)<br>Corrected name of gene 81401 CYFB-MYH11 to CBFB-MYH11 in COVERED MOLECULAR PATHOLOGY PROCEDURES section.<br><br>CPT code 81519 (ONCOLOGY (BREAST), MRNA)<br>Removed CPT code 81519 from Group 7, COVERED MULTIANALYTE ASSAYS with ALGORITHMIC ANALYSES PROCEDURES and added to CPT/HCPCS Codes section, GROUP 1- COVERED MOLECULAR PATHOLOGY PROCEDURES.<br><br>CPT code 81595 (CARDIOLOGY (HEART TRANSPLANT), MRNA,)<br>Removed CPT code 81595 from Group 7, COVERED MULTIANALYTE ASSAYS with ALGORITHMIC ANALYSES PROCEDURES and added to CPT/HCPCS Codes section, GROUP 1- COVERED MOLECULAR PATHOLOGY PROCEDURES.<br><br>CPT code 81599 UNLISTED MULTIANALYTE ASSAY WITH ALGORITHMIC ANALYSIS<br>Removed CPT code from Group 6- MULTIANALYTE ASSAYS with ALGORITHMIC ANALYSES PROCEDURES THAT REQUIRE INDIVIDUAL REVIEW and added CPT code 81599 to GROUP 2- MOLECULAR PATHOLOGY PROCEDURES THAT REQUIRE INDIVIDUAL REVIEW<br><br>CPT code 0008M (Prosigna® Breast Cancer Prognostic Gene Signature Assay)<br>Added criteria to Indications and Limitations of Coverage section. Removed CPT code 0008M from NON-COVERED GENOMIC SEQUENCING PROCEDURES AND OTHER MULTIANALYTE ASSAYS WITH ALGORITHMIC ANALYSES PROCEDURES, Group 5 and added CPT code 0008M to GROUP 1- COVERED MOLECULAR PATHOLOGY PROCEDURES. Added CPT code 0008M to the ICD-10 Codes that Support Medical Necessity section, Group 27. | |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| 10/01/2016 | R5 | Added ICD-10-CM diagnosis code range C49.A0-C49.A9 to the ICD-10 Codes that Support Medical Necessity section that relates to CPT code 81272 (Group 12). | • Revisions Due To ICD-10-CM Code Changes |
| 04/01/2016 | R4 | The LCD has been revised during the notice period to remove codes 81442, 81490-81595 from Group 5 CPT Code section and to delete Group 6 CPT Code section (NON-COVERED ADMINISTRATIVE CODES FOR MULTIANALYTE ASSAYS WITH ALGORITHMIC ANALYSES (MAAA) that contained codes 0001M-0004M and 0006M-0010M. | • Other (The CPT codes were not included in DL35000.) |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| 04/01/2016 | R3 | Added the following CPT codes and indications and limitations of coverage to the **TIER 1 AND TIER 2 INDICATIONS AND LIMITATIONS OF COVERAGE** section: 81170, 81162, 81216, 81218, 81219, 81227, 81245, 81246, 81271, 81273, 81276, 81301, 81311, 81314, 81370-81383, 81401, 81404, 81405, 81406<br><br>Added the following CPT codes to the CPT HCPCS Group 1 **TIER 1 COVERED MOLECULAR PATHOLOGY PROCEDURES** section: 81170, 81218, 81225, 81272, 81273, 81276, 81310, 81311, 81314, 81370-81383<br><br>Added the following CPT codes to the CPT HCPCS Group 2 **TIER 1 AND TIER 2 MOLECULAR PATHOLOGY PROCEDURES THAT REQUIRE INDIVIDUAL REVIEW** section: 81162, 81216, 81301<br><br>Added the following CPT codes to the CPT HCPCS Group 3 **TIER 1 NON-COVERED MOLECULAR PATHOLOGY PROCEDURES** section: 81219, 81227, 81355<br><br>Added the following CPT codes to the CPT HCPCS Group 5 **NON-COVERED GENOMIC SEQUENCING PROCEDURES AND MULTIANALYTE ASSAYS WITH ALGORITHMIC ANALYSES (MAAA)** section: 81442, 81490, 81493, 81500-81507, 81525, 81535, 81538, 81540, 81595<br><br>Added CPT code and ICD-10-CM diagnosis code groupings in **ICD-10-CM Diagnosis Codes that Support Medical Necessity** section for the following CPT codes: 81170, 81218, 81245-81246, 81272-81273, 81275-81276, 81311, 81314, 81401, 81404, 81405, 81406<br><br>Added the following CPT code ranges to the CPT HCPCS Group 6 NON-COVERED ADMINISTRATIVE MULTIANALYTE ASSAYS WITH ALGORITHMIC ANALYSES (MAAA) section: 0001M-0004M, 0006M-0010M<br><br>Added the following language to bullet number 6 in the Indications of Coverage section: "Exceptions include clinical scenarios whereby repeat testing of somatically-acquired mutations (for example, pre- and post- therapy) may be required to inform appropriate therapeutic decision-making.” | • Provider Education/Guidance<br>• Revisions Due To CPT/HCPCS Code Changes |
| 01/01/2016 | R2 | Based on the CPT/HCPCS annual update, the descriptions for the following codes have been changed: 81210, 81275, 81355, 81402. | • Revisions Due To CPT/HCPCS Code Changes |

| Revision History Date | Revision History Number | Revision History Explanation | Reasons for Change |
|---|---|---|---|
| 10/01/2015 | R1 | LCD updated to reflect administrative changes. | • Provider Education/Guidance |

## Associated Documents

### Attachments

N/A

### Related Local Coverage Documents

Articles

A56199 - Billing and Coding: Molecular Pathology Procedures

A59968 - Response to Comments: Molecular Pathology Procedures

### Related National Coverage Documents

NCDs

90.2 - Next Generation Sequencing (NGS)

### Public Versions

| Updated On | Effective Dates | Status | |
|---|---|---|---|
| 05/21/2025 | 07/13/2025 - N/A | Currently in Effect | You are here |
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| 06/15/2023 | 08/06/2023 - N/A | Superseded | View |

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## Keywords

N/A