Medicare Local Coverage Determination Policy

J6 NGS - Molecular Pathology Procedures

CPT: 81120,81121,81162,81165,81168,81170,81206,81207,81210,81212,81215,81218,81225,81226,81227,81245, 81246,81256,81261,81263,81264,81270,81272,81273,81275,81276,81279,81287,81301,81305,01310,81311, 81314,81315,81332,81335,81338,81339,81340,81342,81351,81352,81404,81405,81406,81520

CMS Policy for Illinois, Minnesota, and Wisconsin

Local policies are determined by the performing test location. This is determined by the state in which your performing laboratory resides and where your testing is commonly performed.

Medically Supportive ICD Codes are listed on subsequent page(s) of this document.

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,
- Diagnosis and Monitoring Non-Cancer Indications, and
- Several Pharmacogenomic applications.

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.

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CMS Policy for Illinois, Minnesota, and Wisconsin (continued)

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.

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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.

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.

CYP2C6 19-cytochrome P450 CYP2C6 19-cytochrome P450 Based on the FDA's Black Box warning for clopidogrel, the effectiveness of clopidogrel is dependent on its activation to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. CYP2C619 genotyping may be medically necessary once per lifetime to identify individuals:

- Who are poor metabolizers of clopidogrel, so that alternative treatment or treatment strategies can be considered
- Who are poor metabolizers of clopidogrel with acute coronary syndrome or who are undergoing percutaneous coronary intervention

CYP2C9 (cytochrome P450, family 2, subfamily D polypeptide 9) (e.g., drug metabolism), gene analysis, is only considered medically necessary for individuals who have relapsing forms of multiple sclerosis, and require CYP2C9 genotyping for dosing in accordance with the FDA prescribing information for Mayzent. CYP2C9 testing must include the *1, *2, and *3 alleles that are necessary to safely dose the FDA-approved drug Mayzent.

CYP2D6 (cytochrome P450, family 2, subfamily D polypeptide 6) (e.g., drug metabolism), gene analysis, is only considered medically necessary for individuals with Huntington's disease for whom doses of tetrabenazine greater than 50 mg per day are being considered, and for testing prior to the initiation of Cerdelga™ (eliglustat) for Gaucher's disease.

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.

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CMS Policy for Illinois, Minnesota, and Wisconsin (continued)

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:
  - Standard of care testing to diagnose certain HLA related drug hypersensitivity reactions when the testing is supported by the clinical literature and is informative for the direct management of a patient bearing a certain allele(s) associated to fatal skin drug reactions (Stevens-Johnson syndrome and toxic epidermal necrolysis). It is not expected that more than one test would be required in a given beneficiary's lifetime. Possible covered indications:
    - HLA –B*5701 when testing performed prior to the initiation of an abacavir-containing regime in the treatment of HIV Infection.
    - HLA-B*1502 when genotyping may be useful for risk stratification when the testing is performed prior to the initiation of carbamazepine therapy in the treatment of patients at high risk of having this allele. HLA-B*1502 occurs almost exclusively in patients with ancestry across broad areas of Asia, including South Asian Indians.
    - Identification of HLA compatible platelets for transfusion when standard typing is not adequate.

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) 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, JAK2-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). Note: JAK2 (exons 12 and 13) (reported with 81403) is medically necessary in individuals for whom PV is a strong consideration.

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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.

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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.

PCA3 testing is considered medically necessary in patients ONLY when all biopsies in previous encounter(s) are negative for prostatic cancer, the subsequent prostate specific antigen (PSA) is rising, and when the patient or physician wants to avoid repeat biopsy ("watchful waiting"). When the physician plans to biopsy the prostate, NGS will consider a PCA3 test as not medically necessary, and thus, not a covered Medicare benefit. NGS considers all other indications for PCA3 not reasonable and necessary. Medical record documentation must indicate the rationale to perform a PCA3 assay.

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 L36376).

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 or Myeloplastic 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.

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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)

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CMS Policy for Illinois, Minnesota, and Wisconsin (continued)

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):

ABCC8

AADM

ACADS (acyl-CoA dehydrogenase)

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)

J6 NGS - Molecular Pathology Procedures

CPT: 81120,81121,81162,81165,81168,81170,81206,81207,81210,81212,81215,81218,81225,81226,81227,81245, 81246,81256,81261,81263,81264,81270,81272,81273,81275,81276,81279,81287,81301,81305,01310,81311, 81314,81315,81332,81335,81338,81339,81340,81342,81351,81352,81404,81405,81406,81520

CMS Policy for Illinois, Minnesota, and Wisconsin (continued)

DYT1 (TOR1A)

EGR2 (early growth response 2) (eg, Charcot-Marie-Tooth)

F8 (coagulation factor VIII)

F8 (coagulation factor VIII)

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

Level 8 Molecular Pathology Procedures

Level 9 Molecular Pathology Procedures

LMNA (lamin A/C)

LPA intron 25 genotype

J6 NGS - Molecular Pathology Procedures

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CMS Policy for Illinois, Minnesota, and Wisconsin (continued)

LPA intron 25 genotype

MEFV (Mediterranean fever) (eg, familial Mediterranean fever)

MEG3/DLK1

MEK1

MLH1

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)

J6 NGS - Molecular Pathology Procedures

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CMS Policy for Illinois, Minnesota, and Wisconsin (continued)

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)

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.

Medicare Local Coverage Determination Policy

J6 NGS - Molecular Pathology Procedures

CPT: 81120,81121,81162,81165,81168,81170,81206,81207,81210,81212,81215,81218,81225,81226,81227,81245, 81246,81256,81261,81263,81264,81270,81272,81273,81275,81276,81279,81287,81301,81305,01310,81311, 81314,81315,81332,81335,81338,81339,81340,81342,81351,81352,81404,81405,81406,81520

CMS Policy for Illinois, Minnesota, and Wisconsin

Local policies are determined by the performing test location. This is determined by the state in which your performing laboratory resides and where your testing is commonly performed.

The ICD10 codes listed below are the top diagnosis codes currently utilized by ordering physicians for the limited coverage test highlighted above that are also listed as medically supportive under Medicare's limited coverage policy. **If you are ordering this test for diagnostic reasons that are not covered under Medicare policy, an Advance Beneficiary Notice form is required.**
Note—Bolded diagnoses below have the highest utilization

Code	Description
81206	
C92.10	
C92.11	
81270	
D45	
D751	
D7589	

Visit **QuestDiagnostics.com/MLCP** to view current limited coverage tests, reference guides, and policy information.
To view the complete policy and the full list of medically supportive codes, please refer to the CMS website reference www.cms.gov ▶

Last updated: