Laboratory Developed Test Coverage Criteria Guide

Genetic Test Name	Description	Coverage Criteria
ALK	Molecular cytogenetics; DNA probe, each (for example, FISH) Cytogenetics and molecular cytogenetics, interpretation and report	• to determine response to tyrosine kinase inhibitor (TKI) therapy in patients with adenocarcinoma of the lung or mixed lung cancer with adenocarcinoma component of the lung
APC	Adenomatous polyposis coli (APC) (for example, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; full gene sequence Known familial variants Duplication/deletion variants	• testing for APC variants in individuals with clinical symptoms consistent with FAP • testing for APC variants in individuals with clinical symptoms consistent with attenuated familial adenomatous polyposis (AFAP) • testing for APC variants in individuals with clinical symptoms consistent with Turcot's or Gardner's syndromes • testing individuals with an APC-associated polyposis syndrome for the purpose of identifying a variant that may be used to screen at-risk relatives • for the pre-symptomatic testing of at-risk relatives for a known familial variant
ATXN1	ATXN1 (ataxin1) (for example, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (for example, expanded) alleles	• diagnosis of spinocerebellar ataxia type 1 (SCA1) in patients with cerebellar ataxia of known etiology, along with extracerebellar symptoms associated with SCA1 and/or a family history consistent with autosomal dominant inheritance • diagnosis of SCA1 in symptomatic family members of known SCA1 patients
ATXN2	ATXN2 (ataxin2) (for example, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (for example, expanded) alleles	• diagnosis of spinocerebellar ataxia type 2 (SCA2) in patients with cerebellar ataxia of known etiology, along with extracerebellar symptoms associated with SCA2 and/or a family history consistent with autosomal dominant inheritance • diagnosis of SCA2 in symptomatic family members of known SCA2 patients
ATXN3	ATXN3 (ataxin3) (for example, spinocerebellar ataxia, Machado-Joseph disase) gene analysis, evaluation to detect abnormal (for example, expanded) alleles	• diagnosis of spinocerebellar ataxia type 3 (SCA3) in patients with cerebellar ataxia of known etiology, along with extracerebellar symptoms associated with SCA3 and/or a family history consistent with autosomal dominant inheritance • diagnosis of SCA3 in symptomatic family members of known SCA3 patients
ATXN7	ATXN7 (ataxin7) (for example, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (for example, expanded) alleles	• diagnosis of spinocerebellar ataxia type 7 (SCA7) in patients with cerebellar ataxia and visual disturbance • diagnosis of SCA7 in symptomatic family members of known SCA7 patients
ATXN10	ATXN10 (ataxin10) (for example, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (for example, expanded) alleles	• diagnosis of spinocerebellar ataxia type 10 (SCA10) in ataxia patients whose ancestry is of American Indian origin, and whose family history is consistent with autosomal dominant inheritance • diagnosis of SCA10 in symptomatic family members of known SCA10 patients
Afirma Thyroid FNA Analysis	Oncology (thyroid), gene expression analysis of 142 genes, utilizing fine needle aspirate, algorithm reported as a categorical result (for example, benign or suspicious)	• to aid in thyroid nodule diagnosis by reducing unnecessary surgeries in patients with indeterminate thyroid nodules

Genetic Test Name	Description	Coverage Criteria
BCR/ABL1	ABL1 BCR/ABL1 gene major bp BCR/ABL1 gene minor bp BCR/ABL1 gene other bp Mol Path, level 2 ABL1 (ABL proto oncogene 1, non-receptor tyrosine kinase) (for example, acquired imatinib resistance), T315I variant Oncology (hematolymphoid neoplasia), RNA, BCR/ABL1 major and minor breakpoint fusion transcripts, quantitative PCR amplification, blood or bone marrow, report of fusion not detected or detected with quantitation BCR/ABL1 (t9;22)) (for example, chronic myelogenous leukemia) translocation analysis, major breakpoint quantitative	• diagnostic assessment of individuals with suspected Chronic Myelogenous Leukemia (CML) by quantitative RT-PCR (RQ-PCR) • diagnostic assessment of individuals with suspected CML by qualitative RT-PCR • monitoring response to tyrosine kinase inhibitor (TKI) therapy, such as imatinib, in individuals with CML by RQ-PCR • testing for the presence of the BCR/ABL1 p.Thr315IlE variant in CML patients to guide treatment selection following resistance to first-line imatinib therapy • testing for the presence of BCR/ABL1 variants other than p.Thr315Ile in CML patients to guide treatment selection following resistance to first-line imatinib therapy
BMPR1A	Unlisted molecular pathology procedure	• to clarify the diagnosis of individuals with juvenile polyposis syndrome (JPS) • a known SMAD4 mutation is in the family (genetic testing should be performed in the first six months of life due to hereditary hemorrhagic telangiectasia risk)
BRAF	BRAF gene MolPath, level 7 BRAF (B-Raf protooncogene, serine/threonine kinase) (for example, Noonan syndrome), full gene sequence	• to predict response to vemurafenib therapy in patients with a positive cobas 4800 BRAF mutation test result • to predict response to trametinib monotherapy in advanced melanoma patients with a positive BRAF p.Val600Glu and/or p.Val600Lys test result. • to predict response to dabrafenib monotherapy in advanced melanoma patients with a positive BRAF p.Val600Glu test result. • to predict response to trametinib and dabrafenib combination therapy in advanced melanoma patients with a positive BRAF p.Val600Glu and/or p.Val600Lys test result • for individuals with indeterminate thyroid fine-needle aspiration (FNA) biopsy cytology for diagnosis of papillary thyroid carcinoma
BRCA1/ BRCA2 or BRAC Analysis®	BRCA 1 & 2 seq & full dup/del Gene analysis (BRCA1 & 2) of full sequence Gene analysis (BRCA1 & 2) for duplication or deletion variants Gene analysis (BRCA1) of full sequence Gene analysis (BRCA1) for duplication or deletion variants Gene analysis (BRCA2) for duplication or deletion variants BRCA 1 & 2 185&538&6174 var BRCA 1 gene known familial variant BRCA2 gene full sequence BRCA 2 gene known familial variant	• BRCA1/BRCA2 gene testing must be in accordance with current National Comprehensive Cancer Network (NCCN) guidelines for breast cancer.
CACNA1A	CACNA1A (calcium channel, voltage-dependent, P/Q type, alpha 1A subunit) (for example, spinocerebellar ataxia), evaluation to detect abnormal (for example, expanded) alleles Gene analysis (calcium voltage- gated channel subunit alpha1 A) for abnormal alleles Gene analysis (calcium voltage- gated channel subunit alpha1 A) of full sequence Gene analysis (calcium voltage- gated channel subunit alpha1 A) for known familial variant	• diagnosis of spinocerebellar ataxia type 6 (SCA6) in patients with cerebellar ataxia with dysarthria and/or nystagmus • diagnosis of SCA6 in symptomatic family members of known SCA6 patients
CALM 1, CASQ2, RYR2, and TRDN	Mopath procedure level 6 Mopath procedure level 9 Unlisted molecular pathology	• to confirm a diagnosis of Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) in patients with clinically diagnosed or suspected CPVT

Genetic Test Name	Description	Coverage Criteria
CDH1	Mopath procedure level 7	• for large rearrangements in the CDH1 gene for the treatment of Hereditary Diffuse Gastric Cancer (HDGC)
CEBPA	CEBPA gene full sequence	• to guide the treatment decisions for individuals with acute myeloid leukemia (AML)
Chromosome 22q11.2	Molecular cytogentics; DNA probe each (for example, FISH) Cytogenetics and molecular cytogenetics, interpretation and report	• confirmation of diagnosis in an individual suspected of chromosome 22q11.2 deletion syndrome based on clinical findings
Chimerism Analysis	Str markers specimen anal Str markers spec anal addl Chimerism anal no cell select Chimerism anal w/cell select	• for the management and treatment of stem cell transplant patients
COL1A1/ COL1A2	Mopath procedure level 9	• for sequence variants in the COL1A1/COL1A2 genes for the diagnosis of Osteogenesis Imperfecta (OI) when clinical and radiological examination and family history provide inadequate information for diagnosis of OI
COL3A1	Unlisted molecular pathology procedure	• to confirm or establish a diagnosis of Ehlers-Danlos syndrome type 4 (EDS IV), also known as vascular EDS, in patients with clinical symptoms or features of EDS IV
CYP2C19	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (for example, drug metabolism), gene analysis, common variants (for example, *2, *3, *4, *8, *17)	• to manage dosing of clopidogrel
CYP2C9	CYP2C9 gene com variants	• for the initiation and management of warfarin treatment
Cystic fibrosis/CFTR testing	CFTR (cystic fibrosis transmembrane conductance regulator) (for example, cystic fibrosis) gene analysis; common variants Known familial variants Duplication/deletion variants Full gene sequence Intron 8 poly-T analysis (for example, male infertility)	• confirmation of diagnosis in individuals showing clinical symptoms of cystic fibrosis or having a high sweat chloride level • identification of newborns who are affected with cystic fibrosis • identification of individuals with the p.Gly551Asp variant who will respond to treatment with ivacaftor • male infertility testing and treatment • preconception and prenatal carrier screening in accordance with the most current ACOG guidelines • patient has not previously been genetically tested for cystic fibrosis **Note:** If a patient has previously been tested, a repeat genetic test is not covered.
Cytogenomic Constitutional Microarray Analysis	Cytoenomic constitutional (genomewide) microarray analysis; interrogation of genomic regions for copy number variants (for example, bacterial artificial chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis) Interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities Cytogenomic microarray analysis, neoplasia (for example, interrogation of copy number, and loss-of-heterozygosity via single nucleotide polymorphism [SNP]-based CGH microarray analysis)	• diagnostic evaluation of patients suspected of having a genetic syndrome (in other words, have congenital anomalies, dysmorphic features, developmental delay and/or intellectual disability) • diagnostic evaluation of individuals with autism spectrum disorder (ASD), including autism, Asperger's syndrome and pervasive developmental disorder
DAZ/SRY	DAZ/SRY (deleted in azoospermia and sex determining region Y) (for example, male infertility), common deletions (for example, AZFa, AZFb, AZFc, AZFd)	• to detect submicroscopic deletions involving the Y chromosome in the evaluation of men with infertility secondary to azoospermia, oligozoospermia, or teratozoospermia
DMD	DMD dup/delet analysis Mopath procedure level 9	• for diagnostic DMD testing (deletion and duplication analysis with reflect to complete gene sequencing) in males or females exhibiting symptoms of Duchenne muscular dystrophy or Becker muscular dystrophy
DMPK	DMPK (DM1 protein kinase) (for example, myotonic dystrophy type 1) gene analysis; evaluation to detect abnormal (expanded) alleles DMPK (DM1 protein kinase) (for example, myotonic dystrophy type 1) gene analysis; characterization of alleles (expanded size)	• confirmation of a diagnosis of myotonic dystrophy type 1 (DM1) or type 2 (DM2) in symptomatic patients • diagnosis of DM1 or DM2 in asymptomatic adults who are at an increased risk of DM1 or DM2 through a positive family history

Genetic Test Name	Description	Coverage Criteria
DSC2, DSG2, DSP, JUP, PKP2, RYR2, TGFB3 and TMEM43	Mopath procedure level 7 MolPath procedure, level 9, 50 exons in a single gene by DNA sequence analysis, full gene sequence DMPK (dystrophia myotonica-protein kinase (for example, myotonic dystrophy type 1), characterization of abnormal (for example, expanded) alleles	• for sequence variants in the DSC2, DSG2, DSP, JUP, PKP2, RYR2, TGFB3, and TMEM43 genes to confirm a diagnosis of Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy (ARVD/C) in probands • for a known familial sequence variant in the DSC2, DSG2, DSP, PKP2, or TMEM43 gene for at-risk relatives of probands with International Task Force (ITF)-confirmed ARVD/C to confirm a diagnosis of ARVD/C in those whose symptoms meet the ITF diagnostic criteria
DYT1/TOR1A	Mol Path, level 1, TOR1A (torsin family 1, member A [torsin A]) (for example, early-onset primary dystonia [DYT1]), 907_909 delGAG (904_906del-GAG) variant Mol Path, level 5, TOR1A (torsin family 1, member A [torsin A]) (for example, torsion dystonia), full gene sequence	• for genetic testing for sequence variants of DYT1 for patients with primary dystonia with onset < 30 years of age. • for genetic testing for sequence variants of DYT1 for patients with primary dystonia with onset ≥ 30 years of age who have a relative who developed dystonia aged < 30 years.
EGFR	GFR (epidermal growth factor receptor) (for example, non-small cell lung cancer) gene analysis, common variants (for example, exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)	• to help guide administration of EGFR TKIs in the first-line treatment of non-small cell lung cancer
F2	F2 (prothrombin, coagulation factor II) (for example, hereditary hypercoagulability) gene analysis, 20210G>A variant F2 (coagulation factor II) (for example, hereditary hypercoagulability), 1199G>A variant	• diagnostic evaluation of individuals with a prior venous thromboembolism (VTE) during pregnancy or puerperium for patients with VTE with a personal or family history of recurrent VTE (more than two in the same person) • for patients with their first VTE before age 50 with no precipitating factors • for venous thrombosis at unusual sites such as the cerebral, mesenteric, portal, or hepatic veins • for VTE associated with the use of estrogen-containing oral contraceptives, selective estrogen receptor modulators (SERMs), or hormone replacement therapy • to diagnose an inherited thrombophilia in female family members of individuals with an inherited thrombophilia if the female family member is pregnant or considering pregnancy or oral contraceptive use
F5	F5 (coagulation factor V) (for example, Hereditary hypercoagulability) gene analysis, Leiden variant F5 (coagulation factor V) (for example, hereditary hypercoagulability), HR2 variant	• diagnostic evaluation of individuals with a prior venous thromboembolism (VTE) during pregnancy or puerperium • for patients with VTE with a personal or family history of recurrent VTE (more than two in the same person) • for patients with their first VTE before age 50 with no precipitating factors • for venous thrombosis at unusual sites such as the cerebral, mesenteric, portal, or hepatic veins • For VTE associated with the use of estrogen-containing oral contraceptives, selective estrogen receptor modulators (SERMs), or hormone replacement therapy • to diagnose an inherited thrombophilia in female family members of individuals with an inherited thrombophilia if the female family member is pregnant or considering pregnancy or oral contraceptive use
FBN1	FBN1 (fibrillin 1) (for example, Marfan syndrome), full gene sequence	• to facilitate the diagnosis of Marfan syndrome in patients who do not fulfill the Ghent diagnostic criteria, but have at least one major feature of the condition • to facilitate the diagnosis of Marfan syndrome in the at-risk relatives of patients carrying known disease-causing variants
FLCN	Unlisted molecular pathology	• to confirm a diagnosis of Birt-Hogg-Dube' Syndrome (BHD) in patients with suspected BHD
FLT3	FLT3 gene FLT3 gene analysis FLT3 (FMS related tyrosine kinase 3) (for example, acute myeloid leukemia) internal tandem duplication (ITD) variances, quantitative	• for diagnosis and prognosis in AML

Genetic Test Name	Description	Coverage Criteria
FMR1	FMR1 (fragile X mental retardation 1) (for example, fragile X mental retardation) gene analysis; evaluation to detect abnormal (for example, expanded) alleles Characterization of alleles (for example, expanded size and methylation status)	FMR1 gene testing is covered for the following indications: • testing for CGG repeat length for diagnosis of patients of either sex with mental retardation, intellectual disability, developmental delay, or autism FMR1 testing for fragile X-associated tremor/ataxia syndrome is covered for the following individuals: • males and females older than age 50 years who have progressive cerebellar ataxia and intention tremor with or without a positive family history of FMR1-related disorders in whom other common causes of ataxia have been excluded • women with unexplained premature ovarian insufficiency (POI)
GCK	GCK (glucokinase [hexokinase 4]) (for example, maturity-onset diabetes of the young [MODY]), full gene sequence	• diagnosis of maturity-onset diabetes of the young type 2 (MODY2) in patients with hyperglycemia or non-insulin-dependent diabetes who have a family history of abnormal glucose metabolism in at least two consecutive generations, with the patient or at least one family member diagnosed before age 25
GJB2	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (for example, nonsyndromic hearing loss) gene analysis; full gene sequence Known familial variants	• diagnosis of DFNB1 or DFNA3 in individuals with nonsyndromic hearing loss to aid in treatment
GJB6	GJB6 (gap junction protein, beta 6, 30kDa, connexin 30) (for example, nonsyndromic hearing loss) gene analysis, common variants (for example 309kb [del(GJB6-D13S1830)] and 232kb [del(GJB6-D13S1854)])	• diagnosis of DFNB1 or DFNA3 in individuals with nonsyndromic hearing loss to aid in treatment
HBA1/HBA2	HBA1/BHA2 (alpha globin 1 and alpha globin 2) (for example, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis, for common deletions or variant (for example, Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, alpha4.2, alpha20.5, and Constant Spring) HBA1/HBA2 (alpha globin 1 and alpha globin 2) (for example, alpha thalassemia, HB bart hydrops fetalis syndrome, HBH disease), gene analysis; known familial variant HBA1/HBA2 (alpha globin 1 and alpha globin 2) (for example, alpha thalassemia, HB bart hydrops fetalis syndrom, HBH disease), gene analysis; full gene sequence HBA1/HBA2 (alpha globin 1 and alpha globin 2) (for example, alpha thalassemia, HB bart hydrops fetalis sydrome, HBH disease), gene analysis; duplication/deletion variants	• to confirm the diagnosis of alpha-thalassemia in a symptomatic individual • to confirm the diagnosis in a pregnant woman with low hemoglobin when alpha-thalassemia is suspected
HEXA	HEXA (hexosaminidase A [alpha polypeptide]) (for example, Tay-Sachs disease) gene analysis, common variants (for example, 1278insTATC, 1421+1G>C, G269S) Mol Path, level 7, HNF4A (hepatocyte nuclear factor 4, alpha) (for example, maturity-onset diabetes of the young [MODY]), full gene sequence	• as an adjunct to biochemical testing in patients with low hexosaminidase A levels in blood • when individuals are identified with apparent deficiency of hexosaminidase A enzymatic activity, targeted mutation analysis can then be used to distinguish pseudodeficiency alleles from disease-causing alleles
HFE	HFE (hemochromatosis) (for example, hereditary hemochromatosis) gene analysis, common variants (for example, C282Y, H63D)	• diagnosis of patients with or without symptoms of iron overload with a serum transferrin saturation > 45 percent and/or elevated serum ferritin

Genetic Test Name	Description	Coverage Criteria
HLA	HLA Class I and II typing, low resolution (for example, antigen equivalents); HLA-A, HLA-B, HLA-C, HLA-DRB1,HLA-DRB3, HHLA-DRB4, HLA-DRB5 and HLA-DQB1 HLA-A, HLA-B and HLA-DRB1 (for example, verification typing) HLA Class I typing, low resolution (for example, antigen equivalents); complete (for example, HLA-A, HLA-B, HLA-C) One locus (for example, HLA-A, HLA-B or HLA-C) each One antigen equivalent (for example, B*27), each HLA Class II typing, low resolution (for example, antigen equivalents); HLA-DRB1, HLA-DRB3, HLA-DRB4, HLA-DRB5 and HLA-DQB1 One locus (for example, HLA-DRB1, HLA-DRB3, HLA-DRB4, HLA-DRB5, HLA-DQB1, HLA-DQA1, HLA-DPB1, HLA-DPA1), each One anitgen equivalent, each HLA Class I and II typing, high resolution (for example, alleles or allele groups), HLA-A, HLA-B, HLA-C and HLA-DRB1 HLA Class I typing, high resolution (for example, alleles or allele groups); complete (for example, HLA-A, HLA-B and HLA-C) One locus (for example, HLA-A, HLA-B or HLA-C), each One allele or allele group (for example, B*57:01P), each HLA Class II typing, high resolution (for example, alleles or allele groups); one locus (for example, HLA-DRB!, HLA-DRB3, HLA-DRB4, HLA-DRB5, HLA-DQB1, HLA-DQA1, HLA-DPB1, HLA-DPA1), each One allele or allele group (for example, HLA-DQB1*06:02P), each	• to determine histocompatibility of tissue between organ and bone marrow donors and recipients prior to transplant • for platelet transfusion for patients refractory to treatment due to alloimmunization • diagnosis of celiac disease in symptomatic patients with equivocal results on small bowel biopsy and serology, or in previously symptomatic patients who are asymptomatic while on a gluten free diet • testing for the HLA-B*1502 allele prior to initiating treatment with carbamazepine in patients from high risk ethnic groups • testing for the HLA-B*5701 allele for hypersensitivity reactions in patients prior to initiation or re-initiation with treatments containing abacavir • testing for the HLA-B*58:01 allele in patients prior to initiating treatment with allopurinol
HNF1A	HNF1A (HNF1 homeobox A) (for example, maturity-onset diabetes of the young [MODY]), full gene sequence	• diagnosis of maturity-onset diabetes of the young type 3 (MODY3) in patients with hyperglycemia or non-insulin-dependent diabetes who have a family history of abnormal glucose metabolism in at least two consecutive generations, with the patient or at least one family member diagnosed before age 25
HNF1B	MolPath, level 5, HNF1B (HNF1 homeobox B) (for example, maturity-onset diabetes of the young [MODY]), duplication/deletion analysis MolPath, level 6, HNF1B (HNF1 homeobox B) (for example, maturity-onset diabetes of the young [MODY]), full gene sequence	• diagnosis of Maturity-Onset Diabetes of the Young Type 5 (MODY5) in patients with hyperglycemia or non-insulin-dependent diabetes who have a family history of abnormal glucose metabolism in at least two consecutive generations, with the patient or ≥ 1 family member(s) diagnosed before age 25, and who have structural or functional abnormalities of the kidneys
HNF4A	MolPath, level 7, HNF4A (hepatocyte nuclear factor 4, alpha) (for example, maturity-onset diabetes of the young [MODY]), full gene sequence Unlisted molecular pathology procedure	• diagnosis of maturity-onset diabetes of the young type 1 (MODY1) in patients with hyperglycemia or non-insulin-dependent diabetes who have a family history of abnormal glucose metabolism in at least two consecutive generations, with the patient or ≥ 1 family member(s) diagnosed before age 25.
HTT	Gene analysis (Huntington) for abnormal alleles Gene analysis (Huntington) for characterization of alleles	• to test for CAG repeat length for diagnosis of Huntington's/Chorea disease (HD) in patients suspected of having HD in the absence of a family history of HD

Genetic Test Name	Description	Coverage Criteria
IGH	IGH gene rearrange amp meth IGH gene rearrange dir probe IGH vari regional mutation	• for medical management of patients with Acute Lymphoblastic Leukemia (ALL) through analysis of rearrangements in the IGH gene to estimate Minimal Residual Disease (MRD) levels • for diagnostic evaluation of rearrangements in the IGH gene in patients with suspected B-cell Non-Hodgkin's Lymphoma (NHL), but in whom clinical, immunophenotypic, and histologic evaluation have provided inconclusive results
IGK	IGK rearrangeabn clonal pop	• for medical management of patients with ALL through analysis of rearrangements in the IGK gene to estimate MRD levels • for diagnostic evaluation of rearrangements in the IGK gene in patients with suspected B-cell NHL, but in whom clinical, immunophenotypic, and histologic evaluation have provided inconclusive results
IL28B	IFNL3 (interferon, lambda 3) (for example, drug response), gene analysis, rs12979860 variant	• for IL28B single nucleotide polymorphism (SNP) testing in patients with chronic Hepatitis C Virus (HCV) genotype 1 being considered for treatment with PegIFN/RBV dual therapy
JAK2	JAK2 (janus kinase 2) (for example, myeloproliferative disorder) gene analysis, p.Val617Phe (V617F) variant Exon 12 sequence and exon 13 sequence, if performed JAK2 (janus kinase 2) (for example, myeloproliferative disorder) gene anaylsis, targeted sequence analysis exons 12-15 Oncology (hematolymphoid neoplasia), JAK2 Mutation DNA, PCR amplification of exons 12-14 and sequence analysis, blood or bone marrow, report of JAK2 mutation not detected or detected	• diagnostic evaluation of individuals presenting with clinical, laboratory, or pathological findings suggesting classic forms of myeloproliferative neoplasms (MPN), that is, polycythemia vera (PV), essential thrombocythemia (ET), or primary myelofibrosis (PMF) • diagnostic evaluation of PV through JAK2 exon 12 variant detection in JAK2 p.Val617Phe negative individuals
KCNQ1, KCNH2, SCN5A, KCNE1 and KCNE2	KCNH2 (potassium voltage-gated channel, subfamily H [eag-related], member 2) (for example, short QT syndrome, long QT syndrome), full gene sequence; KCNQ1 (potassium voltage-gated channel, KQT-like subfamily, member 1) (eg, short QT syndrome, long QT syndrome), full gene sequence; KCNQ2 (potassium voltage-gated channel, KQT-like subfamily, member 2) (for example, epileptic encephalopathy), full gene sequence; MolPath 8, SCN5A (sodium channel, voltage-gated, type V, alpha subunit) (for example, familial dilated cardiomyopathy), full gene sequence	• for patients with suspected familial Long QT syndrome for confirmation of diagnosis and treatment
KIT	Kit gene targeted seq analysis Kit gene analysis d816 variant	• to confirm a diagnosis of a gastrointestinal stromal tumor (GIST) in patients who are negative by immunostaining • to determine primary resistance to treatment with TKIs in patients with an advanced metastatic or unresectable GIST • to determine primary resistance to preoperative or postoperative treatment of a GIST with TKIs
KMT2D and/ or KDM6A	Unlisted molecular pathology procedure	• diagnosis of Kabuki Syndrome (KS) in patients with symptoms compatible with KS
KRAS	KRAS gene variants exon 2 KRAS gene addl variants	• to help guide administration of anti-EGFR monoclonal antibodies
MECP2	MECP2 (methyl CpG binding protein 2) (for example, Rett syndrome) gene analysis; full sequence analysis Known familial variant Duplication/deletion variants	• testing for MECP2 sequence variants in patients who meet established clinical diagnostic criteria for classic or variant Rett syndrome • testing for MECP2 sequence variants in patients who have symptoms of Rett syndrome, but do not meet established clinical diagnostic criteria
MEFV	MolPath, level 3, MEFV (mediterranean fever) (for example, familial mediterranean fever), common variants (for example, E148Q, P369S, F479L, M680I, I692del, M694V, M694I, K695R, V726A, A744S, R761H) MolPath, level 5, MEFV (mediterranean fever) (for example, familial mediterranean fever), full gene sequence	• in patients exhibiting symptoms of Familial Mediterranean Fever (FMF), including periodic episodes of fever in combination with peritonitis, pleuritic, arthritis, and erysipelas-like erythema. - In patients from ethnic groups considered at high risk for FMF who present with nephrotic syndrome or amyloidosis, but do not meet the diagnostic criteria for FMF

Genetic Test Name	Description	Coverage Criteria
MLH1, MHS2, MSH6, MSI, PMS2, and EPCAM	MLH1 gene MLH1 gene full MLH1 gene known variants MLH1 gene dup/del variant MSH2 gene full MSH2 gene known variants MSH2 gene dup/delete variant MSH6 gene full seq MSH6 gene known MSH6 gene dup/delete variant Microsatellite instability PMS2 gene full seq PMS2 gene known familial variants PMS2 gene dup/delete variants	• Genetic testing for Lynch Sydrome (LS) must be in accordance with current National Comprehensive Cancer Network (NCCN) guidelines for colon cancer.
MPL	MPL (myeloprolifereative leukemia virus oncogene, thrombopoietin receptor) (for example, myeloproliferative disorder), common variants (for example, W515A, W515K, W515L, W515R) MPL (myeloproliferative leukemia virus oncogene, thrombopoietin receptor) (for example, myloproliferative disorder), exon 10 sequence	• diagnostic evaluation of MPL variants to include Trp515Leu and Trp515Lys in JAK2 p.Val617Phe-negative individuals showing symptoms
MUTYH	MUTYH (mutY homolog [E. coli]) (for example, MYH-associated polyposis), common variants (for example, Y165C, G382D) MUTYH (mutY homolog [E. coli]) (for example, MYH-associated polyposis), full gene sequence	• diagnosis of MYH-associated polyposis (MAP) in APC-negative colorectal polyposis patients, or in polyposis patients who have a family history consistent with autosomal recessive inheritance • diagnosis of MAP in asymptomatic siblings of patients with known MYH variants
Noninvasive Prenatal Screening for Trisomies 13, 18, 21, X&Y	Fetal chrmoml aneuploidy Unlisted molecular pathology Fetal aneuploidy trisomy risk Unlisted maaa	• in singleton pregnancies with a high risk of fetal aneuploidy
NPM1	NPM1 (nucleophosmin) (for example, acute myeloid leukemia [AML]) gene analysis, exon 12 variants NPM1 (nucleophosmin) (for example, acute myeloid leukemia) gene analysis, quantitative	• to guide treatment decisions for individuals with AML
NRAS	NRAS gene variants exon 2 & 3	• for patients with metastatic colorectal cancer who are being considered for treatment with anti-EGFR monoclonal antibodies, and who have had negative KRAS gene testing
Oncotype Dx Breast Cancer Assay	mRNA gene analysis of 21 genes in breast tumor tissue	• estrogen receptor (ER) positive (+), lymph node (LN) negative (-), human EGFR 2 negative (HER2-) breast cancer patients who are considering whether to use adjuvant chemotherapy in addition to standard hormone therapy • ER+, HER2- breast cancer patients with 1–3 involved ipsilateral axillary lymph nodes who are considering whether to use adjuvant chemotherapy in addition to hormonal therapy
PAX8	PAX8/PPARG (t(2;3) (q13;p25)) (for example, follicular thyroid carcinoma), translocation analysis	• for individuals with indeterminate thyroid FNA biopsy cytology for diagnosis of papillary thyroid carcinoma
PDGFRA	PDGFRA (platelet-derived growth factor receptor, alpha polypeptide) (for example, gastrointestinal stromal tumor [GIST]), gene analysis, targeted sequence analysis (for example, exons 12, 18)	• to confirm a diagnosis of a GIST in patients who are negative by immunostaining • to determine primary resistance to treatment with TKIs in patients with an advanced metastatic or unresectable GIST • to determine primary resistance to preoperative or postoperative treatment of a GIST with TKIs
PML/ RARalpha	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha (for example, promyelocytic leukemia) translocation analysis; common breakpoints (for example, intron 3 and intron 6), qualitative or quantitative Single breakpoint (for example, intron 3, intron 6 or exon 6), qualitative or quantitative	• diagnostic assessment of individuals with suspected acute promyelocytic leukemia (APL) by quantitative RT-PCR (RQ-PCR) • diagnostic assessment of individuals with suspected APL by qualitative RT-PCR • monitoring response to treatment and disease progression in individuals with APL by RQ-PCR

Genetic Test Name	Description	Coverage Criteria
PMP22	PMP22 (peripheral myelin protein 22) (for example, Charcot-Marie- Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; duplication/deletion analysis Full sequence analysis Known familial variant	• for the accurate diagnosis and classification of hereditary polyneuropathies
PPP2R2B	Gene analysis (protein phosphatase 2 regulatory subunit Bbeta) for abnormal alleles	• diagnosis of spinocerebellar ataxia type 12 (SCA12) in patients with action tremor of the upper extremities and signs of cerebellar and cortical dysfunction, in addition to Indian ancestry and a family history consistent with autosomal dominant inheritance • diagnosis of SCA12 in symptomatic family members of known SCA12 patients

PRSS1	PRSS1 (protease, serine, 1 [trypsin 1]) (for example, hereditary pancreatitis), common variants (for example, N29I, A16V, R122H)
	Molecular pathology procedure level 5, PRSS1 (protease, serine, 1 [trypsin 1]) (for example, hereditary pancreatitis), full gene sequence
		• to confirm diagnosis of hereditary pancreatitis in symptomatic patients with any of the following:
		  • a family history of pancreatitis in a first-degree (parent, sibling, child) or second-degree (aunt, uncle, grandparent) relative;
		  • an unexplained episode of documented pancreatitis occurring in a child that has required hospitalization, and where there is significant concern that hereditary pancreatitis should be excluded;
		  • recurrent (two or more separate, documented episodes with hyperamylasemia) attacks of acute pancreatitis for which there is no explanation (anatomical anomalies, ampullary or main pancreatic strictures, trauma, viral infection, gallstones, alcohol, drugs, hyperlipidemia, etc); or
		  • unexplained (idiopathic) chronic pancreatitis

PTEN	PTEN (phosphatase and tensin homolog) (for example, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis Known familial variant Duplication/deletion variant	• for patients with autism spectrum disorders (ASDs) and macrocephaly (head circumference greater than 2 standard above the mean for age) • PTEN variant testing in individuals suspected of being affected with Cowden syndrome (CS) or Bannayan-Riley-Ruvalcaba syndrome (BRRS)
RET	RET (ret proto-oncogene) (for example, multiple endocrine neoplasia, type 2B and familial medullary thyroid carcinoma), common variants (for example, M918T, 2647_2648delinsTT, A883F) RET (for example, multiple endocrine neoplasia, type 2A and familial medullary thyroid carcinoma), targeted sequence analysis (for example, exons 10, 11, 13-16) MolPath, level 7, RET (ret proto-oncogene) (for example, Hirschsprung disease), full gene sequence	• multiple endocrine neoplasia type 2 (MEN2) gene testing in patients with the clinical manifestations of MEN2A, MEN2B, or familial medullary thyroid carcinoma (FMTC), including those with apparently sporadic medullary thyroid carcinoma (MTC) or pheochromocytoma • MEN2 gene testing to confirm a diagnosis in the at-risk relatives of genetically confirmed MEN2 patients
ROS1	Cytogenetics 25-99	• for patients who have wild type (negative) EGFR or ALK gene testing, reflex testing to ROS1 should be ordered for the treatment of non-small cell lung carcinoma
RYR1	Molecular pathology procedure, level 9, 50 exons in a single gene by DNA sequence analysis, full gene sequence (RYR1 (ryanodine receptor 1, skeletal) (for example, malignant hyperthermia), full gene sequence) Molecular pathology procedure level 7, RYR1 (ryanodine receptor 1, skeletal) (for example, malignant hyperthermia), targeted sequence analysis of exons with functionally-confirmed mutations	• to test clinically confirmed malignant hyperthermia susceptibility (MHS) patients for variants in the RYR1 gene to facilitate diagnostic testing in at-risk relatives • to diagnose MHS in at-risk relatives of patients with clinically confirmed MHS

Genetic Test Name	Description	Coverage Criteria
SDHA, SDHB, SDHC, SDHD, SDHAF2, MAX, and/or TMEM127	MolPath, Level 5, SDHC (succinate dehydrogenase complex, subunit C, integral membrane protein, 15kDa) (for example, hereditary paraganglioma-pheochromocytoma syndrome), duplication/deletion analysis MolPath, level 6, SDHC (succinate dehydrogenase complex, subunit C, integral membrane protein, 15kDa) (for example, hereditary paraganglioma-pheochromocytoma syndrome), full gene sequence MolPath, level 7, SDHA (succinate dehydrogenase complex, subunit A, flavoprotein [Fp]) (for example, Leigh syndrome, mitochondrial complex II deficiency), full gene sequence Hereditary neuroendocrine tumor disorders (for example, 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. (However, panel must include VHL gene, which isn't on this grouping.) Hereditary neuroendocrine tumor disorders (for example, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma pr paraganglioma); duplication/deletion analysis panel, must include analysis for SDHB, SDHC, SDHD, AND VHL Unlisted molecular pathology procedure	• to diagnose a hereditary paraganglioma (PGL) or pheochromocytoma (PCC) syndrome in patients with PGLs and/or PCCs
SERPINA1	SERPINA1 gene	• for guidance in diagnosis of inconclusive cases of Alpha-1 Antitrypsin Deficiency (AATD) in individuals with Chronic Obstructive Pulmonary Disease (COPD), unexplained liver disease, family history of AATD, or environmental exposures leading to airflow obstruction after serum Alpha-1 Antitrypsin (AAT) protein levels and protein phenotyping has been completed
SMAD4	SMAD4 (SMAD family member 4) (for example, hemorrhagic telangiectasia syndrome, juvenile polyposis), duplication/deletion analysis Full gene sequence	• to clarify the diagnosis of individuals with JPS or a known SMAD4 mutation is in the family (Genetic testing should be performed in the first six months of life due to hereditary hemorrhagic telangiectasia risk)
SMN1/SMN2	SMN1 (survival of motor neuron 1, telomeric) (for example, spinal muscular atrophy), exon 7 deletion SMN1/SMN2 (survival of motor neuron 1, telomeric/survival of motor neuron 2, centromeric) (for example, spinal muscular atrophy), dosage analysis (for example, carrier testing) SMN1, known familial sequence variant(s) SMN1, full gene sequence Gene analysis (survival of motor neuron 1, telomeric) for dosage/deletion Gene analysis (survival of motor neuron 1, telomeric) of full sequence Gene analysis (survival of motor neuron 1, telomeric) for known familial sequence variants	• diagnosis of patients with hypotonia and muscle weakness who are suspected of having spinal muscular atrophy (SMA)

Genetic Test Name	Description	Coverage Criteria
SNRPN/ UBE3A	SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (for example, Prader-Willi syndrome and/or Angelman syndrome), methylation analysis	When a clinical diagnosis of Prader-Willi syndrome is suspected, the following findings justify genetic testing: • from birth to age two: hypotonia with poor suck (neonatal period) • from age two to age six: hypotonia with history of poor suck, global developmental delay • from age six to age 12: hypotonia with history of poor suck, global developmental delay, excessive eating with central obesity if uncontrolled • from age 13 years to adulthood: cognitive impairment, usually mild intellectual disability; excessive eating with central obesity if uncontrolled, hypothalamic hypogonadism and/or typical behavior problems When a clinical diagnosis of Angelman Syndrome is suspected, the following findings justify genetic testing: • as part of the evaluation of patients with developmental delay, regardless of age • as part of the evaluation of patients with a balance or movement disorder such as ataxia of gait (May not appear as frank ataxia but can be forward lurching, unsteadiness, clumsiness, or quick, jerky motions.) • as part of the evaluation of patients with uniqueness of behavior: any combination of frequent laughter/smiling; apparent happy demeanor; easily excitable personality, often with uplifted hand-flapping or waving movements; hypermotoric behavior • speech impairment, none or minimal use of words; receptive and non-verbal communication skills higher than verbal ones
STK11	STK11 (serine/threonine kinase 11) (for example, Peutz-Jeghers syndrome [PJS]), duplication/ deletion analysis Full gene sequence	• to confirm a diagnosis of Peutz-Jeghers syndrome (PJS) in proband patients with a presumptive or probable diagnosis of PJS
TBP	TBP (TATA box binding protein) (for example, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (for example, expanded) alleles	• diagnosis of spinocerebellar ataxia type 17 (SCA17) in ataxia patients exhibiting variable combinations of cognitive decline, psychiatric disturbance, and movement disorders • diagnosis of SCA17 in symptomatic family members of known SCA17 patients • diagnosis of SCA17 in patients suspected of having Huntington Disease (HD) who have tested negative for a pathogenic variant in the HD gene
TGFBR2	MolPath, level 6, TGFBR2 (transforming growth factor, beta receptor 2) (for example, Marfan syndrome), full gene sequence	• to facilitate the diagnosis of Marfan syndrome in patients testing negative for FBN1 gene variants
TP53	TP53 (tumor protein 53) (for example, tumor samples), targeted sequence analysis of 2–5 exons TP53 (for example, Li-Fraumeni syndrome, tumor samples), full gene sequence or targeted sequence analysis of > 5 exons	• diagnosis of patients satisfying the criteria for classic Li-Fraumeni syndrome or Li-Fraumeni-like syndrome, or the Chompret criteria for TP53 gene testing
TPMT	TPMT (thiopurine S-methyltransferase) (for example, drug metabolism), gene analysis, common variants (for example, *2, *3)	• TPMT genotyping or phenotyping in patients with Inflammatory Bowel Disease (IBD) prior to administration of thiopurines (azathioprine, 6-MP, and 6-TG)
TRG	TRG (T-cell antigen receptor, gamma) (for example, leukemia and lymphoma), gene rearrangement analysis, evaluation to detect abnormal clonal populations	• diagnosis and treatment of T-cell neoplasms
UPD	Uniparental disomy (UPD) (for example, Russell-Silver syndrome, Prader-Willi-Angelman syndrome), short tandem repeat (STR) analysis	• for neonates, infants, children or adults symptomatic for Beckwith-Wiedermann syndrome (BWS) to diagnose uniparental disomy (UPD) for chromosome 11
UGT1A1	UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (for example, irinotecan metabolism), gene analysis, common variants (for example, *28, *36, *37)	• prior to irinotecan administration in patients with colorectal cancer (CRC) to lower the starting does of irinotecan in patients with the UGT1A1*28/UGT1A1*28 genotype • prior to irinotecan administration in patients with CRC to increase the starting does of irinotecan in patients with the UGT1A1*1/ UGT1A1*1 or UGT1A1*1/UGT1A1*28 genotypes

Genetic Test Name	Description	Coverage Criteria
VHL	VHL (Von Hippel-Lindau tumor suppression) (for example, VHL familial cancer syndrome), deletion/duplication analysis Full gene sequence	• diagnosis of Von Hippel-Lindau (VHL) syndrome in patients presenting with pheochromocytoma, paraganglioma or central nervous system hemangioblastoma • confirmation of diagnosis in individuals with symptoms consistent with VHL syndrome
VKORC1	VKORC1 gene	• for the initiation and management of warfarin treatment
Y Chromosome Microdeletion Analysis	Mol Path, level 4, DAZ/SRY (deleted in azoospermia and sex determining region Y) (for example, male infertility), common deletions (for example, AZFa, AZFb, AZFc, AZFd) Unlisted molecular pathology procedure	• for detecting submicroscopic deletions involving the Y chromosome in men with azoospermia, oligozoospermia, or teratozoospermia

Authorizations and Referrals • PO Box 9108 • Virginia Beach, VA 23450-9108