

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 meets 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.
 - d. Testing for Cystic Fibrosis (CF) and Spinal Muscular Atrophy (SMA) will be covered as part of standard care
 - e. Moda health does not provide coverage for the determination of fetal sex

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.

B. Pre/Post Symptomatic Testing (*all members – refer to Moda Health Medical Necessity Criteria (MHMNC) or Milliman Care Guidelines (MCG) for specific genetic disorder testing. If guidelines neither are 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.
- 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 (81522) – 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 (81518) for continuation of endocrine therapy is considered medically necessary when **All** of the following criteria are met; (reference LCD 38722)
 1. Member has early-stage disease (Tumor, Node, Metastasis (TNM) stage T1-3, pNO-N1, MO)
 2. Breast tumor is estrogen receptor positive (ER+) and/or progesterone receptor positive (PR+)
 3. Breast tumor is Human Epidermal Growth Factor Receptor 2 negative(HER2-)
 4. There is no evidence of distant breast cancer metastasis
 5. Test results will be used to guide therapy

- iii. Decision DX-UM (Uveal Melanoma) (81552) – risk stratification for uveal (eye) melanoma is considered medically necessary for members presenting with primary, localized uveal melanoma
- 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. Amyotrophic 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. The following **pharmacogenetic testing panels are considered experimental and investigational** as there is insufficient evidence in peer-reviewed literature to support the clinical utility. This is not an all-inclusive list:

- 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 the following **genetic tests/panels experimental and investigational** as there is insufficient evidence in peer-reviewed literature to support their clinical utility. This is not an all-inclusive list:

- a. BRCAplus (Ambry Genetics Corp.)
- b. CancerNext (Ambry Genetics Corp.)
- c. ColoNext (Ambry Genetics Corp.)
- d. DecisionDX – Glioblastoma multiforme (GBM) or Cutaneous Melanoma (CM)
- e. epiSEEK
- f. Genesight ADHD (Assurance Health)
- g. Gene Trails
- h. Guardant 360

- i. Macula Risk PGX
- j. mtSEEK Whole Mitochondrial Genome Analysis (Courtagen Life Sciences, Inc.)
- k. OncoGeneDX (GeneDX)
- l. Oncotype DX Prostate Cancer Assay (Genomic Health)
- m. Oncotype DX Colon Cancer Assay (Genomic Health)
- n. OncoVue for Breast Cancer Risk (Intergenetics, Inc.)
- o. OvaNext Next-Gen Cancer Panel
- p. OvaSure (LabCorp)
- q. PancNext Gen Cancer Panel (Ambry Genetics Corp)
- r. 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 (if available):

1. Provider chart notes
2. Family history
3. Documentation of pre-test genetic counseling from a qualified and appropriately trained provider

IV. Applicable CPT or HCPC codes if criteria requirements are met;

Codes	Description
81105	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	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	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	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	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	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	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
81168	CCND1/IGH (t(11;14)) (eg, mantle cell lymphoma) translocation analysis, major breakpoint, qualitative and quantitative, if performed
81191	NTRK1 (neurotrophic receptor tyrosine kinase 1) (eg, solid tumors) translocation analysis
81192	NTRK2 (neurotrophic receptor tyrosine kinase 2) (eg, solid tumors) translocation analysis
81193	NTRK3 (neurotrophic receptor tyrosine kinase 3) (eg, solid tumors) translocation analysis
81194	NTRK (neurotrophic-tropomyosin receptor tyrosine kinase 1, 2, and 3) (eg, solid tumors) translocation 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
81212	BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants
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	F9 (coagulation factor IX) (eg, hemophilia B), full gene sequence
81247	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; common variant(s) (eg, A, A-)
81248	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; known familial variant(s)
81249	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	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	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	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis;
81277	Cytogenomic neoplasia (genome-wide) microarray analysis, interrogation of genomic regions for copy number and loss-of-heterozygosity variants for chromosomal abnormalities
81278	IGH@/BCL2 (t(14;18)) (eg, follicular lymphoma) translocation analysis, major breakpoint region (MBR) and minor cluster region (mcr) breakpoints, qualitative or quantitative
81279	JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) targeted sequence analysis (eg, exons 12 and 13)
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, Mucopolipidosis, 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
81307	PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) gene analysis; full gene sequence
81308	PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) gene analysis; known familial variant
81309	PIK3CA (phosphatidylinositol-4, 5-biphosphate 3-kinase, catalytic subunit alpha) (eg, colorectal and breast cancer) gene analysis, targeted sequence analysis (eg, exons 7, 9, 20)
81317	PMS2 (postmeiotic segregation increased 2 [<i>S. cerevisiae</i>]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81318	PMS2 (postmeiotic segregation increased 2 [<i>S. cerevisiae</i>]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81319	PMS2 (postmeiotic segregation increased 2 [<i>S. cerevisiae</i>]) (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	TPMT (thiopurine S-methyltransferase) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3)
81338	MPL (MPL proto-oncogene, thrombopoietin receptor) (eg, myeloproliferative disorder) gene analysis; common variants (eg, W515A, W515K, W515L, W515R)
81339	MPL (MPL proto-oncogene, thrombopoietin receptor) (eg, myeloproliferative disorder) gene analysis; sequence analysis, exon 10
81347	SF3B1 (splicing factor [3b] subunit B1) (eg, myelodysplastic syndrome/acute myeloid leukemia) gene analysis, common variants (eg, A672T, E622D, L833F, R625C, R625L)
81348	SRSF2 (serine and arginine-rich splicing factor 2) (eg, myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variants (eg, P95H, P95L)
81351	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; full gene sequence
81352	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; targeted sequence analysis (eg, 4 oncology)
81353	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; known familial variant
81357	U2AF1 (U2 small nuclear RNA auxiliary factor 1) (eg, myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variants (eg, S34F, S34Y, Q157R, Q157P)

81360	ZRSR2 (zinc finger CCCH-type, RNA binding motif and serine/arginine-rich 2) (eg, myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variant(s) (eg, E65fs, E122fs, R448fs)
81362	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); common variant(s) (eg, HbS, HbC, HbE)
81363	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); duplication/deletion variant(s)
81364	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)
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
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
81419	Epilepsy genomic sequence analysis panel, must include analyses for ALDH7A1, CACNA1A, CDKL5, CHD2, GABRG2, GRIN2A, KCNQ2, MECP2, PCDH19, POLG, PRRT2, SCN1A, SCN1B, SCN2A, SCN8A, SLC2A1, SLC9A6, STXB1, SYNGAP1, TCF4, TPP1, TSC1, TSC2, and ZEB2
81422	Fetal chromosomal microdeletion(s) genomic sequence analysis (eg, DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood
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
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
81435	Hereditary colon cancer syndromes (eg, Lynch syndrome, familial adenomatous 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
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	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
81513	Infectious disease, bacterial vaginosis, quantitative real-time amplification of RNA markers for Atopobium vaginae, Gardnerella vaginalis, and Lactobacillus species, utilizing vaginal-fluid specimens, algorithm reported as a positive or negative result for bacterial vaginosis
81514	Infectious disease, bacterial vaginosis and vaginitis, quantitative real-time amplification of DNA markers for Gardnerella vaginalis, Atopobium vaginae, Megasphaera type 1, Bacterial Vaginosis Associated Bacteria-2 (BVAB-2), and Lactobacillus species
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
81520	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
81522	Oncology (breast), mRNA, gene expression profiling by RT-PCR of 12 genes (8 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as 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
81542	Oncology (prostate), mRNA, microarray gene expression profiling of 22 content genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as metastasis 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)

81546	Oncology (thyroid), mRNA, gene expression analysis of 10,196 genes, utilizing fine needle aspirate, algorithm reported as a categorical result (eg, benign or suspicious)
81554	Pulmonary disease (idiopathic pulmonary fibrosis [IPF]), mRNA, gene expression analysis of 190 genes, utilizing transbronchial biopsies, diagnostic algorithm reported as categorical result (eg, positive or negative for high probability of usual interstitial pneumonia [UIP])
81552	Oncology (uveal melanoma), mRNA, gene expression profiling by real-time RT-PCR of 15 genes (12 content and 3 housekeeping), utilizing fine needle aspirate or formalin-fixed paraffin-embedded tissue, algorithm reported as risk of metastasis
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	ASXL1 (additional sex combs like 1, transcriptional regulator) (eg, myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; full gene sequence
81176	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	CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis, common variant(s)
81231	CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *7)
81232	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
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 analysis
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)
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
81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
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
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
81529	Oncology (cutaneous melanoma), mRNA, gene expression profiling by real-time RT-PCR of 31 genes (28 content and 3 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence risk, including likelihood of sentinel lymph node metastasis
81551	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

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12. Local Coverage Determination (LCD):MoIDX: Breast Cancer Index® (BCI) Gene Expression Test (L37822) [Local Coverage Determination for MoIDX: Breast Cancer Index® \(BCI\) Gene Expression Test \(L37822\) \(cms.gov\)](https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=37822)

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 14 pharmacogenetics 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
06/2019	Annual Review: No changes	07/01/2019
11/2019	Updated codes on covered and non-covered list	11/01/2019
11/2019	Code 81551 indicated as Investigational, added to non-covered list Code updated; Endopredict (81520)	11/15/2019
1/2020	Updates: 2020 new codes added; coverage of Cystic Fibrosis (CF) and Spinal Muscular Atrophy (SMA) testing as part of standard care; no coverage for fetal sex determination	1/17/2020
06/2020	Annual Review: No content changes	07/01/2020
08/2020	Update: Endopredict CPT code 81520 to 81522	
01/2021	Update: replaced LCD L36316 with L37824, A57774 Added 2021 New CPT codes	
03/2021	Update: Breast Cancer Index, replaced CPT 81479 with 81518. CPT code 81529 always not covered	
07/2021	Annual Review: Expanded the requirements for Breast Cancer Index. Added coverage requirements for risk stratification for uveal melanoma	08/01/2021
08/2021	Update: reworded indications for Breast Cancer Index, LCD 38722	
06/2022	Annual Review: No changes	07/01/2022
06/2023	Annual Review: No changes	07/01/2023

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

ICD-10	ICD-10 Description
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