Genetic Testing

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Developed By: Medical Necessity Criteria Committee

I. Description

The broadest definition of genetic testing includes all tests that are ordered to look for evidence of inherited traits or diseases. Some genetic tests analyze DNA, the inherited chemical material. Other tests examine the chromosomes or protein. Genetic tests search DNA for specific changes. Some changes could increase a person's chance of developing a particular disease. Other changes might not affect the person, but could put his or her children at risk. Some genetic tests look for changes in proteins, which reflect changes in the DNA. Such tests look for the presence, absence or function of a protein. This information can tell physicians if the gene that makes the protein is working properly. Laboratory tests can determine whether a person carries some of the genetic alterations that can increase a person's risk of developing certain cancers. With the completion of the Human Genome Project, new genetic tests have entered the market. Disease risk testing seeks to identify individuals predisposed toward certain diseases and to identify markers for risk of future disease. However, the information obtained from genetic tests is often complex and difficult to interpret. The decision to undergo genetic testing should therefore be a personal, voluntary one and should only be made in conjunction with appropriate genetic counseling.

II. Criteria: CWQI HCS-0031

A. **Pregnancy related** *(or those planning to become pregnant, as applicable)* for **1 or more** of the following (a, b, or c):

   a. Pregnant woman or couples planning pregnancy with a personal or family history of genetic disorder;
   b. Pregnant woman or couples planning pregnancy with ancestry with high risk of genetic disorder that meet the specific criteria for the test (refer to Clinical Care Guidelines for specific conditions);
   c. Testing of both parents (i.e. chromosome analysis, karyotype) after previous unexplained stillbirth, repeated *(two or more)* first trimester miscarriages, or previous child with abnormality.

In addition, pre-test genetic counseling must be provided by a qualified and appropriately trained practitioner.

The requested procedure or services are considered investigational if they are requested in a quantity or panel of services that may be individually proven but when performed as a group or panel, the evidence-based literature does not support the requested procedures or services. *(i.e. Counsyl Universal, Genecept)*.

B. **Pre/Post Symptomatic Testing** *(all members – refer to Moda Health Clinical Care Guidelines for the specific genetic disorder testing or appropriate NCD/LCD for Medicare)*. If guidelines are **NOT** available then **ALL** of following criteria apply:
    a. Patients who have signs or symptoms of a genetic disease or are at risk of inheriting the disease due to family history or ancestry and **ALL** of the following:
        i. The requested genetic test has been proven in evidenced-based literature to be diagnostic of the specific disease or condition being tested for. Genetic tests that are not proven for the requested diagnosis are considered experimental and investigational.
    b. The results of the test may confirm or deny the diagnosis when standard evaluation does not provide a definitive answer.
    c. The results will directly impact the course of treatment.
    d. The requested procedure or services are considered investigational if they are requested in a quantity or panel of services that may be individually proven but when performed as a group or panel, the evidence-based literature does not support the requested procedures or services*. (i.e. Counsyl Universal, Genecept).*
    e. Pre-test genetic counseling must be provided by a qualified and appropriately trained practitioner.

C. **Tumor Marker Genetic Assays:**
    a. Moda Health considers the following tumor markers medically necessary if **1 or more** of the following:
        i. Gene expression assays for breast cancer risk stratification for 1 or more of the following per primary breast tumor:
            1. Endopredict (81599) – risk stratification for breast cancer staging refer to MCG A-0532 Breast Cancer Gene Expression Assays
            2. Oncotype DX for Breast Cancer assay (81519) - risk stratification for breast cancer staging refer to MCG A-0532 Breast Cancer Gene Expression Assays.
            3. Mammaprint 70 gene breast assay (81521) – refer to MCG A-0532 Breast Cancer Gene Expression Assays
        ii. Breast Cancer Index (81479) for continuation of endocrine therapy refer to Noridian LCD 36316.
        iii. Decision DX-UM (Uveal Melanoma) – risk stratification for uveal (eye) melanoma refer to Noridian LCD 37072
        iv. Prolaris Prostate Cancer Genomic Assay (81541) – refer to Moda Health Medical Necessity Criteria for Prostate Cancer Genomic Assay HCS-0225
        v. Myriad Integrated BRACAnalysis with myRisk (81479) BRCA1 and 2 – refer to MCG A-0499 Breast and Ovarian Cancer, Hereditary
        vi. Myriad Colaris with myRisk – colon cancer (81479) – refer to MCG A-0533 Lynch Syndrome

D. **Genetic testing for the following conditions is considered NOT medically necessary** including but not limited to **ALL** of the following:
    a. Familial Alzheimer Disease
    b. Amyotropic lateral sclerosis
    c. Age-related macular edema
    d. Narcolepsy
    e. Scoliosis
    f. Depression
    g. Mood disorders
    h. Bipolar disorders
    i. Anxiety disorders
    j. Attention deficit hyperactivity disorder
    k. Anorexia nervosa

E. **Pharmacogenetic testing** for effectiveness and dosing of specific drugs are available in Moda Health Clinical Care Guidelines. **All** of the following, but not limited to, **pharmacogenetic testing panels are considered experimental and investigational** as there is insufficient evidence in peer-reviewed literature to support the clinical utility:
    a. Genecept Assay (Clinical Reference Laboratory, Inc.)
    b. GeneSight Assay (Assurex Health, Inc.)
    c. PGXL Broad Spectrum Panel (Pharmacogenetics Diagnostic Laboratory, LLC)
    d. Millenium PGT (Millenium Laboratories, LLC)
    e. AmpliChip
    f. STAR SureGene Test for Antipsychotic and Antidepressant Response

F. Moda Health considers **All** of the following, but not limited to, **genetic tests/panels experimental and investigational** as there is insufficient evidence in peer-reviewed literature to support their clinical utility:
    a. BRCAplus (Ambry Genetics Corp.)
    b. CancerNext (Ambry Genetics Corp.)
    c. ColoNext (Ambry Genetics Corp.)
    d. DecisionDX – Glioblastoma multiforme (GBM) or Cutaneous Melanom (CM)
    e. epiSEEK
    f. Gene Trails
    g. Guardant 360
    h. Macula Risk PGX
    i. mtSEEK Whole Mitochondrial Genome Analysis (Courtagen Life Sciences, Inc.)
    j. OncoGeneDX (GeneDX)
    k. Oncotype DX Prostate Cancer Assay (Genomic Health)
    l. Oncotype DX Colon Cancer Assay (Genomic Health)
    m. OncoVue for Breast Cancer Risk (Intergenetics, Inc.)
    n. OvaNext Next-Gen Cancer Panel
    o. OvaSure (LabCorp)

p. PancNext Gen Cancer Panel (Ambry Genetics Corp)
q. Pathfinder TG Topographic

G. **Direct to consumer genetic testing** is **NOT** covered by Moda Health *(i.e. 23 and me, Color)*. Genetic testing must be ordered by an appropriate provider, performed by a CLIA approved laboratory, and meet the medical necessity criteria for the specific indication.

III. Information Submitted with the Prior Authorization Request:

1. Provider chart notes
2. Family history

a. Documentation of pre-test genetic counseling from a qualified and appropriately trained provider.

IV. Applicable CPT or HCPC codes

Codes	Description
81105 – new code 1/1/18	Human Platelet Antigen 1 genotyping (HPA-1), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa], antigen CD61 [GPIIIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-1a/b (L33P)
81106 – new code 1/1/18	Human Platelet Antigen 2 genotyping (HPA-2), GP1BA (glycoprotein Ib [platelet], alpha polypeptide [GPIba]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-2a/b (T145M)
81107 – new code 1/1/18	Human Platelet Antigen 3 genotyping (HPA-3), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex], antigen CD41 [GPIIb]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-3a/b (I843S)
81108 – new code 1/1/18	Human Platelet Antigen 4 genotyping (HPA-4), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa], antigen CD61 [GPIIIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-4a/b (R143Q)
81109 – new code 1/1/18	Human Platelet Antigen 5 genotyping (HPA-5), ITGA2 (integrin, alpha 2 [CD49B, alpha 2 subunit of VLA-2 receptor] [GPIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant (eg, HPA-5a/b (K505E))
81110 – new code 1/1/18	Human Platelet Antigen 6 genotyping (HPA-6w), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa, antigen CD61] [GPIIIa]) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-6a/b (R489Q)
81111 – new code 1/1/18	Human Platelet Antigen 9 genotyping (HPA-9w), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex, antigen CD41] [GPIIb]) (eg, neonatal

	alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-9a/b (V837M)
81112	Human Platelet Antigen 15 genotyping (HPA-15), CD109 (CD109 molecule) (eg, neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-15a/b (S682Y)
81161	DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed
81162	BRCA1 and BRCA2 (breast cancer 1 and 2) (hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis
81203	APC (adenomatous polyposis coli) (eg familial adenomatous polyposis (FAP) attenuated FAP) gene analysis, duplication/deletion variants
81210	BRAF (v-raf murine sarcoma viral oncogene homolog B1) (eg, colon cancer), gene analysis, V600E variant
81211	BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants in BRCA1 (ie, exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)
81212	BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants
81213	BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; uncommon duplication/deletion variants
81214	BRCA1 (breast cancer 1) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants (ie, exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb
81215	BRCA1 (breast cancer 1) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant
81216	BRCA2 (breast cancer 2) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81217	BRCA2 (breast cancer 2) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence
81228	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (eg, bacterial artificial chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis)
81229	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities.
81238 – new code 1/1/18	F9 (coagulation factor IX) (eg, hemophilia B), full gene sequence
81247 – new code 1/1/18	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; common variant(s) (eg, A, A-)

81248 – new code 1/1/18	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; known familial variant(s)
81249 – new code 1/1/18	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; full gene sequence
81252	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; full gene sequence
81255	HEXA (hexosaminidase A [alpha polypeptide]) (eg, Tay-Sachs disease) gene analysis, common variants (eg, 1278insTATC, 1421+1G>C, G269S)
81257	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis, for common deletions or variant (eg, Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, alpha4.2, alpha20.5, and Constant Spring)
81258 – new code 1/1/18	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; known familial variant
81259 – new code 1/1/18	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; full gene sequence
81269 – new code 1/1/18	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis;
81280	Long QT syndrome gene analyses (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); full sequence analysis
81281	Long QT syndrome gene analyses (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); known familial sequence variant
81282	Long QT syndrome gene analyses (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); duplication/deletion variants
81288	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis
81290	MCOLN1 (mucolipin 1) (eg, Mucolipidosis, type IV) gene analysis, common variants (eg, IVS3-2A>G, del6.4kb)
81292	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81293	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81294	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81295	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81296	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants

81297	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81298	MSH6 (mutS homolog 6 [E. coli]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81299	MSH6 (mutS homolog 6 [E. coli]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81300	MSH6 (mutS homolog 6 [E. coli]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81302	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; full sequence analysis
81303	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; known familial variant
81304	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; duplication/deletion variants
81317	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81318	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81319	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81321	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis
81322	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; known familial variant
81323	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; duplication/deletion variant
81324	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; duplication/deletion analysis
81325	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; full sequence analysis
81326	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; known familial variant
81327	SEPT9 (Septin9) (eg. Colorectal cancer methylation analysis)
81335 – new code 1/1/18	TPMT (thiopurine S-methyltransferase) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3)
81362 – new code 1/1/18	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); common variant(s) (eg, HbS, HbC, HbE)
81363 – new code 1/1/18	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); duplication/deletion variant(s)
81364 – new code 1/1/18	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); full gene sequence

81401	Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)
81402	Molecular pathology procedure, Level 3 (eg, >10 SNPs, 2-10 methylated variants, or 2-10 somatic variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants of 1 exon, loss of heterozygosity [LOH], uniparental disomy [UPD])
81403	Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)
81404	Molecular pathology procedure, Level 5 (eg, analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis)
81405	Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis)
81406	Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia)
81407	Molecular pathology procedure, Level 8 (eg, analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform)
81408	Molecular pathology procedure, Level 9 (eg, analysis of >50 exons in a single gene by DNA sequence analysis)
81412	Ashkenazi Jewish associated disorders (eg, Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group C, Gaucher disease, Tay-Sachs disease), genomic sequence analysis panel, must include sequencing of at least 9 genes, including ASPA, BLM, CFTR, FANCC, GBA, HEXA, IKBKAP, MCOLN1, and SMPD1
81413	Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); genomic sequence analysis panel, must include sequencing of at least 10 genes, including ANK2, CASQ2, CAV3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, RYR2, and SCN5A
81414	Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); duplication/deletion gene analysis panel, must include analysis of at least 2 genes, including KCNH2 and KCNQ1
81422	Fetal chromosomal microdeletion(s) genomic sequence analysis (eg, DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood
81432	Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 14 genes, including ATM,

	BRCA1, BRCA2, BRIP1, CDH1, MLH1, MSH2, MSH6, NBN, PALB2, PTEN, RAD51C, STK11, and TP53
81433	Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11
81434	Hereditary retinal disorders (eg, retinitis pigmentosa, Leber congenital amaurosis, cone-rod dystrophy), genomic sequence analysis panel, must include sequencing of at least 15 genes, including ABCA4, CNGA1, CRB1, EYS, PDE6A, PDE6B, PRPF31, PRPH2, RDH12, RHO, RP1, RP2, RPE65, RPGR, and USH2A
81437	Hereditary neuroendocrine tumor disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); genomic sequence analysis panel, must include sequencing of at least 6 genes, including MAX, SDHB, SDHC, SDHD, TMEM127, and VHL
81438	Hereditary neuroendocrine tumor disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); duplication/deletion analysis panel, must include analyses for SDHB, SDHC, SDHD, and VHL
81439	Inherited cardiomyopathy (eg, hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy) genomic sequence analysis panel, must include sequencing of at least 5 genes, including DSG2, MYBPC3, MYH7, PKP2, and TTN
81442	Noonan spectrum disorders (eg, Noonan syndrome, cardio-facio-cutaneous syndrome, Costello syndrome, LEOPARD syndrome, Noonan-like syndrome), genomic sequence analysis panel, must include sequencing of at least 12 genes, including BRAF, CBL, HRAS, KRAS, MAP2K1, MAP2K2, NRAS, PTPN11, RAF1, RIT1, SHOC2, and SOS1
81448 – new code 1/1/18	Hereditary peripheral neuropathies (eg, Charcot-Marie-Tooth, spastic paraplegia), genomic sequence analysis panel, must include sequencing of at least 5 peripheral neuropathy-related genes (eg, BSCL2, GJB1, MFN2, MPZ, REEP1, SPAST, SPG11, SPTLC1)
81479	Unlisted molecular pathology procedure
81520 – new code 1/1/18	Oncology (breast), mRNA gene expression profiling by hybrid capture of 58 genes (50 content and 8 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence risk score
81528	Oncology (colorectal) screening, quantitative real-time target and signal amplification of 10 DNA markers (KRAS mutations, promoter methylation of NDRG4 and BMP3) and fecal hemoglobin, utilizing stool, algorithm reported as a positive or negative result
81535	Oncology (lung), mass spectrometric 8-protein signature, including amyloid A, utilizing serum, prognostic and predictive algorithm reported as good versus poor overall survival
81538	Oncology (lung), mass spectrometric 8-protein signature, including amyloid A, utilizing serum, prognostic and predictive algorithm reported as good versus poor overall survival

81539	Oncology (high-grade prostate cancer), biochemical assay of four proteins (Total PSA, Free PSA, Intact PSA, and human kallikrein-2 [hK2]), utilizing plasma or serum, prognostic algorithm reported as a probability score
81540	Oncology (tumor of unknown origin), mRNA, gene expression profiling by real-time RT-PCR of 92 genes (87 content and 5 housekeeping) to classify tumor into main cancer type and subtype, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a probability of a predicted main cancer type and subtype
81541	Oncology (prostate), mRNA gene expression profiling by real-time RT-PCR of 46 genes (31 content and 15 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a disease-specific mortality risk score
81545	Oncology (thyroid), gene expression analysis of 142 genes, utilizing fine needle aspirate, algorithm reported as a categorical result (eg, benign or suspicious)
81551 – new code 1/1/18	Oncology (prostate), promoter methylation profiling by real-time PCR of 3 genes (GSTP1, APC, RASSF1), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a likelihood of prostate cancer detection on repeat biopsy
81595	Cardiology (heart transplant), mRNA, gene expression profiling by real-time quantitative PCR of 20 genes (11 content and 9 housekeeping), utilizing subfraction of peripheral blood, algorithm reported as a rejection risk score
81599	Unlisted multianalyte assay with algorithmic analysis

CPT codes NOT covered:

Codes	Description
81175- new code 1/1/18	ASXL1 (additional sex combs like 1, transcriptional regulator) (eg, myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; full gene sequence
81176 – new code 1/1/18	ASXL1 (additional sex combs like 1, transcriptional regulator) (eg, myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; targeted sequence analysis (eg, exon 12)
81225	Cyp2C19 (Cytochrome P450, Family 2, Subfamily C, Polypeptide 19), Gene Analysis, Common Variants
81226	Cyp2D6 (Cytochrome P450, Family 2, Subfamily D, Polypeptide 6), Gene Analysis, Common Variants
81227	Cyp2C9 (Cytochrome P450, Family 2, Subfamily C, Polypeptide 9), Gene Analysis, Common Variants (Eg, *2, *3, *5, *6)
81230 – new code 1/1/18	CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis, common variant(s)
81231 – new code 1/1/18	CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *7)
81232 – new code 1/1/18	DPYD (dihydropyrimidine dehydrogenase) (eg, 5-fluorouracil/5-FU and capecitabine drug metabolism), gene analysis, common variant(s) (eg, *2A, *4, *5, *6)

81291	Mthfr (5,10-Methylenetetrahydrofolate Reductase) (Eg, Hereditary Hypercoagulability) Gene Analysis, Common Variants
81313	PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kallikrein-related peptidase 3 [prostate specific antigen]) ratio (eg, prostate cancer)
81350	Ugt1A1 (Udp Glucuronosyltransferase 1 Family, Polypeptide A1) (Eg, Irinotecan Metabolism), Gene Analysis,Common Variants
81355	Vkorc1 (Vitamin K Epoxide Reductase Complex, Subunit 1) (Eg, Warfarin Metabolism), Gene Analysis, Common Variants
81377	HLA Class II typing, low resolution (eg, antigen equivalents); one antigen equivalent, each
81383	HLA Class II typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, HLA-DQB1*06:02P), each
81410	Aortic dysfunction or dilation (eg, Marfan syndrome, Loeys Dietz syndrome, Ehler Danlos syndrome type IV, arterial tortuosity syndrome); genomic sequence analysis panel, must include sequencing of at least 9 genes, including FBN1, TGFBR1, TGFBR2, COL3A1, MYH11, ACTA2, SLC2A10, SMAD3, and MYLK
81411	Aortic dysfunction or dilation (eg, Marfan syndrome, Loeys Dietz syndrome, Ehler Danlos syndrome type IV, arterial tortuosity syndrome); duplication/deletion analysis panel, must include analyses for TGFBR1, TGFBR2, MYH11, and COL3A1
81415	Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis
81416	sequence analysis, each comparator exome (eg, parents, siblings) (List separately in addition to code for primary procedure)
81417	re-evaluation of previously obtained exome sequence (eg, updated knowledge or unrelated condition/syndrome)
81425	Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analys
81426	Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator genome (eg, parents, siblings) (List separately in addition to code for primary procedure)
81427	Genome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained genome sequence (eg, updated knowledge or unrelated condition/syndrome)
81430	Hearing loss (eg, nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); genomic sequence analysis panel, must include sequencing of at least 60 genes, including CDH23, CLRN1, GJB2, GPR98, MTRNR1, MYO7A, MYO15A, PCDH15, OTOF, SLC26A4, TMC1, TMPRSS3, USH1C, USH1G, USH2A, and WFS1
81431	Hearing loss (eg, nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); duplication/deletion analysis panel, must include copy number analyses for STRC and DFNB1 deletions in GJB2 and GJB6 genes
81435	Hereditary colon cancer syndromes (eg, Lynch syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include analysis of at least 7 genes, including APC, CHEK2, MLH1, MSH2, MSH6, MUTYH, and PMS2
81436	duplication/deletion gene analysis panel, must include analysis of at least 8 genes, including APC, MLH1, MSH2, MSH6, PMS2, EPCAM, CHEK2, and MUTYH

81440	Nuclear encoded mitochondrial genes (eg, neurologic or myopathic phenotypes), genomic sequence panel, must include analysis of at least 100 genes, including BCS1L, C10orf2, COQ2, COX10, DGUOK, MPV17, OPA1, PDSS2, POLG, POLG2, RRM2B, SCO1, SCO2, SLC25A4, SUCLA2, SUCLG1, TAZ, TK2, and TYMP
81460	Whole mitochondrial genome (eg, Leigh syndrome, mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes [MELAS], myoclonic epilepsy with ragged-red fibers [MERFF], neuropathy, ataxia, and retinitis pigmentosa [NARP], Leber hereditary optic neuropathy [LHON]), genomic sequence, must include sequence analysis of entire mitochondrial genome with heteroplasmy detection
81465	Whole mitochondrial genome large deletion analysis panel (eg, Kearns-Sayre syndrome, chronic progressive external ophthalmoplegia), including heteroplasmy detection, if performed
81470	X-linked intellectual disability (XLID) (eg, syndromic and non-syndromic XLID); genomic sequence analysis panel, must include sequencing of at least 60 genes, including ARX, ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, and SLC16A2
81471	X-linked intellectual disability (XLID) (eg, syndromic and non-syndromic XLID); duplication/deletion gene analysis, must include analysis of at least 60 genes, including ARX, ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, and SLC16A2
81490	Autoimmune (rheumatoid arthritis), analysis of 12 biomarkers using immunoassays, utilizing serum, prognostic algorithm reported as a disease activity score
81493	Coronary artery disease, mRNA, gene expression profiling by real-time RT-PCR of 23 genes, utilizing whole peripheral blood, algorithm reported as a risk score
81500	Oncology (Ovarian), Biochemical Assays Of Two Proteins, Serum, W Menopausal Status, Algorithm Reported As A Risk Score
81503	Oncology (Ovarian), Biochemical Assays Of Five Proteins, Utilizing Serum, Algorithm Reported As A Risk Score
81504	Oncology Tissue of Origin
81519	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
81525	Oncology (colon), mRNA, gene expression profiling by real-time RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a recurrence score

V. References

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5. Medical References: Tay - Sachs disease. March of Dimes. Accessed on April 16, 2012 at: http://www.marchofdimes.com/baby/birthdefects_taysachs.html,
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9. Hayes. GTE Report. Alpha-Thalassemia. February 5, 2015.
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11. Physician Advisors
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VI. Annual Review History

Review Date	Revisions	Effective Date
02/2013	Annual Review: Added table with review date, revisions, and effective date.	03/1/2013
09/2013	Review: Added item 2.b related genetic test must be proven for the diagnosis or considered E/I. 2.e – related to multiple genetic panels must be medically necessary for the diagnosis to be covered.	09/25/2014
08/2014	Annual Review: No Changes	8/30/2014
02/2016	Annual Review: Added section I.2. e-g, added section 3 for pharmacogenetic tests, added section 4 for investigational genetic panels. Added new 2016 codes.	02/15/2016
02/2017	Annual Review: Updated to new template, revised statement	02/02/2017
10/2017	Added new genetic testing codes	10/25/2017
6/2018	Annual Review: added Mammaprint to criteria to align with CMS	07/01/2018
11/2018	Added definition of GBM and CM	11/19/2018

Appendix 1 – Covered Diagnosis Codes – including but not limited to:

ICD-10	ICD-10 Description
D56.0-D56.9	Thalassemia
D57.00-D57.819	Sickle cell disorders
D58.0-D58.9	Other hereditary hemolytic anemias
D66	Hereditary factor VIII deficiency
D67	Hereditary factor IX deficiency
D68.0-D68.9	Other coagulation defects
D70.0-D71	Neutropenia
E75.00-E75.6	Disorders of sphingolipid metabolism and other lipid storage disorders (i.e., Tay Sachs, Gaucher disease, Niemann-Pick disease, etc.)
F70-F79	Intellectual Disabilities
G10-G14	Systemic atrophies primarily affecting the CNS (i.e., Huntington's disease, spinal muscular atrophy, etc.)
G60.0-G65.2	Polyneuropathies and other disorders of the peripheral nervous system (i.e., hereditary and idiopathic neuropathy, etc.)
G47.35	Congenital central alveolar hypoventilation
Q75.0-Q75.9	Other congenital malformations of skull and face bones
Z13.0-Z13.89	Encounter for screening for other diseases and disorders
Z82.0-Z82.8	Family history of certain disabilities and chronic diseases (leading to disablement)

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

Jurisdiction(s): 5, 8	NCD/LCD Document (s):
Multiple LCD's apply to various genetic tests: Check Noridian website at: https://med.noridianmedicare.com/web/jfb/policies/lcd/active	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC