MEDICAL POLICY	Genetic and Molecular Testing (Medicare Only)
Effective Date: 5/1/2022  5/1/2022 Medical Officer Date	Medical Policy Number: 317 Medical Policy Committee Approved Date: 10/2021; 3/2022

See Policy CPT/HCPCS CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:

Medicare only

DOCUMENTATION REQUIREMENTS

In order to review for medical necessity, the following documentation **must** be provided. If any of these items are not submitted, the review may be delayed and the decision outcome could be affected:

- Test name;
  - If the test is a panel test, the name of the panel test;
  - For single gene/variant testing, the name of the gene(s) and/or components of the test;
- Name and location of laboratory that performed or will be performing the test;
- Clinical notes should include the following:
  - Documentation supporting the member was advised what tests were being ordered;
  - Condition or suspected condition;
  - What test results are expected to provide (e.g., make diagnosis, determine medication therapy(ies), etc.);
  - Signs/symptoms/prior test results related to reason for genetic testing;
  - Family history, if applicable;
  - How test results will impact clinical decision making
- CPT and/or HCPCS code(s) billed

POLICY CRITERIA

Notes:

- **The list of genetic tests addressed in this policy is not all-inclusive.**
- **In compliance with Medicare guidelines, some LCDs and LCAs used may be for service areas outside of the Company's primary service area, because they are based on where the performing laboratory is located.**
- Other Company Medical Policies may be available for specific tests or indications:
  - Most of these tests are listed within Criteria VI, IX and X below.
  - See Cross References section for medical policies which may apply to specific hereditary or oncologic conditions.
  - If a test is not found in this policy, see the separate genetic testing policies to confirm coverage resources are not provided in another location. For example, if a panel test for colorectal cancer is not found in this policy, see the separate *Genetic Testing: Inherited Susceptibility to Colorectal Cancer (Medicare Only)* medical policy.
- Due to the rapidly changing field of genetic testing, panel names, genes included, and coding may change subsequent to the last update of this policy.
- CMS guidance is also subject to change at any time.

Medical Policy Criteria Quick Links

Excluded Genes

I. The following single gene tests are **not medically necessary** in many service areas *(**NOTE:** This list is NOT all-inclusive and there may be exceptions to non-coverage for some of the genes listed, depending on location of and purpose for testing. See the applicable LCA or LCD for information.)**:**

GENE	LOCATION/MEDICARE CONTRACTOR					
	NORIDIAN J-F OR, WA, AK, ID, UT, AZ, MT, ND, SD, and WY	***NORIDIAN J-E*** CA and NV	***PALMETTO GBA J-J AND J-M*** NC, SC, AL, GA, TN, VA, and WV	***WISCONSIN J-5 AND J-8*** IA, KS, MO, NE, IN, and MI	***CGS ADMINISTRATORS J-15*** KY and OH	***NATIONAL GOVERNMENT SERVICES J-6 and J-K*** IL, MN, WI, CT, NY, ME, MA, NH, RI, VT
ACVRL1*	A55182	A55181	A53536	A55159	A54262	
ASPA	A55089	A55088	A53602	A55142	A54253	A56199
ATP7B	A55098	A55097	A53550	A55143	A54254	A56199
BCKDHB	A55099	A55100	A53600	A55145	A54255	A56199
BLM	A55114	A55113	A53540	A55148	A54256	A56199
CFTR	L38337 / A57385	L38335 / A57384	L38294 / A58318	L38435 / A58395	L38394 / A58324	L35000 / A56199
ENG*	A55182	A55181	A53536	A55159	A54262	
F5	L36159	L36155	L36089	L36400	L35984	L35000 / A56199
F2	L36159	L36155	L36089	L36400	L35984	L35000 / A56199
FANCC	A55183	A55184	A53628	A55160	A54263	A56199
FMR1	A55242	A55241	A53638	A55163	A54264	A56199
GBA	A55244	A55243	A53542	A55164	A54265	A56199
HAX1	A55252	A55249	A53619	A55165	A54266	A56199
HBB	A55254	A55253	A53493	A55166	A54267	A56199

HEXA	A55256	A55255	A53598	A55168	A54268	A56199
IKBKAP	A55613	A55612	A53596	A55170	A54270	A56199
MCOLN1	A55284	A55283	A53630	A55176	A54277	A56199
MECP2	A55286	A55285	A53574	A55189	A54278	A56199
MMACHC	A55289	A55288	A54035	A55191	A54209	
MTHFR	L36159 / L36362	L36155 / L36358	L36089 / L36129	L36400 / L36523	L35984 / L36139	L35000 / A56199
NSD1	A55615	A55609	A53585	A55198	A54291	A56199
SMPD1	A55631	A55627	A53624	A55208	A54285	A56199
SULT4A1	A55601	A55596	A53538	A55210	A54283	
VEGFR2	A55469	A55468	A53548	A55232	A54279	A56199

Non-Covered Tests

II. Based on the Medicare Benefit requirements, **all** of the following test types and scenarios are excluded and are denied as **not medically necessary** on a national basis:
   A. Tests performed in the absence of clinical signs and symptoms of disease are considered screening and are non-covered UNLESS specifically identified by the law (this includes genetic testing requested due to family history alone);
   B. Tests that do not provide the clinician with actionable data for the member (information that will not improve patient outcomes and/or change physician care and treatment of the patient) (this includes testing at-risk relative testing);
   C. Tests that confirm a diagnosis or known information;
   D. Tests to determine risk for developing a disease or condition;
   E. Tests performed to measure the quality of a process, or tests performed to confirm the sample belongs to a particular member;
   F. Tests without diagnosis specific indications;
   G. Carrier testing (tests to determine if they or offspring are potential carriers of a genetic variant);
   H. Tests identified as investigational by all available literature and/or the literature supplied by the developer and are not a part of a clinical trial as determined by LCD, LCA, or the MolDX program (when applicable)

III. Genetic panel tests for the evaluation of **arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) (CPT code 81439)** are considered **not medically necessary**. Applicable Medicare references include the following:

A. Local Coverage Articles (LCA):
   i. Billing and Coding: MolDX: Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy (ARVD/C) Testing
      1. Testing performed in OH and KY: A54685 (CGS Administrators, LLC)
      2. Testing performed in CA and NV: A54975 (Noridian Healthcare Solutions, LLC; J-E)
      3. Testing performed in AK, ID, OR, WA, UT, AZ, MT, ND, SD, and WY: A54976 (Noridian Healthcare Solutions, LLC; J-F)
      4. Testing performed in VA, WV, NC, SC, GA, TN, AL: A53605 (Palmetto GBA)
      5. Testing performed in IA, KS, MO, and NE: A55235 (Wisconsin Physician Services)
   ii. Billing and Coding: Molecular Pathology Procedures (A56199) for testing performed in IL, MN, WI, CT, NY, ME, MA, NH, RI, and VT (National Government Services, Inc.)

IV. **Whole exome and whole genome sequencing/testing** are considered **not medically necessary** for Medicare under *Social Security Act, §1862(a)(1)(A).* Applicable Medicare references include the following:
A. Testing performed in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY: LCD attachment for L36256, Excluded Test List – as of 08/01/2016
B. Testing performed in CA and NV: LCD attachment for L35160, Excluded Test List – as of 08/01/2016
C. Testing performed in in IL, MN, WI, CT, NY, ME, MA, NH, RI, or VT: LCA for Billing and Coding: Molecular Pathology Procedures (A56199)
   i. Non-coverage of genome and exome analysis includes the EXaCT-1 Whole Exome Test (0036U), GPS Cancer® (NantHealth, D/B/A NantOmics; California), Praxis Whole Genome Sequencing (Praxis Genomics LLC; 0265U) and the Praxis Combined Whole Genome Sequencing and Optical Genome Mapping (Praxis Genomics LLC; 0267U). Since current codes for whole exome and genome sequencing are non-covered, all whole exome sequencing tests are considered non-covered, regardless of what CPT code is used, until LCDs or LCAs indicate otherwise.

V. Single gene and panel testing for **hereditary hearing loss** (genes GJB2 [81252, 81253] and GJB6 [81254], and panel tests [81430, 81431]) are considered **not medically necessary** for Medicare. Applicable Medicare references include the following:
A. Testing performed in AK, ID, OR, WA, UT, AZ, MT, ND, SD, WY: LCD attachment for L36256, Excluded Test List – as of 08/01/2016
B. Testing performed in CA and NV: LCD attachment for L35160, Excluded Test List – as of 08/01/2016
C. C. Testing performed in in IL, MN, WI, CT, NY, ME, MA, NH, RI, or VT: LCA for Billing and Coding: Molecular Pathology Procedures (A56199)

VI. The following **reproductive planning and prenatal genetic tests** are considered **not medically necessary** for Medicare (this list may not be all-inclusive. Medicare guidance pertaining to this testing can be found in the "Policy Guidelines" section below).
- A. Carrier screening.
- B. Preimplantation genetic testing.
- C. Noninvasive prenatal screening (e.g., PGIF Preeclampsia Screen [PerkinElmer Genetics, Inc.] [0243U], PreTRM® [Sera Prognostics] [0247U]).
- D. Pregnancy loss.
- E. Direct-to-consumer testing for reproductive planning or prenatal testing.

Miscellaneous Genetic or Molecular Tests

VII. **Chimerism analysis (CPT codes 81265-81268)** may be **medically necessary** for some indications. Applicable Medicare references include the following:
- A. Billing and Coding: MolDX: Short Tandem Repeat (STR) Markers and Chimerism (codes 81265-81268)
  - i. Testing performed in AK, ID, OR, WA, UT, AZ, MT, ND, SD, and WY: A57843 (Noridian J-F)
  - ii. Testing performed in CA or NV: A57842 (Noridian J-E)
  - iii. Testing performed in OH and KY: A54830 (CGS Administrators, LLC)
  - iv. Testing performed in VA, WV, NC, SC, GA, TN, and AL: A54832 (Palmetto GBA)
  - v. Testing performed in IA, KS, MO, and NE: A55621 (Wisconsin Physician Services)
- B. Billing and Coding: Molecular Pathology Procedures (A56199) for testing performed in IL, MN, WI, CT, NY, ME, MA, NH, RI, and VT (National Government Services, Inc.)

VIII. **Colorectal cancer screening and pre-screening tests** are **not medically necessary** when they are not called out as eligible preventive benefits under Medicare's NCD 210.3. These non-covered tests include, but may not be limited to
- A. BeScreened™-CRC (0163U) and Colonsentry® (81479).
- B. Some tests may be addressed in separate Company policies, such as the *Colorectal Cancer Screening* policy (Cologuard™ Colorectal Screening [81528], Epi proColon [G0327]) or *Circulating Tumor Cell and DNA Assays For Cancer Management (Medicare Only)* policy (e.g., FirstSight^{CRC} [0091U]) (See Cross References).

IX. **Cytogenetic studies** for genetic disorders in a fetus may be **medically necessary**, as determined by the national coverage determination (NCD) for Cytogenetic Studies (190.3)

Genetic and Molecular Panel Tests

X. The tests in **Table 1** have specific LCD policies or LCA articles available. Additional notes are provided when necessary.

Table 1

Proprietary Test Name	Laboratory (Location)	Medicare Policy Cross Reference or Medicare Citation/Rationale
AlloMap® (81595)	CareDx, Inc. (California)	Apply the LCD L38629. The LCD requires successful completion of TA review of the test; this test meets this LCD requirement.
AlloSure® Donor-Derived Cell-Free DNA Tests (AlloSure® Heart and AlloSure® Kidney)	CareDx, Inc. (California)	Apply the LCD L38629. The LCD requires successful completion of TA review of the test; these tests both meet this LCD requirement.
CancerTypeID (81540)	bioTheranostics, Inc. (California)	Apply the LCA A54386. While it doesn't give specific *criteria*, it does provide a list of ICD-10 codes that support medically necessity. These are used to determine coverage.
Clarava™ and Tuteva™	Verici Dx (Tennessee)	Apply the LCD L38568. The LCD requires successful completion of TA review of the test; these tests **do not** meet this LCD requirement and therefore are **not medically necessary**.
GeneTrails Comprehensive Solid Tumor Panel (81479)	Knight Diagnostics/OHSU (Oregon)	Apply the LCD L38121. The LCD requires successful completion of TA review of the test; this test meets this LCD requirement.
GeneTrails Hematologic Malignancies 220 Gene Panel (81450) *(genes related to hematolymphoid malignancies, including precursor lesions, acute myelogenous / lymphoid leukemias, myelodysplasias, myeloproliferative disorders, and lymphomas)*	Knight Diagnostics/OHSU (Oregon)	Apply the LCD L38125. The LCD requires successful completion of TA review of the test; this test meets this LCD requirement.
High Risk HLA Panel *(this test consists of HLA-A*31:01, HLA-B*15:02, HLA-B*57:01, HLA-B*58:01)*	Genelex Corporation (Washington)	• For ***non-transplant*** testing: *Genetic Testing: Pharmacogenetic Testing (Medicare Only)* • For ***transplant*** testing: LCA A57975

Memorial Sloan Kettering-Integrated Mutation Profiling of Actionable Cancer Targets™ (MSK-IMPACT™) (0048U)	Memorial Sloan Kettering (New York)	Apply the LCD L37810. See the *Non-Small Cell Lung Cancer: Molecular Testing for Targeted Therapy (Medicare Only)* policy when testing is used for NSCLC and *Genetic Testing: Inherited Susceptibility to Colorectal Cancer (Medicare Only)* when testing is used for colorectal cancer.
MI Profile and MI *TumorSeek* (81479)	Caris Life Sciences (Arizona)	Apply the LCD L38121. The LCD requires successful completion of TA review of the test; this test meets this LCD requirement. **Note:** If the MI *TumorSeek* is deemed medically necessary, the MI Profile may be approved. **Background:** MI *TumorSeek* is a next-generation sequencing (NGS) tumor profiling assay that covers DNA mutations, copy number alterations, insertions/deletions, and RNA fusions for select lineages. When microsatellite instability (MSI) and tumor mutational burden (TMB) are included, the full comprehensive genomic profile (CGP) assay is known as the MI *Profile* test. According to MolDX, the MI *Profile* in its entirety has been approved for coverage when the medical necessity criteria for the MI *TumorSeek* component are met. As of January 2019, MolDX determined CPT 81455 is no longer appropriate for this test. As a CGP assay, a single code (CPT 81479) should be used to report the test in its entirety (see A56518 for CGP test coding instructions).
Oncotype MAP® Pan-Cancer Tissue Test (formerly Paradigm PCDx) (0244U)	Paradigm Diagnostics (Arizona) (Test may be billed by Genomic Health, but it is performed by Paradigm Diagnostics)	Apply the LCD L38121. The LCD requires successful completion of TA review of the test; this test meets this LCD requirement.
Ova1™ (81503) and **Overa** (0003U)	Aspira Labs, Inc., a Vermillion Company (Texas)	Apply the LCD L35396. Allow these tests when performed according to the Food and Drug Administration [FDA] label. For coding, see companion article, which can be accessed directly from the LCD.)

PancraGEN (aka Pathfinder® Pancreas) (81479)	Interspace Diagnostics (Pennsylvania)	Apply the LCD L34864. The PancraGEN test is specific to pancreatic masses or cysts and uses a proprietary platform known as PathfinderTG®.
Prospera™ (81479)	Natera, Inc. (California)	Apply the LCD L38629. The LCD requires successful completion of TA review of the test; this test meets this LCD requirement.
Providence Personalized Medicine Panel, Solid Tumor (aka, ProvSeq523)	Providence St. Joseph (Oregon)	Apply the LCD L38121. The LCD requires successful completion of TA review of the test; this test meets this LCD requirement.
Risk of Ovarian Malignancy Algorithm (ROMA™) (81500)	Quest Diagnostics (Headquartered in New Jersey) ***or*** LabCorp (Headquartered in North Carolina)	• For testing performed in laboratories in OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY, CA, NV, HI, NC, SC, AL, GA, TN, VA, WV, KY, OH, IA, KS, MO, NE, IN, and MI: The ROMA™ test is noted as a covered test by MolDX when Medicare medical necessity criteria are met. This means documentation must support that the test is ordered to provide actionable data to be used promptly by the treating physician to treat or diagnose an illness or condition in order to be considered medically reasonable and necessary. *(Medicare Benefit Policy Manual, Ch. 15 – Covered Medical and Other Health Services, §80.1 - Clinical Laboratory Services) (See U.S. Food and Drug Administration [FDA] label here)* • For testing performed in laboratories in IL, MN, WI, CT, NY, ME, MA, NH, RI, VT: LCD L38371 *(Search for "Risk of Ovarian Malignancy Algorithm")* • For testing performed in laboratories in CO, NM, OK, TX, AR, LA, MS, DE, MD, NJ, PA: LCD L35396 *(Search for "Risk of Ovarian Malignancy Algorithm")*
TruGraf® (81479)	Transplant Genomics (California)	Apply the LCD L38629. The LCD requires successful completion of TA review of the test; this test meets this LCD requirement.
Vectra DA (81490)	Crescendo Bioscience (Any state)	Apply the LCA A53110. While it doesn't give specific *criteria*, it does provide a list of ICD-10 codes that support medically necessity for this test, up to two times per year. These ICD-10 codes are used to determine coverage.

XI. These tests are addressed in **<u>one or more</u>** of the following separate Company medical policies:

A. These tests are addressed in the separate ***Genetic Testing: Hereditary Breast and Ovarian Cancer Genetic Testing (Medicare Only)*** policy:

i. BRCAplus (Ambry Genetics; California)
ii. BRCAplus-Expanded (Ambry Genetics; California)
iii. Breast Next (Ambry Genetics; California) *(No longer offered)*
iv. GYNPlus® (Ambry Genetics; California) *(No longer offered)*
v. OvaNext® (Ambry Genetics; California)
vi. VistaSeq Breast and Gyn Cancer Profile (LabCorp / Integrated Genetics / Integrated Oncology)
vii. VistaSeq Breast Cancer Profile (LabCorp / Integrated Genetics / Integrated Oncology)
viii. VistaSeq High/Moderate Risk Breast Cancer Profile (LabCorp / Integrated Genetics / Integrated Oncology)

B. These tests are addressed in the separate ***Genetic Testing: Inherited Susceptibility to Colorectal Cancer (Medicare Only)*** policy:

i. ColoNext (Ambry Genetics; California)
ii. ColoNext +RNAinsight™ (Ambry Genetics; California)
iii. RenalNext (Ambry Genetics; California)
iv. VistaSeq Colorectal Cancer Profile (LabCorp / Integrated Genetics / Integrated Oncology)

C. These tests are found in **both** of these separate ***Genetic Testing: Hereditary Breast and Ovarian Cancer Genetic Testing (Medicare Only)*** and ***Genetic Testing: Inherited Susceptibility to Colorectal Cancer (Medicare Only)*** policies *<u>(Policy selection will be based on the clinical presentation of the individual for which testing is requested)</u>:*

i. Cancer Next (Ambry Genetics; California)
ii. CancerNext-Expanded (Ambry Genetics; California)
iii. CancerNext-Expanded +RNAinsight™ (Ambry Genetics; California)
iv. CancerNext +RNAinsight™ (Ambry Genetics; California)
v. myRisk® Hereditary Cancer (Myriad Genetics; Utah)
vi. myRisk® Hereditary Cancer Update (Myriad Genetics; Utah)
vii. VistaSeq Hereditary Cancer Panel (LabCorp / Integrated Genetics / Integrated Oncology)
viii. VistaSeq Hereditary Cancer without BRCA (LabCorp / Integrated Genetics / Integrated Oncology)

D. These tests are addressed in the separate ***Genetic Testing: Pharmacogenetic Testing (Medicare Only)*** policy.

i. Mental Health DNA Insight™ (Pathway Genomics®; California)
ii. Neuro IDGenetix (AltheaDx, Inc.; California)

iii. Pain Medication DNA Insight™ (Pathway Genomics®)
iv. Personalized Medicine Panel (Alpha Genomix)
v. CNT (CEP72, TPMT and NUDT15) Genotyping Panel (0286U) (RPRD Diagnostics)
vi. Focused Pharmacogenomics Panel (0029U) (Mayo Clinic, Mayo Medical Laboratories; Headquartered in Minnesota)
vii. Genecept™ Assay (Genomind; Pennsylvania)
viii. GenoMind Professional PGx Express™, Full Mental Health Report (24 Genes) (Genomind; Pennsylvania)
ix. GenoMind Professional PGx Express™, CORE Anxiety & Depression Report (15 Genes) (Genomind; Pennsylvania)
x. PGxOne™ Plus Pharmacogenomics Test (Admera Health; New Jersey)
xi. RightMed Comprehensive Test (OneOme; Minnesota)
xii. Warfarin Response Genotype (0030U) (Mayo Clinic, Mayo Medical Laboratories; Headquartered in Minnesota)

XII. The following tests are **not medically necessary**.
A. The following tests are **not medically necessary** based on **Table 2** in the Policy Guidelines section.
i. Copper Metabolism Disorders Panel (Invitae; California)
ii. Nervous System/Brain Cancer (Invitae; California)
iii. DCMNext (Ambry Genetics; California)
iv. HCMNext (Ambry Genetics; California)
v. GeneTrails® GIST Genotyping Panel (OHSU Knight Diagnostic Laboratories; Oregon)
vi. GeneTrails® Hematologic Malignancies 76 Gene Panel (OHSU Knight Diagnostic Laboratories; Oregon)
vii. Lymph3Cx Lymphoma Molecular Subtyping Assay (Mayo Clinic; Test developed and performed in Arizona)
viii. NextStep DX Plus (Lineagen, Inc.; Utah)
ix. Skeletal Dysplasias Core Panel (Blueprint Genetics; Washington)
x. Megalencephaly Panel (Seattle Children's Hospital, UW Medical Center; Washington)
xi. Oncoplex Select Cancer Gene Panel (University of Washington; Washington)
xii. Retinal Dystrophy Panel (Blueprint Genetics; Washington)
xiii. UW-OncoPlex - Cancer Gene Panel (University of Washington; Washington)
xiv. Riscover Hereditary Cancer Panel (Progenity; Michigan) *(No longer offered)*
xv. Macula Risk PGx (ArcticDX Inc. / Arctic Medical Laboratories; Michigan)
xvi. Vita Risk® (ArcticDX Inc. / Arctic Medical Laboratories; Michigan)
xvii. OtoSCOPE® Panel (University of Iowa, D/B/A Molecular Otolaryngology and Renal Research Laboratories; Iowa)
xviii. DecisionDx®-SCC (Castle Biosciences, Inc.; Arizona)
xix. EpiSign Complete (Greenwood Genetic Center)

xx. Bridge Urinary Tract Infection Detection and Resistance Test (Bridge Diagnostics; California)

B. The following tests are **not medically necessary** based on **Table 3** in the Policy Guidelines section.

i. Arrhythmia Panel (GeneDx, Maryland)
ii. Ataxia Comprehensive Evaluation Panel (Athena Diagnostics; Massachusetts)
iii. Breast/Gyn Cancer Panel (GeneDx, Maryland)
iv. Cardiomyopathy Panel (GeneDx, Maryland)
v. CNGnome™ PerkinElmer Genomics (Pennsylvania)
vi. Colorectal Cancer Panel (GeneDx, Maryland)
vii. CxBladder Detect (0012M) and CxBladder Monitor (0013M) and CxBladder Triage (81479) Pacific Edge, Ltd. (Pennsylvania)
viii. Genomic Unity® Ataxia Repeat Expansion Analysis (0216U) (Variantyx Inc.; Massachusetts)
ix. Genomic Unity® Comprehensive Ataxia Repeat Expansion and Sequence Analysis (0217U) (Variantyx Inc.; Massachusetts)
x. Genomic Unity® DMD Analysis (0218U) (Variantyx Inc.; Massachusetts)
xi. Hemiplegic Migraine Panels (GeneDx, Maryland)
xii. Infantile Epilepsy Panel (GeneDx, Maryland)
xiii. myTAIHEART (TAI Diagnostics, Inc.; Wisconsin)
xiv. OmniSeq Advance℠ (OmniSeq®Corporation; New York)
xv. OmniSeq Comprehensive® (OmniSeq®Corporation; New York)
xvi. OtoGenome™ (Laboratory for Molecular Medicine / Partners HealthCare; Massachusetts)
xvii. Tissue of Origin® (TOO®) – Endometrial (Cancer Genetics Inc.; New Jersey, with labs also in California and North Carolina)
xviii. Tissue of Origin® (TOO®) – Head & Neck (Cancer Genetics Inc.; New Jersey, with labs also in California and North Carolina)
xix. ERA® (Endometrial Receptivity Analysis) (Igenomix®; Florida) - In vitro fertilization (IVF) services are not a covered Medicare benefit. See member benefits. In addition, testing to ensure successful IVF does not meet Medicare's definition of medical necessity. Therefore, this test is **not medically necessary** under *Social Security Act, §1862(a)(1)(A)* for Medicare.
xx. PancreaSeq® Genomic Classifier (Molecular and Genomic Pathology Laboratory, University of Pittsburgh Medical Center)
xxi. Versiti™ Thrombosis Panel (0278U) (Versiti™ Diagnostic Laboratories; Wisconsin)

XIII. The following tests may be **medically necessary** as FDA-approved or cleared companion diagnostic (CDx) in vitro tests when all other applicable criteria from the national coverage determination (NCD) for *Next Generation Sequencing (NGS)* (90.2) are met:

i. FoundationOne CDx™ (F1CDx) (0037U) (Foundation Medicine, Inc., Massachusetts) *(See the Non-Small Cell Lung Cancer: Molecular Testing for Targeted Therapy (Medicare Only) policy when testing is used for NSCLC.)*

ii. FoundationOne®Liquid CDx (0239U) (Foundation Medicine, Inc., Massachusetts) *(See the Non-Small Cell Lung Cancer: Molecular Testing for Targeted Therapy (Medicare Only) policy when testing is used for NSCLC.)*
iii. Guardant360® CDx (0242U) (Guardant Health, California) *(See the Non-Small Cell Lung Cancer: Molecular Testing for Targeted Therapy (Medicare Only) policy when testing is used for NSCLC.)*
iv. MyChoice® CDx (0172U, 81479, 81599, 81162) (Myriad Genetics, Utah)
v. Oncomine™ Dx Target Test (0022U) (Thermo Fisher Scientific, Massachusetts) *(See the Non-Small Cell Lung Cancer: Molecular Testing for Targeted Therapy (Medicare Only) policy when testing is used for NSCLC.)*
vi. Praxis™ Extended RAS Panel (0111U) (Illumina, Inc., California)

POLICY GUIDELINES

Genetic and Molecular Testing

Genetic testing is performed to detect variants in DNA, RNA, and/or chromosomes. Within the Medicare program, genetic testing may also be referred to as molecular or biomarker testing.

According to Human Genome Variation Society (HGVS) nomenclature, the term "variant" is used to describe a change in a DNA or protein sequence, replacing previously-used terms, such as "mutation." Pathogenic variants are variants associated with disease, while benign variants are not. However, the majority of genetic changes have unknown effects on human health. These are referred to as "variants of uncertain significance."

Such testing may be requested for a variety of purposes, such as diagnosing a condition, predicting susceptibility for inherited conditions, determining carrier status, diagnostic and prognostic testing, screening for common disorders, or selecting appropriate treatments (also known as pharmacogenetic testing). However, this is not a complete list of reasons genetic testing may be requested or performed.

Some genetic tests may be eligible for Medicare coverage, while others are potentially covered in select individuals or for certain conditions. Still other tests may not be eligible for Medicare coverage at all due to Medicare's reasonable and necessary requirements for diagnostic testing.

Some tests may be single gene testing, while other tests are offered as multi-gene panels. Panel testing technology, such as next generation sequencing (NGS) and chromosomal microarray, is a testing method that examines multiple genes or mutations simultaneously. There is currently no standardization of the design and composition of panel tests. Therefore, panels can vary by laboratory. Thus, different commercially available test options that appear to be for the same condition may test different sets of genes. In addition, the composition of any individual panel is likely to change over time, as genes are added to or removed from existing panels.

Some tests are performed at one single laboratory, while other tests may be developed as "test kits," which can be sent out by a manufacturer to any laboratory for processing.

While genetic testing has potential benefits for certain conditions, especially cancer, there are also risks associated with genetic testing. These include emotional, social, or financial consequences. Reasons include what test results may reveal, and the feelings that can arise with such test results (e.g., results revealing information about other family members who were not the intended individual the testing was performed for, etc.). In addition, there are limitations to what genetic and molecular tests can provide regarding an inherited condition. Even if a positive result is received, the test may be unable to determine if a person will ever show symptoms of a disorder, how severe the symptoms will be, or whether the disorder will progress over time. Another limitation of molecular testing is that there may not be treatments or cures available for conditions related to an identified genetic variant or genetic disorder. Therefore, it is very important that any individual who is considering genetic testing understand all aspects of the test results before making a decision. While not a requirement for Medicare coverage in most cases, individuals considering genetic testing may wish to consult with a

genetics professional to explain in detail both benefits and risks of testing, as well as any potential and significant limitations of a particular test. (Genetics Home Reference U.S. National Library of Medicine, https://ghr.nlm.nih.gov/primer/testing/genetictesting)

Medicare Coverage and Medical Necessity Background

In order for a laboratory service (including genetic and molecular testing) to be considered for coverage, Medicare requires that the test in question meet all of the following:

- **Not be excluded from coverage** by statute, regulation, National Coverage Determination, (NCD), or Local Coverage Determination (LCD);[2]
- **Be ordered by a physician or practitioner** who is treating the beneficiary;[7,8]
- Provide data that will be **directly used in the management** of a beneficiary's specific medical problem;[7,8]
- **Be considered medically reasonable and necessary**, as required per the *Social Security Act, §1862(a)(1)(A)*. This means the service must be considered reasonable and necessary in the diagnosis or treatment of an illness or injury, or to rule out or confirm a suspected diagnosis because the patient has signs and/or symptoms.[4,5]
    - This also means services deemed ***not*** medically necessary for any reason (including lack of safety and efficacy for investigational services) are also non-covered.[6]

In addition to the above general Medicare requirements, under Chapter 13 of the Medicare Program Integrity Manual, Medicare allows contractors to consider a service "reasonable and necessary" when the service is appropriate for the member's condition. This includes appropriateness in duration, frequency, and that the service is furnished in accordance with accepted standards of medical practice for the condition, furnished in a setting appropriate to the medical needs and condition, ordered and furnished by qualified personnel, that the service meets, but does not exceed, the medical need; and is at least as beneficial as an existing and available medically appropriate alternative.[11]

To effectively manage a patient's specific medical problem using genetic or molecular diagnostic testing, the genetic tests performed must be relevant to the medical condition **and** have established clinical utility and analytical validity for that condition. Therefore, ordering physicians must be familiar with the genetic tests they order to ensure all test result components are clinically actionable.

Medicare Guidance on Genetic Screening Tests

According to the Medicare Claims Processing Manual, Chapter 16[1]:

> "Tests that are performed in the absence of signs, symptoms, complaints, personal history of disease, or injury are **not covered** except when there is a statutory provision that explicitly covers tests for screening as described.
>
> If a person is tested to rule out or to confirm a suspected diagnosis because the patient has a sign and/or symptoms, this is considered a diagnostic test, not a screening test. A/B MACs (A)

and (B) have discretionary authority to make reasonable and necessary scope of benefit determinations."

Reproductive Planning and Prenatal Genetic Testing

Tests performed in the absence of clinical signs/symptoms are considered "screening" tests. For Medicare members of child-bearing age, there are many routine tests, including screening tests, performed during a pregnancy which are covered tests; however, other tests are not eligible for Medicare coverage. These include, but are not limited to, tests performed to determine gender of fetus and carrier screening.

While reproductive planning and prenatal tests may provide useful information, test results are not generally used to diagnose or make direct treatment decisions for an illness or injury, as defined by Medicare. Some tests are not used in the management of a beneficiary's specific medical problem because they are performed in the absence of signs or symptoms. Since these tests do not meet Medicare's medical and reasonable threshold requirements under *Title XVIII of the Social Security Act, Section 1862(a)(1)(A)*, they are considered not medically necessary for Medicare.

Direct-to-Consumer (DTC) and over-the-counter (OTC) tests are also considered not medically necessary for Medicare. Tests must be ordered by a treating provider to provide actionable data to be used promptly by the treating physician to treat or diagnose an illness or condition in order to be considered medically reasonable and necessary.[8] DTC and OTC testing also do not meet this Medicare laboratory testing coverage requirement and therefore, are not medically reasonable or necessary under *Title XVIII of the Social Security Act, Section 1862(a)(1)(A)*.

National Coverage Determination (NCD) for Next Generation Sequencing (NGS)

Medicare does have a national coverage determination (NCD) applicable to some next-generation sequencing (NGS) somatic and germline testing (90.2). However, this NCD has limitations. Specifically, this NCD is only applicable to:

- NGS testing for ***DNA*** sequencing to detect genomic mutations;
- Tests **with** FDA approval or clearance as a companion in vitro diagnostic (CDx) test;
- Tests used for cancer-related indications.

According to this NCD, coverage for NGS tests not otherwise addressed by the NCD is left to local Medicare Administrative Contractor (MAC) discretion. This includes, but is not necessarily limited to, tests using NGS for *RNA* sequencing and protein analysis, tests **without** FDA approval or clearance as a CDx test, and testing used for **non**-cancer related indications.

Diagnostic Laboratory Test Jurisdiction

The Company policy *PHA Medicare Medical Policy Development and Application* (MP# 50) describes the Plan's hierarchy with respect to Medicare medical policy development. In compliance with Medicare guidelines, some LCDs and LCAs used may be for test service areas **outside** of the Company service area.

This is because Medicare's general rule regarding jurisdiction of claims furnished by an independent laboratory is that jurisdiction lies with the A/B MAC (B) (aka, Medicare Contractor) serving the **area in which the laboratory test is performed**.[10]

However, there may be exceptions to this rule. According to Medicare, while jurisdiction for laboratory services normally lies with the carrier serving the performing laboratory service area, there are situations where a regional or national lab chain jurisdiction (e.g., Quest Diagnostics, LabCorp, etc.) lies with a single carrier.[16] Therefore, tests performed by a national laboratory chain may have a single carrier established within the Company medical policies for all laboratory services they perform, regardless of the individual laboratory location. This allows for consistent outcomes for all members who receive the same test by the same lab chain.

Another exception to this rule involves "referring laboratory tests." This is when one laboratory sends the sample to another laboratory for processing. Under Medicare rules for referred tests, the location of the **billing** provider determines jurisdiction for claim payment and coverage criteria. Note, also under Medicare rules, only one laboratory is allowed to bill for the services rendered. If the performing laboratory and billing provider both submit a claim, then the performing laboratory's claim is the claim that would adjudicate according to member benefits.[18-20]

Medicare's Molecular Diagnostic (MolDX) Program Contractor

While many Medicare contractors (MACs) have adopted guidelines developed and published by the Molecular Diagnostic Services (MolDX) Program for their service areas, the program is **not** national in scope. MolDX-related reference materials only apply to genetic and molecular tests performed in the following states: OR, WA, AK, ID, UT, AZ, MT, ND, SD, WY, CA, NV, HI, NC, SC, AL, GA, TN, VA, WV, KY, OH, IA, KS, MO, NE, IN, and MI.[12]

The MolDX Program was developed by Palmetto GBA in 2011. The MolDX Contractor performs the following functions[12,14]:

- Establish clinical utility expectations.
- Complete technical assessments of published test data to determine clinical utility and coverage of individual tests.
- Develop unique test identifiers (Z-codes), adding to the DEX™ register of molecular diagnostic tests to allow for automated claims processing and to track utilization.
- Establish reimbursement.

Table 2

Genetic tests performed within a MolDX service area are required to undergo a technical assessment (TA) review by MolDX. The LCDs in Table 2 detail this requirement:

	LOCATION/MEDICARE CONTRACTOR				
	NORIDIAN J-F	***NORIDIAN J-E*** CA and NV	***PALMETTO GBA J-J AND J-M***	***WPS J-5 AND J-8***	***CGS J-15*** KY and OH

	OR, WA, AK, ID, UT, AZ, MT, ND, SD, and WY		NC, SC, AL, GA, TN, VA, and WV	IA, KS, MO, NE, IN, and MI	
General MolDX Requirements	L36256	L35160	L35025	L36807	L36021

The outcome of these TA reviews is maintained in the DEX™ Diagnostics Exchange registry catalog and when possible, the coverage outcome is included within this medical policy to assist with coverage decision-making.

- Tests listed as "not covered" in this catalog have had clinical utility and analytical validity (CU/AV) reviewed and were determined to be **not medically reasonable or necessary** for Medicare under *Social Security Act, §1862(a)(1)(A)*.
- Tests which have **not yet** completed the required TA review are by default also considered to be **not medically reasonable or necessary** for Medicare under *§1862(a)(1)(A)*, based on the requirements found in the LCDs noted in Table 1 above.
- Tests listed as "covered" in this catalog have completed the required TA review and have been determined to be **medically reasonable or necessary** for Medicare under *§1862(a)(1)(A)*; however, this coverage is not automatic, as both of the following must be met:
    - Applicable NCD, LCD, and LCA criteria are met; and,
    - The member has signs/symptoms of a relevant disease or condition.

If a test is not specifically called out in this medical policy, additional research is required to determine coverage.

Note, test coverage or non-coverage positions included in this medical policy were accurate at the time of policy publication, but they are subject to change by the Medicare MolDX Program contractor at any time. Appeals to dispute non-coverage should include documentation by the MolDX Contractor which reflects a positive coverage decision (e.g., copy of the MolDX determination letter).

Non-MolDX Service Area Genetic Testing

Services areas which have **not** adopted MolDX guidelines include testing performed in the following states: FL, CO, NM, OK, TX, AR, LA, MS, DE, MD, NJ, PA, IL, MN, WI, CT, NY, ME, MA, NH, RI, and VT.

Table 3

The LCDs in Table 3 provide general coverage requirements for each jurisdiction area:

	LOCATION/MEDICARE CONTRACTOR		
STATE(S)	**MEDICARE CONTRACTOR**	**LCD**	**COVERAGE REQUIREMENTS**
IL, MN, WI, CT, NY, ME,	***National Government***	L35000	This LCD requires clinical utility and analytical validity be established, but it doesn't address all tests by name

MA, NH, RI, and VT	***Services (NGS) J-6 and J-K***		specifically. For panels, this LCD also states, "testing would be covered ONLY for the number of genes or test that are reasonable and necessary to obtain necessary information for therapeutic decision making." In the absence of specific guidance in this LCD, the PHP Company policies for genetic tests provide a peer review of medical literature to evaluate clinical utility/analytical validity. When the biomarkers included in a test do not have proven clinical validity/utility, the test is not medically reasonable or necessary under *Social Security Act, §1862(a)(1)(A)* for Medicare members.
CO, NM, OK, TX, AR, LA, MI, DE, MD, NJ, and PA	***Novitas J-H and J-L***	L35062 / L35396	The LCD L35062 requires clinical utility and analytical validity be established, but it doesn't address all tests by name specifically. Additionally, for multi-biomarker panel test, the LCD L35396 requires evidence to support how "each requested biomarker can be individually contributory." In the absence of specific guidance in these LCDs, the PHP Company policies for genetic tests provide a peer review of medical literature to evaluate clinical utility/analytical validity. When the biomarkers included in a test do not have proven clinical validity/utility, the test is not medically reasonable or necessary under *Social Security Act, §1862(a)(1)(A)* for Medicare members.
FL	***First Coast Service Options J-N***	L34519	The LCD L34519 requires tests to undergo evaluation to establish clinical utility and analytical validity, based on published peer reviewed medical literature, or be FDA-approved, in order to be eligible for coverage. However, it doesn't address all tests by name specifically. For panels, this LCD also states, "testing would be covered ONLY for the number of genes or test that are reasonable and necessary to establish a diagnosis." In the absence of specific guidance in this LCD, the PHP Company policies for genetic tests provide a peer review of medical literature to evaluate clinical utility/analytical validity. When the biomarkers included in a test do not have proven clinical validity/utility, the test is not medically reasonable or necessary under *Social Security Act, §1862(a)(1)(A)* for Medicare members.

As noted in Table 3, all of the listed LCDs require tests undergo evaluation to establish clinical utility (CU) and analytical validity (AV) in order to be eligible for coverage. However, due to the large number of proprietary tests marketed and available, most genetic tests – particularly panel tests – are not specifically called out by name within an LCD or LCA, nor do LCDs or LCAs provide the outcome for the peer-reviewed CU/AV for most tests.

The Company policy *PHA Medicare Medical Policy Development and Application* (MP# 50) describes the Plan's hierarchy with respect to Medicare medical policy development. Medicare rules and regulations state that when no NCD, LCD, LCA, or other Medicare coverage guideline exists, Medicare allows Medicare Advantage Organizations (MAOs) to make coverage determinations based on an objective, evidenced-based process. Therefore, in the absence of a specific Medicare policy or reference for a test, Company Commercial medical policy criteria may be applied to panel tests which do not have clinical utility or analytical validity documented within an LCD directly. Tests which are considered "investigational" in a Company Commercial policy will be denied as not medically reasonable or necessary under *Social Security Act, §1862(a)(1)(A)* for Medicare members.

Genetic Panel Testing

According to the MolDX program, a test panel is defined as "A predetermined set of medical tests composed of individual laboratory tests, related by medical condition, specimen type, frequency ordered, methodology or types of components to aid in the diagnosis/treatment of disease."[12]

Genetic panel tests may be used for a number of indications and they may be either be proprietary, "off-the-shelf", tests with a set number of genes (subject to change without notice), or they may be customized, "a la cart", tests with genes selected by the ordering provider or genetic counselor based on a patient's symptoms.

In addition to targeted tumor panels, there are also comprehensive genomic profile (CGP) tests. Targeted next generation sequencing (NGS) tumor panels are "tests that identify somatic alterations known to occur in certain regions (i.e., 'hotspots') within specific genes of interest for cancer management (i.e., diagnosis, selection of molecularly targeted therapies, prognosis in a context where prognostic classification is essential for treatment selection)."[17]

CGP tests are "NGS-based molecular assays that provide additional insight beyond individual gene hotspots; these assays seek to describe the genomic makeup of a tumor and can help identify underlying mechanisms of disease to guide clinical decision making. These tests include not only mutations in individual relevant genes, but also patterns of mutations across related genes in established cancer pathways and often include an assessment of overall mutational burden."[17]

BILLING GUIDELINES

Some, but not all, panel tests may have a specific CPT or HCPCS code assigned (81410-81471, 815XX multianalyte assays with algorithmic analyses [MAAA] codes or newly developed proprietary laboratory analyses [PLA] codes). However, many panels may not have a specific code available. When no specific CPT or HCPCS code exists for the panel, the provider is required to bill using an unlisted code (e.g., 81479 or 81599). It is not appropriate for the provider to bill any of the tests in a panel separately as if they were performed individually. This is a misrepresentation of services performed and is not appropriate based on either CPT or CMS guidelines. In a "Healthcare Fraud Prevention Partnership" white paper, the unbundling of claims for lab panels was identified as an area of concern for inappropriate billing.[13]

According to Noridian, under the instruction by the MolDX Contractor, to report targeted NGS gene panel services for somatic variant detection of 5 or more genes, providers are to first consider CPT® codes 81445 and 81450, with a unit of service (UOS) of one (UOS=1). Laboratories providing panel tests of 2 to 4 genes should use CPT® 81479 and one (1) UOS.[17]

Since CGP testing is not defined as a targeted panel by MolDX and it is not currently satisfactorily described by any existing CPT code, to report a CGP test, providers should use CPT® code 81479 at this time. Coverage of CGP is limited to one test per surgical specimen and precludes the use of any other molecular testing on that specimen.[17]

For NGS-based tests that do not fit under the Medicare definitions of "targeted" or "Comprehensive" panels, claims should be reported using the "Not Otherwise Classified" (NOC) code 81479. Tier 1 and/or Tier 2 individual biomarker CPT codes should not be used for a single gene or any combination of genes when testing is performed as part of a NGS or other multiplexing technology panel.[17]

Consistent with all HCPCS S-codes, the *National Physician Fee Schedule Relative Value File (NPFSRVF)*, published by Medicare[1] indicates HCPCS codes S3844 and S3870 have been assigned a Status Indicator of "I." This is defined as "Not valid for Medicare purposes." HCPCS codes S3844 and S3870 are not covered unless allowed under a Medicare Advantage provider contract exception, as indicated in the relevant Company coding policy.

CPT/HCPCS CODES

Note: Codes addressed by this policy, may include, but are not limited to, the following:

Medicare Only	
Prior Authorization Required	
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)
81120	IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (eg, glioma), common variants (eg, R132H, R132C)
81121	IDH2 (isocitrate dehydrogenase 2 [NADP+], mitochondrial) (eg, glioma), common variants (eg, R140W, R172M)
81161	DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed
81162	BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis
81163	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81164	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81165	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81166	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81167	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81168	CCND1/IGH (t(11;14)) (eg, mantle cell lymphoma) translocation analysis, major breakpoint, qualitative and quantitative, if performed
81171	AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81172	AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; characterization of alleles (eg, expanded size and methylation status)
81173	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; full gene sequence
81174	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; known familial variant
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)
81177	ATN1 (atrophin 1) (eg, dentatorubral-pallidoluysian atrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81178	ATXN1 (ataxin 1) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81179	ATXN2 (ataxin 2) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81180	ATXN3 (ataxin 3) (eg, spinocerebellar ataxia, Machado-Joseph disease) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81181	ATXN7 (ataxin 7) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81182	ATXN8OS (ATXN8 opposite strand [non-protein coding]) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81183	ATXN10 (ataxin 10) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81184	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81185	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; full gene sequence
81186	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; known familial variant
81187	CNBP (CCHC-type zinc finger nucleic acid binding protein) (eg, myotonic dystrophy type 2) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81188	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81189	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; full gene sequence
81190	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; known familial variant(s)
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
81201	APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; full gene sequence
81202	APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; known familial variants
81203	APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; duplication/deletion variants
81204	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; characterization of alleles (eg, expanded size or methylation status)

81212	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants
81215	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant
81216	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81217	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant
81218	CEBPA (CCAAT/enhancer binding protein [C/EBP], alpha) (eg, acute myeloid leukemia), gene analysis, full gene sequence
81219	CALR (calreticulin)(eg myeloproliferative disorders, gene analysis, common variants in exon 9)
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines)
81221	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; known familial variants
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; duplication/deletion variants
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence
81224	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; intron 8 poly-T analysis (eg, male infertility)
81225	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *8, *17)
81226	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN)
81227	CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (eg, drug metabolism), 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) (eg, *2, *22)
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)
81233	BTK (Bruton's tyrosine kinase) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, C481S, C481R, C481F)
81234	DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; evaluation to detect abnormal (expanded) alleles
81236	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, myelodysplastic syndrome, myeloproliferative neoplasms) gene analysis, full gene sequence
81237	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, diffuse large B-cell lymphoma) gene analysis, common variant(s) (eg, codon 646)
81238	F9 (coagulation factor IX) (eg, hemophilia B), full gene sequence

81239	DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; characterization of alleles (eg, expanded size)
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
81250	G6PC (glucose-6-phosphatase, catalytic subunit) (e.g., Glycogen storage disease, type 1a, von Gierke disease) gene analysis, common variants (e.g., R83C, Q347X)
81256	HFE (hemochromatosis) (e.g. hereditary hemochromatosis) gene analysis, common variants (e.g. C282Y, H63D)
81257	HBA1/HBA2 (alpha globin 1 and alpha globin 2)(e.g. alpha thalsemmia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis, for common deletions or variant (e.g., Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, 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
81265	Comparative analysis using Short Tandem Repeat (STR) markers; patient and comparative specimen (eg, pre-transplant recipient and donor germline testing, post-transplant non-hematopoietic recipient germline [eg, buccal swab or other germline tissue sample] and donor testing, twin zygosity testing, or maternal cell contamination of fetal cells)
81266	Comparative analysis using Short Tandem Repeat (STR) markers; each additional specimen (eg, additional cord blood donor, additional fetal samples from different cultures, or additional zygosity in multiple birth pregnancies) (List separately in addition to code for primary procedure)
81267	Chimerism (engraftment) analysis, post transplantation specimen (eg, hematopoietic stem cell), includes comparison to previously performed baseline analyses; without cell selection
81268	Chimerism (engraftment) analysis, post transplantation specimen (eg, hematopoietic stem cell), includes comparison to previously performed baseline analyses; with cell selection (eg, CD3, CD33), each cell type
81269	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; duplication/deletion variants
81270	JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) gene analysis, p.Val617Phe (V617F) variant
81271	HTT (huntingtin) (eg, Huntington disease) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
81274	HTT (huntingtin) (eg, Huntington disease) gene analysis; characterization of alleles (eg, expanded size)
81275	KRAS ((V-KI-RAS2 Kirsten Rat Sarcoma Viral Oncogene)(EG carcinoma) gene analysis, variants in codons 12 and 13
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (eg, carcinoma) gene analysis; additional variant(s) (eg, codon 61, codon 146)

81277	Cytogenomic neoplasia (genome-wide) microarray analysis, interrogation of genomic regions for copy number and loss-ofheterozygosity variants for chromosomal abnormalities
81279	JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) targeted sequence analysis (eg, exons 12 and 13)
81283	IFNL3 (interferon, lambda 3) (eg, drug response), gene analysis, rs12979860 variant
81284	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; evaluation to detect abnormal (expanded) alleles
81285	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; characterization of alleles (eg, expanded size)
81286	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; full gene sequence
81287	MGMT (O-6-methylguanine-DNA methyltransferase) (eg, glioblastoma multiforme) promoter methylation analysis
81288	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis
81289	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; known familial variant(s)
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
81305	MYD88 (myeloid differentiation primary response 88) (eg, Waldenstrom's macroglobulinemia, lymphoplasmacytic leukemia) gene analysis, p.Leu265Pro (L265P) variant
81306	NUDT15 (nudix hydrolase 15) (eg, drug metabolism) gene analysis, common variant(s) (eg, *2, *3, *4, *5, *6)
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)
81310	NPM1 (nucleophosmin) (eg, acute myeloid leukemia) gene analysis, exon 12 variants
81311	NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (eg, colorectal carcinoma), gene analysis, variants in exon 2 (eg, codons 12 and 13) and exon 3 (eg, codon 61)
81312	PABPN1 (poly[A] binding protein nuclear 1) (eg, oculopharyngeal muscular dystrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81314	PDGFRA (platelet-derived growth factor receptor, alpha polypeptide) (eg, gastrointestinal stromal tumor [GIST]), gene analysis, targeted sequence analysis (eg, exons 12, 18)
81315	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative
81316	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; single breakpoint (eg, intron 3, intron 6 or exon 6), qualitative or quantitative
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
81320	PLCG2 (phospholipase C gamma 2) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, R665W, S707F, L845F)
81321	PTEN (phosphatase and tensin)(e.g., Cowden Syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis
81322	PTEN (phosphatase and tensin)(e.g., Cowden Syndrome, PTEN hamartoma tumor syndrome) gene analysis; known familial variant
81323	PTEN (phosphatase and tensin)(e.g., Cowden Syndrome, PTEN hamartoma tumor syndrome) gene analysis; duplication/deletion variant
81324	PMP22 (peripheral myelin protein 22)(e.g., Charcot-Marie-Tooth hereditary neuropathy with liability to pressure palsies) gene analysis; duplication/deletion analysis
81325	PMP22 (peripheral myelin protein 22)(e.g., Charcot-Marie-Tooth hereditary neuropathy with liability to pressure palsies) gene analysis; full sequence
81326	PMP22 (peripheral myelin protein 22) (e.g., Charcot-Marie-Tooth hereditary neuropathy with liability to pressure palsies) gene analysis; know familial variant
81327	SEPT9 (Septin9) (eg, colorectal cancer) methylation analysis
81328	SLCO1B1 (solute carrier organic anion transporter family, member 1B1) (eg, adverse drug reaction), gene analysis, common variant(s) (eg, *5)
81329	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; dosage/deletion analysis (eg, carrier testing), includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed
81331	SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and Ubiquitin protein ligase E3A) (e.g., Prader-Willi syndrome and/or Angelman syndrome methylation analysis

81332	SERPINA 1 (serpin peptidase inhibitor, clade A, alpha-1 antiproteinase variants (e.g., *S and *Z)
81333	TGFBI (transforming growth factor beta-induced) (eg, corneal dystrophy) gene analysis, common variants (eg, R124H, R124C, R124L, R555W, R555Q)
81334	RUNX1 (runt related transcription factor 1) (eg, acute myeloid leukemia, familial platelet disorder with associated myeloid malignancy), gene analysis, targeted sequence analysis (eg, exons 3-8)
81335	TPMT (thiopurine S-methyltransferase) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3)
81336	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; full gene sequence
81337	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)
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
81343	PPP2R2B (protein phosphatase 2 regulatory subunit Bbeta) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81344	TBP (TATA box binding protein) (eg, spinocerebellar ataxia) gene analabnormal (eg, expanded) alleles
81345	TERT (telomerase reverse transcriptase) (eg, thyroid carcinoma, glioblastoma multiforme) gene analysis, targeted sequence analysis (eg, promoter region)
81346	TYMS (thymidylate synthetase) (eg, 5-fluorouracil/5-FU drug metabolism), gene analysis, common variant(s) (eg, tandem repeat variant)
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)
81349	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and loss-of-heterozygosity variants, low-pass sequencing analysis
81350	UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (eg, irinotecan metabolism), gene analysis, common variants (eg, *28, *36, *37)
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
81355	VKORC1 (vitamin K epoxide reductase complex, subunit 1) (eg, warfarin metabolism), gene analysis, common variant(s) (eg, -1639G>A, c.173+1000C>T)
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)
81400	Molecular pathology procedure, Level 1 (e.g., identification of single germline variant [e.g., SNP] by techniques such as restriction enzyme digestion or melt curve analysis)
81401	Molecular pathology procedure, Level 2 (e.g., 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 (e.g.,>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 1 exon)
81403	Molecular pathology procedure, level 4 (e.g. 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 (e.g., 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 (e.g., analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons)
81406	Molecular pathology procedure, Level 7 (e.g., 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 (e.g., 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, level 9 (e.g., 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
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
81415	Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis

81416	Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator exome (eg, parents, siblings) (List separately in addition to code for primary procedure)
81417	Exome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained exome sequence (eg, updated knowledge or unrelated condition/syndrome)
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, STXBP1, SYNGAP1, TCF4, TPP1, TSC1, TSC2, and ZEB2
81420	Fetal chromosomal aneuploidy (eg, trisomy 21, monosomy X) genomic sequence analysis panel, circulating cell-free fetal DNA in maternal blood, must include analysis of chromosomes 13, 18, and 21
81422	Fetal chromosomal microdeletion(s) genomic sequence analysis (eg, DiGeorge syndrome, Cri-du-chat syndrome), circulating cell-free fetal DNA in maternal blood
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)
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 10 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 disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include analysis of at least 10 genes, including APC, BMPR1A, CDH1, MLH1, MSH2, MSH6, MUTYH, PTEN, SMAD4, and STK11
81436	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); duplication/deletion of gene analysis panel, must include analysis of at least 5 genes, including MLH1, MSH2, EPCAM, SMAD4, and STK11
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	Hereditary cardiomyopathy (eg, hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy), genomic sequence analysis panel, must include sequencing of at least 5 cardiomyopathy-related genes (eg, DSG2, MYBPC3, MYH7, PKP2, TTN)
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
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
81443	Genetic testing for severe inherited conditions (eg, cystic fibrosis, Ashkenazi Jewish-associated disorders [eg, Bloom syndrome, Canavan disease, Fanconi anemia type C, mucolipidosis type VI, Gaucher disease, Tay-Sachs disease], beta hemoglobinopathies, phenylketonuria, galactosemia), genomic sequence analysis panel, must include sequencing of at least 15 genes (eg, ACADM, ARSA, ASPA, ATP7B, BCKDHA, BCKDHB, BLM, CFTR, DHCR7, FANCC, G6PC, GAA, GALT, GBA, GBE1, HBB, HEXA, IKBKAP, MCOLN1, PAH)
81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
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)
81450	Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KRAS, KIT, MLL, NRAS, NPM1, NOTCH1), interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed
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, IDH2, 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
81500	Oncology (ovarian), biochemical assays of two proteins (CA-125 and HE4), utilizing serum, with menopausal status, algorithm reported as a risk score
81503	Oncology (ovarian), biochemical assays of five proteins (CA-125, apolipoprotein A1, beta-2 microglobulin, transferrin, and pre-albumin), utilizing serum, algorithm reported as a risk score
81504	Oncology (tissue of origin), microarray gene expression profiling of > 2000 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as tissue similarity scores
81506	Endocrinology (type 2 diabetes), biochemical assays of seven analytes (glucose, HbA1c, insulin, hs-CRP, adiponectin, ferritin, interleukin 2-receptor alpha), utilizing serum or plasma, algorithm reporting a risk score
81507	Fetal aneuploidy (trisomy 21, 18, and 13) DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy
81508	Fetal congenital abnormalities, biochemical assays of two proteins (PAPP-A, hCG [any form]), utilizing maternal serum, algorithm reported as a risk score
81509	Fetal congenital abnormalities, biochemical assays of three proteins (PAPP-A, hCG [any form], DIA), utilizing maternal serum, algorithm reported as a risk score
81510	Fetal congenital abnormalities, biochemical assays of three analytes (AFP, uE3, hCG [any form]), utilizing maternal serum, algorithm reported as a risk score
81511	Fetal congenital abnormalities, biochemical assays of four analytes (AFP, uE3, hCG [any form], DIA) utilizing maternal serum, algorithm reported as a risk score (may include additional results from previous biochemical testing)
81512	Fetal congenital abnormalities, biochemical assays of five analytes (AFP, uE3, total hCG, hyperglycosylated hCG, DIA) utilizing maternal serum, algorithm reported as a risk 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
81538	Oncology (lung), mass spectrometric 8-protein signature, including amyloid A, utilizing serum, prognostic and predictive algorithm reported as good versus poor overall survival
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
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
0003U	Oncology (ovarian) biochemical assays of five proteins (apolipoprotein A-1, CA 125 II, follicle stimulating hormone, human epididymis protein 4, transferrin), utilizing serum, algorithm reported as a likelihood score *(Overa (Ova1 Next Generation), by Aspira Labs Inc.; Texas)*
0004M	Scoliosis, DNA analysis of 53 single nucleotide polymorphisms (SNPs), using saliva, prognostic algorithm reported as a risk score *(ScoliScore™)*
0006M	Oncology (hepatic), mRNA expression levels of 161 genes, utilizing fresh hepatocellular carcinoma tumor tissue, with alpha-fetoprotein level, algorithm reported as a risk classifier *(HeproDX™)*
0007M	Oncology (gastrointestinal neuroendocrine tumors), real-time PCR expression analysis of 51 genes, utilizing whole peripheral blood, algorithm reported as a nomogram of tumor disease index *(NETest)*
0009M	Fetal aneuploidy (trisomy 21, and 18) DNA sequence analysis of selected regions using maternal plasma, algorithm reported as a risk score for each trisomy
0012M	Oncology (urothelial), mRNA, gene expression profiling by real-time quantitative PCR of five genes (MDK, HOXA13, CDC2 [CDK1], IGFBP5, and XCR2), utilizing urine, algorithm reported as a risk score for having urothelial carcinoma
0013M	Oncology (urothelial), mRNA, gene expression profiling by real-time quantitative PCR of five genes (MDK, HOXA13, CDC2 [CDK1], IGFBP5, and CXCR2), utilizing urine, algorithm reported as a risk score for having recurrent urothelial carcinoma
0015M	Adrenal cortical tumor, biochemical assay of 25 steroid markers, utilizing 24-hour urine specimen and clinical parameters, prognostic algorithm reported as a clinical risk and integrated clinical steroid risk for adrenal cortical carcinoma, adenoma, or other adrenal malignancy
0016M	Oncology (bladder), mRNA, microarray gene expression profiling of 209 genes, utilizing formalinfixed paraffin-embedded tissue, algorithm reported as molecular subtype (luminal, luminal infiltrated, basal, basal claudin-low, neuroendocrine-like)
0017M	Oncology (diffuse large B-cell lymphoma [DLBCL]), mRNA, gene expression profiling by fluorescent probe hybridization of 20 genes, formalin-fixed paraffin-embedded tissue, algorithm reported as cell of origin
0019U	Oncology, RNA, gene expression by whole transcriptome sequencing, formalin-fixed paraffin embedded tissue or fresh frozen tissue, predictive algorithm reported as potential targets for therapeutic agents *(OncoTarget/OncoTreat, by Columbia University Department of Pathology and Cell Biology; New York)*
0022U	Targeted genomic sequence analysis panel, cholangiocarcinoma and non-small cell lung neoplasia, DNA and RNA analysis, 1-23 genes, interrogation for sequence variants and rearrangements, reported as presence/absence of variants and associated therapy(ies) to consider *(Oncomine™ Dx Target Test, by Thermo Fisher Scientific; Massachusetts)*

0029U	Drug metabolism (adverse drug reactions and drug response), targeted sequence analysis (ie, CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, SLCO1B1, VKORC1 and rs12777823) *(Focused Pharmacogenomics Panel, by Mayo Clinic; Minnesota)*
0030U	Drug metabolism (warfarin drug response), targeted sequence analysis (ie, CYP2C9, CYP4F2, VKORC1, rs12777823) *(Warfarin Response Genotype, by Mayo Clinic; Minnesota)*
0031U	CYP1A2 (cytochrome P450 family 1, subfamily A, member 2)(eg, drug metabolism) gene analysis, common variants (ie, *1F, *1K, *6, *7) *(Cytochrome P450 1A2 Genotype, by Mayo Clinic; Minnesota)*
0032U	COMT (catechol-O-methyltransferase)(drug metabolism) gene analysis, c.472G>A (rs4680) variant *(Catechol-Omethyltransferase (COMT) Genotype, by Mayo Clinic; Minnesota)*
0033U	HTR2A (5-hydroxytryptamine receptor 2A), HTR2C (5-hydroxytryptamine receptor 2C) (eg, citalopram metabolism) gene analysis, common variants (ie, HTR2A rs7997012 [c.614-2211T>C], HTR2C rs3813929 [c.-759C>T] and rs1414334 [c.551-3008C>G]) *(Serotonin Receptor Genotype (HTR2A and HTR2C), by Mayo Clinic; Minnesota)*
0034U	TPMT (thiopurine S-methyltransferase), NUDT15 (nudix hydroxylase 15)(eg, thiopurine metabolism) gene analysis, common variants (ie, TPMT *2, *3A, *3B, *3C, *4, *5, *6, *8, *12; NUDT15 *3, *4, *5) *(Thiopurine Methyltransferase (TPMT) and Nudix Hydrolase (NUDT15) Genotyping, by Mayo Clinic; Minnesota)*
0036U	Oncology (somatic mutations). Whole Exome 22,000 genes by Next Generation Sequencing. DNA extracted and analyzed from formalin fixed paraffin embedded tissue and Whole Blood. Algorithm result type is predictive and prognostic. Report of specific gene mutations, alterations as targets for therapeutic agents. *(EXaCT-1 Whole Exome Testing, by Weill Cornell Medicine- Clinical Genomics Laboratory; New York)*
0037U	Broad next generation sequencing in vitro diagnostic device, solid malignant neoplasms, DNA analysis, 324 genes, detection of substitutions, insertion and deletion alterations (indels), copy number alterations (CNAs), and select gene rearrangements as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB), reported as presence/absence of variants and discrete levels of MSI and TMB, and associated therapy(ies) including multiple FDA-approved companion diagnostics, using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens *(FoundationOne CDx™ (F1CDx), by Foundation Medicine Inc.; Massachusetts)*
0046U	FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia) internal tandem duplication (ITD) variants, quantitative *(FLT3 ITD MRD by NGS, by LabPMM LLC; California)*
0048U	Oncology (solid organ neoplasia), DNA, targeted sequencing of protein-coding exons of 468 cancer-associated genes, including interrogation for somatic mutations and microsatellite instability, matched with normal specimens, utilizing formalin-fixed paraffin-embedded tumor tissue, report of clinically significant mutation(s) *(MSK-IMPACT (Integrated Mutation Profiling of Actionable Cancer Targets), by Memorial Sloan Kettering Cancer Center; New York)*
0049U	NPM1 (nucleophosmin) (eg, acute myeloid leukemia) gene analysis, quantitative *(NPM1 MRD by NGS, by LabPMM LLC; California)*
0050U	Targeted genomic sequence analysis panel, acute myelogenous leukemia, DNA analysis, 194 genes, interrogation for sequence variants, copy number variants or rearrangements *(MyAML NGS Panel, by LabPMM LLC; California)*

0055U	Cardiology (heart transplant), cell-free DNA, PCR assay of 96 DNA target sequences (94 single nucleotide polymorphism targets and two control targets), plasma *(myTAIHEART, by TAI Diagnostics, Inc.; Wisconsin)*
0056U	Hematology (acute myelogenous leukemia), DNA, whole genome next-generation sequencing to detect gene rearrangement(s), blood or bone marrow, report of specific gene rearrangement(s) *(MatePair Acute Myeloid Leukemia Panel, by Mayo Clinic; Minnesota)*
0057U	Oncology (solid organ neoplasia), mRNA, gene expression profiling by massively parallel sequencing for analysis of 51 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a normalized percentile rank *(RNA-Sequencing by NGS, by NGS OmniSeq, Inc.; New York)*
0067U	Oncology (breast), immunohistochemistry, protein expression profiling of 4 biomarkers (matrix metalloproteinase-1 [MMP-1], carcinoembryonic antigen-related cell adhesion molecule 6 [CEACAM6], hyaluronoglucosaminidase [HYAL1], highly expressed in cancer protein [HEC1]), formalin-fixed paraffin-embedded precancerous breast tissue, algorithm reported as carcinoma risk score *(BBDRisk Dx™, by Silbiotech, Inc.; Maryland)*
0078U	Pain management (opioid-use disorder) genotyping panel, 16 common variants (ie, ABCB1, COMT, DAT1, DBH, DOR, DRD1, DRD2, DRD4, GABA, GAL, HTR2A, HTTLPR, MTHFR, MUOR, OPRK1, OPRM1), buccal swab or other germline tissue sample, algorithm reported as positive or negative risk of opioid-use disorder *(INFINITI® Neural Response Panel, by PersonalizeDx Labs; California)*
0087U	Cardiology (heart transplant), mRNA gene expression profiling by microarray of 1283 genes, transplant biopsy tissue, allograft rejection and injury algorithm reported as a probability score *(Molecular Microscope® MMDx—Heart, by Kashi Clinical Laboratories; Oregon)*
0088U	Transplantation medicine (kidney allograft rejection) microarray gene expression profiling of 1494 genes, utilizing transplant biopsy tissue, algorithm reported as a probability score for rejection *(Molecular Microscope® MMDx—Kidney, by Kashi Clinical Laboratories; Oregon)*
0092U	Oncology (lung), three protein biomarkers, immunoassay using magnetic nanosensor technology, plasma, algorithm reported as risk score for likelihood of malignancy *(REVEAL Lung Nodule Characterization, by MagArray, Inc.; California)*
0094U	Genome (eg, unexplained constitutional or heritable disorder or syndrome), rapid sequence analysis *(RCIGM Rapid Whole Genome Sequencing, by Rady Children's Institute for Genomic Medicine (RCIGM); California)*
0101U	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA and array CGH, with MRNA analytics to resolve variants of unknown significance when indicated [15 genes (sequencing and deletion/duplication), EPCAM and GREM1 (deletion/duplication only)] *(ColoNext®, by Ambry Genetics; California)*
0102U	Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA and array CGH, with MRNA analytics to resolve variants of unknown significance when indicated [17 genes (sequencing and deletion/duplication)] *(BreastNext®, by Ambry Genetics; California)*

0103U	Hereditary ovarian cancer (eg, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA and array CGH, with MRNA analytics to resolve variants of unknown significance when indicated [24 genes (sequencing and deletion/duplication); EPCAM (deletion/duplication only)] *(OvaNext®, by Ambry Genetics; California)*
0105U	Nephrology (chronic kidney disease), multiplex electrochemiluminescent immunoassay (ECLIA) of tumor necrosis factor receptor 1A, receptor superfamily 2 (TNFR1, TNFR2), and kidney injury molecule-1 (KIM-1) combined with longitudinal clinical data, including APOL1 genotype if available, and plasma (isolated fresh or frozen), algorithm reported as probability score for rapid kidney function decline (RKFD) *(KidneyIntelX™, by RenalytixAI; New York)*
0108U	Gastroenterology (Barrett's esophagus), whole slide–digital imaging, including morphometric analysis, computer-assisted quantitative immunolabeling of 9 protein biomarkers (p16, AMACR, p53, CD68, COX-2, CD45RO, HIF1a, HER-2, K20) and morphology, formalinfixed paraffin-embedded tissue, algorithm reported as risk of progression to high-grade dysplasia or cancer *(TissueCypher® Barrett's Esophagus Assay, by Cernostics; Pennsylvania)*
0111U	Oncology (colon cancer), targeted KRAS (codons 12, 13, and 61) and NRAS (codons 12, 13, and 61) gene analysis utilizing formalinfixed paraffin-embedded tissue *(Praxis™ Extended RAS Panel, by Illumina; California)*
0118U	Transplantation medicine, quantification of donor-derived cell-free DNA using whole genome next-generation sequencing, plasma, reported as percentage of donor-derived cell-free DNA in the total cell-free DNA *(Viracor TRACTM; dd-cfDNA, by Viracore Eurofins; Missouri)*
0120U	Oncology (B-cell lymphoma classification), mRNA, gene expression profiling by fluorescent probe hybridization of 58 genes (45 content and 13 housekeeping genes), formalin-fixed paraffin-embedded tissue, algorithm reported as likelihood for primary mediastinal B-cell lymphoma (PMBCL) and diffuse large B-cell lymphoma (DLBCL) with cell of origin subtyping in the latter *(Lymph3Cx Lymphoma Molecular Subtyping Assay, by Mayo Clinic; Minnesota)*
0124U	Fetal congenital abnormalities, biochemical assays of 3 analytes (free beta-hCG, PAPP-A, AFP), time-resolved fluorescence immunoassay, maternal dried-blood spot, algorithm reported as risk scores for fetal trisomies 13/18 and 21
0129U	Hereditary breast cancer–related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), genomic sequence analysis and deletion/duplication analysis panel (ATM, BRCA1, BRCA2, CDH1, CHEK2, PALB2, PTEN, and TP53) *(BRCAplus, by Ambry Genetics; California)*
0153U	Oncology (breast), mRNA, gene expression profiling by next-generation sequencing of 101 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a triple negative breast cancer clinical subtype(s) with information on immune cell involvement *(Insight TNBCtype, by Insight Molecular Labs; Tennessee)*
0169U	NUDT15 (nudix hydrolase 15) and TPMT (thiopurine Smethyltransferase) (eg, drug metabolism) gene analysis, common variants *(NT [NUDT15 and TPMT] Genotyping Panel, by RPRD Diagnostics; Wisconsin)*

0171U	Targeted genomic sequence analysis panel, acute myeloid leukemia, myelodysplastic syndrome, and myeloproliferative neoplasms, DNA analysis, 23 genes, interrogation for sequence variants, rearrangements and minimal residual disease, reported as presence/absence *(MyMRD® NGS Panel, by Laboratory for Personalized Molecular Medicine; California)*
0172U	Oncology (solid tumor as indicated by the label), somatic mutation analysis of BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) and analysis of homologous recombination deficiency pathways, DNA, formalin-fixed paraffin-embedded tissue, algorithm quantifying tumor genomic instability score *(myChoice® CDx, by Myriad Genetic Laboratories; Utah)*
0173U	Psychiatry (ie, depression, anxiety), genomic analysis panel, includes variant analysis of 14 genes *(Psych HealthPGx Panel, by RPRD Diagnostics; Wisconsin)*
0174U	Oncology (solid tumor), mass spectrometric 30 protein targets, formalin-fixed paraffin-embedded tissue, prognostic and predictive algorithm reported as likely, unlikely, or uncertain benefit of 39 chemotherapy and targeted therapeutic oncology agents *(LC-MS/MS Targeted Proteomic Assay, by OncoOmicDx Laboratory, LDT; Maryland)*
0175U	Psychiatry (eg, depression, anxiety), genomic analysis panel, variant analysis of 15 genes *(Genomind® Professional PGx Express™ CORE, by Genomind, Inc.; Pennsylvania)*
0179U	Oncology (solid tumor as indicated by the label), somatic mutation analysis of BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) and analysis of homologous recombination deficiency pathways, DNA, formalin-fixed paraffin-embedded tissue, algorithm quantifying tumor genomic instability score *(Resolution ctDx Lung™, by Resolution Bioscience, Inc.; Washington)*
0203U	Autoimmune (inflammatory bowel disease), mRNA, gene expression profiling by quantitative RT-PCR, 17 genes (15 target and 2 reference genes), whole blood, reported as a continuous risk score and classification of inflammatory bowel disease aggressiveness *(PredictSURE IBD™ Test, by KSL Diagnostics; New York)*
0205U	Ophthalmology (age-related macular degeneration), analysis of 3 gene variants (2 CFH gene, 1 ARMS2 gene), using PCR and MALDI-TOF, buccal swab, reported as positive or negative for neovascular age-related macular-degeneration risk associated with zinc supplements *(Vita Risk, by Arctic Medical Laboratories; Michigan)*
0209U	Cytogenomic constitutional (genome-wide) analysis, interrogation of genomic regions for copy number, structural changes and areas of homozygosity for chromosomal abnormalities *(CNGnome, by PerkinElmer Genomics; Pennsylvania)*
0211U	Oncology (pan-tumor), DNA and RNA by next-generation sequencing, utilizing formalin-fixed paraffin-embedded tissue, interpretative report for single nucleotide variants, copy number alterations, tumor mutational burden, and microsatellite instability, with therapy association *(MI Cancer Seek™ NGS Analysis, by Caris Life Sciences; Arizona)*
0212U	Rare diseases (constitutional/heritable disorders), whole genome and mitochondrial DNA sequence analysis, including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants, proband *(Genomic Unity® Whole Genome Analysis, by Variantyx Inc.; Massachusetts)*

0213U	Rare diseases (constitutional/heritable disorders), whole genome and mitochondrial DNA sequence analysis, including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants, each comparator genome (eg, parent, sibling) *(Genomic Unity® Whole Genome Analysis – Comparator, by Variantyx Inc.; Massachusetts)*
0214U	Rare diseases (constitutional/heritable disorders), whole exome and mitochondrial DNA sequence analysis, including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants, proband *(Genomic Unity® Exome Plus Analysis – Proband, by Variantyx Inc.; Massachusetts)*
0215U	Rare diseases (constitutional/heritable disorders), whole exome and mitochondrial DNA sequence analysis, including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants, each comparator exome (eg, parent, sibling) *(Genomic Unity® Exome Plus Analysis – Comparator, by Variantyx Inc.; Massachusetts)*
0216U	Neurology (inherited ataxias), genomic DNA sequence analysis of 12 common genes including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants *(Genomic Unity® Ataxia Repeat Expansion and Sequence Analysis, by Variantyx Inc.; Massachusetts)*
0217U	Neurology (inherited ataxias), genomic DNA sequence analysis of 51 genes including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants *(Genomic Unity® Comprehensive Ataxia Repeat Expansion and Sequence Analysis, by Variantyx Inc.; Massachusetts)*
0218U	Neurology (muscular dystrophy), DMD gene sequence analysis, including small sequence changes, deletions, duplications, and variants in non-uniquely mappable regions, blood or saliva, identification and characterization of genetic variants *(Genomic Unity® DMD Analysis, by Variantyx Inc.; Massachusetts)*
0228U	Oncology (prostate), multianalyte molecular profile by photometric detection of macromolecules adsorbed on nanosponge array slides with machine learning, utilizing first morning voided urine, algorithm reported as likelihood of prostate cancer *(PanGIA Prostate, by Genetics Institute of America; Florida)*
0229U	BCAT1 (Branched chain amino acid transaminase 1) or IKZF1 (IKAROS family zinc finger 1) (eg, colorectal cancer) promoter methylation analysis *(Colvera, by Clinical Genomics Pathology Inc.; New Jersey)*
0230U	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation), full sequence analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, short tandem repeat (STR) expansions, mobile element insertions, and variants in non-uniquely mappable regions *(Genomic Unity® AR Analysis, by Variantyx Inc.; Massachusetts)*

0231U	CACNA1A (calcium voltage-gated channel subunit alpha 1A) (eg, spinocerebellar ataxia), full gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, short tandem repeat (STR) gene expansions, mobile element insertions, and variants in non-uniquely mappable regions *(Genomic Unity® CACNA1A Analysis, by Variantyx Inc.; Massachusetts)*
0232U	CSTB (cystatin B) (eg, progressive myoclonic epilepsy type 1A, Unverricht-Lundborg disease), full gene analysis, including small sequence changes in exonic and intronic regions, deletions,duplications, short tandem repeat (STR) expansions, mobile element insertions, and variants in non-uniquely mappable regions *(Genomic Unity® CSTB Analysis, by Variantyx Inc.; Massachusetts)*
0233U	FXN (frataxin) (eg, Friedreich ataxia), gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, short tandem repeat (STR) expansions, mobile element insertions, and variants in non-uniquely mappable regions *(Genomic Unity® FXN Analysis, by Variantyx Inc.; Massachusetts)*
0234U	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome), full gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions *(Genomic Unity® MECP2 Analysis, by Variantyx Inc.; Massachusetts)*
0235U	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome), full gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions *(Genomic Unity® PTEN Analysis, by Variantyx Inc.; Massachusetts)*
0236U	SMN1 (survival of motor neuron 1, telomeric) and SMN2 (survival of motor neuron 2, centromeric) (eg, spinal muscular atrophy) full gene analysis, including small sequence changes in exonic and intronic regions, duplications and deletions, and mobile element insertions *(Genomic Unity® SMN1/2 Analysis, by Variantyx Inc.; Massachusetts)*
0237U	Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia), genomic sequence analysis panel including ANK2, CASQ2, CAV3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, RYR2, and SCN5A, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions *(Genomic Unity® Cardiac Ion Channelopathies Analysis, by Variantyx Inc.; Massachusetts)*
0238U	Oncology (Lynch syndrome), genomic DNA sequence analysis of MLH1, MSH2, MSH6, PMS2, and EPCAM, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions *(Genomic Unity® Lynch Syndrome Analysis, by Variantyx Inc.; Massachusetts)*
0239U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free DNA, analysis of 311 or more genes, interrogation for sequence variants, including substitutions, insertions, deletions, select rearrangements, and copy number variations *(FoundationOne Liquid CDx, by Foundation Medicine, Inc.; Massachusetts)*
0242U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free circulating DNA analysis of 55-74 genes, interrogation for sequence variants, gene copy number amplifications, and gene rearrangements *(Guardant360® CDx, by Guardant Health, Inc.; Washington)*

0243U	Obstetrics (preeclampsia), biochemical assay of placental-growth factor, time-resolved fluorescence immunoassay, maternal serum, predictive algorithm reported as a risk score for preeclampsia *(PlGF Preeclampsia Screen, by PerkinElmer Genomics; Pennsylvania)*
0244U	Oncology (solid organ), DNA, comprehensive genomic profiling, 257 genes, interrogation for single-nucleotide variants, insertions/deletions, copy number alterations, gene rearrangements, tumor-mutational burden and microsatellite instability, utilizing formalin-fixed paraffin-embedded tumor tissue *(Oncotype MAP™ PanCancer Tissue Test, by Paradigm Diagnostics, Inc,; Arizona)*
0249U	Oncology (breast), semiquantitative analysis of 32 phosphoproteins and protein analytes, includes laser capture microdissection, with algorithmic analysis and interpretative report *(Theralink® Reverse Phase Protein Array (RPPA), by Theralink® Technologies, Inc.; Colorado)*
0250U	Oncology (solid organ neoplasm), targeted genomic sequence DNA analysis of 505 genes, interrogation for somatic alterations (SNVs [single nucleotide variant], small insertions and deletions, one amplification, and four translocations), microsatellite instability and tumor-mutation burden *(PGDx elio^{TM} tissue complete, by Personal Genome Diagnostics, Inc.; Maryland)*
0258U	Autoimmune (psoriasis), mRNA, next generation sequencing, gene expression profiling of 50-100 genes, skin-surface collection using adhesive patch, algorithm reported as likelihood of response to psoriasis biologic *(Mind.Px, by Mindera Corporation; California)*
0260U	Rare diseases (constitutional/heritable disorders), identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping *(Augusta Optical Genome Mapping, by Bionano Genomics Inc.; California)*
0264U	Rare diseases (constitutional/heritable disorders), identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping *(Praxis Optical Genome Mapping, by Praxis Genomics LLC; Georgia)*
0265U	Rare constitutional and other heritable disorders, whole genome and mitochondrial DNA sequence analysis, blood, frozen and formalin-fixed paraffin embedded (FFPE) tissue, saliva, buccal swabs or cell lines, identification of single nucleotide and copy number variants *(Praxis Whole Genome Sequencing, by Praxis Genomics LLC; Georgia)*
0266U	Unexplained constitutional or other heritable disorders or syndromes, tissue specific gene expression by whole transcriptome and next-generation sequencing, blood, formalin-fixed paraffin embedded (FFPE) tissue or fresh frozen tissue, reported as presence or absence of splicing or expression changes *(Praxis Transcriptome, by Praxis Genomics LLC; Georgia)*
0267U	Rare constitutional and other heritable disorders, identification of copy number variations, inversions, insertions, translocations, and other structural variants by optical genome mapping and whole genome sequencing *(Praxis Combined Whole Genome Sequencing and Optical Genome Mapping, by Praxis Genomics LLC; Georgia)*
0268U	Hematology (atypical hemolytic uremic syndrome [aHUS]), genomic sequence analysis of 15 genes, blood, buccal swab, or amniotic fluid *(Versiti™ aHUS Genetic Evaluation, by Versiti™ Diagnostic Laboratories; Wisconsin)*
0269U	Hematology (autosomal dominant congenital thrombocytopenia), genomic sequence analysis of 14 genes, blood, buccal swab, or amniotic fluid *(Versiti™ Autosomal Dominant Thrombocytopenia Panel, by Versiti™ Diagnostic Laboratories; Wisconsin)*

0271U	Hematology (congenital neutropenia), genomic sequence analysis of 23 genes, blood, buccal swab, or amniotic fluid *(Versiti™ Congenital Neutropenia Panel, by Versiti™ Diagnostic Laboratories; Wisconsin)*
0273U	Hematology (genetic hyperfibrinolysis, delayed bleeding), genomic sequence analysis of 8 genes (F13A1, F13B, FGA, FGB, FGG, SERPINA1, SERPINE1, SERPINF2, PLAU), blood, buccal swab, or amniotic fluid *(Versiti™ Fibrinolytic Disorder Panel, by Versiti™ Diagnostic Laboratories; Wisconsin)*
0274U	Hematology (genetic platelet disorders), genomic sequence analysis of 43 genes, blood, buccal swab, or amniotic fluid *(Versiti™ Comprehensive Platelet Panel, by Versiti™ Diagnostic Laboratories; Wisconsin)*
0276U	Hematology (inherited thrombocytopenia), genomic sequence analysis of 23 genes, blood, buccal swab, or amniotic fluid *(Versiti™ Inherited Thrombocytopenia Panel, by Versiti™ Diagnostic Laboratories; Wisconsin)*
0277U	Hematology (genetic platelet function disorder), genomic sequence analysis of 31 genes, blood, buccal swab, or amniotic fluid *(Versiti™ Platelet Function Disorder Panel, by Versiti™ Diagnostic Laboratories; Wisconsin)*
G9143	Warfarin responsiveness testing by genetic technique using any method, any number of specimen(s)

No Prior Authorization Required

Note: Inclusion of a code in this section does not guarantee reimbursement or coverage. The following codes do not require routine review for medical necessity, but they may be subject to audit or benefit denial.

81170	ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase) (eg, acquired imatinib tyrosine kinase inhibitor resistance), gene analysis, variants in the kinase domain
81206	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; major breakpoint, qualitative or quantitative
81207	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; minor breakpoint, qualitative or quantitative
81208	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; other breakpoint, qualitative or quantitative
81210	BRAF(v-raf murine sarcoma viral oncogene homolog B1) (e.g. Colon Cancer) gene analysis, V600E variant
81235	EGFR (Epidermal growth factor receptor)(EG, non-small cell lung cancer) gene analysis, common variants (EG, exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)
81245	FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia), gene analysis; internal tandem duplication (ITD) variants (ie, exons 14, 15)
81246	FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia), gene analysis; tyrosine kinase domain (TKD) variants (eg, D835, I836)
81261	IGH@ (Immunoglobulin heavy chain locus) (eg, leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); amplified methodology (eg, polymerase chain reaction)

No Prior Authorization Required Note: Inclusion of a code in this section does not guarantee reimbursement or coverage. The following codes do not require routine review for medical necessity, but they may be subject to audit or benefit denial.	
81262	IGH@ (Immunoglobulin heavy chain locus) (eg, leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); direct probe methodology (eg, Southern blot)
81263	IGH@ (Immunoglobulin heavy chain locus) (eg, leukemia and lymphoma, B-cell), variable region somatic mutation analysis
81264	IGK@ (Immunoglobulin kappa light chain locus) (eg, leukemia and lymphoma, B-cell), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)
81272	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (eg, gastrointestinal stromal tumor [GIST], acute myeloid leukemia, melanoma), gene analysis, targeted sequence analysis (eg, exons 8, 11, 13, 17, 18)
81273	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (eg, mastocytosis), gene analysis, D816 variant(s)
81278	IGH@/BCL2 (t(14;18)) (eg, follicular lymphoma) translocation analysis, major breakpoint region (MBR) and minor cluster region (mcr) breakpoints, qualitative or quantitative
81301	Microsatellite instability analysis (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) of markers for mismatch repair deficiency (e.g., BAT25, BAT26), includes comparison of neoplastic and normal tissue, if performed
81340	TRB@ (T cell antigen receptor, beta) (eg, leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using amplification methodology (eg, polymerase chain reaction)
81341	TRB@ (T cell antigen receptor, beta) (eg, leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using direct probe methodology (eg, Southern blot)
81342	TRG@ (T cell antigen receptor, gamma) (eg, leukemia and lymphoma), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)
81490	Autoimmune (rheumatoid arthritis), analysis of 12 biomarkers using immunoassays, utilizing serum, prognostic algorithm reported as a disease activity score
88235	Tissue culture for non-neoplastic disorders; amniotic fluid or chorionic villus cells
88261	Chromosome analysis; count 5 cells, l karyotype, with banding
88262	Chromosome analysis; count 15-20 cells, 2 karyotypes, with banding
88263	Chromosome analysis; count 45 cells for mosaicism, 2 Karyotypes, with banding
88264	Chromosome analysis; analyze 20-25 cells
88267	Chromosome analysis, amniotic fluid or chorionic villus, count 15 cells, 1 karyotype, with banding
88269	Chromosome analysis, in situ for amniotic fluid cells, count cells from 6-12 colonies, 1 karyotype, with banding
88271	Molecular cytogenetics; DNA probe, each (eg, FISH)
88272	Molecular cytogenetics; chromosomal in situ hybridization, analyze 3-5 cells (eg, for derivatives and markers)

No Prior Authorization Required

Note: Inclusion of a code in this section does not guarantee reimbursement or coverage. The following codes do not require routine review for medical necessity, but they may be subject to audit or benefit denial.

88273	Molecular cytogenetics; chromosomal in situ hybridization, analyze 10-30 cells (eg, for microdeletions)
88274	Molecular cytogenetics; interphase in situ hybridization, analyze 25-99 cells
88275	Molecular cytogenetics; interphase in situ hybridization, analyze 100-300 cells
88280	Chromosome analysis; additional karyotypes, each study
88283	Chromosome analysis; additional specialized banding technique (eg, NOR, C-banding)
88285	Chromosome analysis; additional cells counted, each study
88289	Chromosome analysis; additional high resolution study
88291	Cytogenetics and molecular cytogenetics, interpretation and report

Not Covered

All codes in this section are **non-covered** by Medicare or Commercial Plan policy.

0060U	Twin zygosity, genomic targeted sequence analysis of chromosome 2, using circulating cell-free fetal DNA in maternal blood *(Panorama® Twin Zygosity test, by Natera, Inc.; California)*
0130U	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis), targeted mRNA sequence analysis panel (APC, CDH1, CHEK2, MLH1, MSH2, MSH6, MUTYH, PMS2, PTEN, and TP53) (List separately in addition to code for primary procedure) (Use 0130U in conjunction with 81435, 0101U) *(RNAinsight™ for ColoNext®, by Ambry Genetics; California)*
0131U	Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), targeted mRNA sequence analysis panel (13 genes) (List separately in addition to code for primary procedure) *(RNAinsight™ for BreastNext®, by Ambry Genetics; California)*
0132U	Hereditary ovarian cancer–related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer), targeted mRNA sequence analysis panel (17 genes) (List separately in addition to code for primary procedure) (Use 0132U in conjunction with 81162, 81432, 0103U) *(RNAinsight™ for OvaNext®, by Ambry Genetics; California)*
0133U	Hereditary prostate cancer–related disorders, targeted mRNA sequence analysis panel (11 genes) (List separately in addition to code for primary procedure) (Use 0133U in conjunction with 81162) *(RNAinsight™ for ProstateNext®, by Ambry Genetics; California)*
0134U	Hereditary pan cancer (eg, hereditary breast and ovarian cancer, hereditary endometrial cancer, hereditary colorectal cancer), targeted mRNA sequence analysis panel (18 genes) (List separately in addition to code for primary procedure) *(RNAinsight™ for CancerNext®, by Ambry Genetics; California)*
0135U	Hereditary gynecological cancer (eg, hereditary breast and ovarian cancer, hereditary endometrial cancer, hereditary colorectal cancer), targeted mRNA sequence analysis panel (12 genes) (List separately in addition to code for primary procedure) (Use 0135U in conjunction with 81162) *(RNAinsight™ for GynPlus®, by Ambry Genetics; California)*

Not Covered All codes in this section are **non-covered** by Medicare or Commercial Plan policy.	
0138U	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) mRNA sequence analysis (List separately in addition to code for primary procedure) (Use 0138U in conjunction with 81162) *(RNAinsight™ for BRCA1/2, by Ambry Genetics; California)*
0157U	APC (APC regulator of WNT signaling pathway) (eg, familial adenomatosis polyposis [FAP]) mRNA sequence analysis (List separately in addition to code for primary procedure) *(CustomNext + RNA: APC, by Ambry Genetics; California)*
0158U	MLH1 (mutL homolog 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) *(CustomNext + RNA: MLH1, by Ambry Genetics; California)*
0159U	MSH2 (mutS homolog 2) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) *(CustomNext + RNA: MSH2, by Ambry Genetics; California)*
0160U	MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) *(CustomNext + RNA: MSH6, by Ambry Genetics; California)*
0161U	PMS2 (PMS1 homolog 2, mismatch repair system component) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) *(CustomNext + RNA: PMS2, by Ambry Genetics; California)*
0162U	Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2) (List separately in addition to code for primary procedure) *(CustomNext + RNA: Lynch (MLH1, MSH2, MSH6, PMS2), by Ambry Genetics; California)*
0163U	Oncology (colorectal) screening, biochemical enzyme-linked immunosorbent assay (ELISA) of 3 plasma or serum proteins (teratocarcinoma derived growth factor-1 [TDGF-1, Cripto-1], carcinoembryonic antigen [CEA], extracellular matrix protein [ECM]), with demographic data (age, gender, CRC-screening compliance) using a proprietary algorithm and reported as likelihood of CRC or advanced adenomas *(BeScreened™-CRC, by Beacon Biomedical Inc.; Arizona)*
0243U	Obstetrics (preeclampsia), biochemical assay of placental-growth factor, time-resolved fluorescence immunoassay, maternal serum, predictive algorithm reported as a risk score for preeclampsia *(PlGF Preeclampsia Screen, by PerkinElmer Genomics; Pennsylvania)*
0247U	Obstetrics (preterm birth), insulin-like growth factor–binding protein 4 (IBP4), sex hormone–binding globulin (SHBG), quantitative measurement by LC-MS/MS, utilizing maternal serum, combined with clinical data, reported as predictive-risk stratification for spontaneous preterm birth *(PreTRM®, by Sera Prognostics; Utah)*
0252U	Fetal aneuploidy short tandem–repeat comparative analysis, fetal DNA from products of conception, reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplications, mosaicism, and segmental aneuploidy *(POC (Products of Conception), by Igenomix; Florida)*
0253U	Reproductive medicine (endometrial receptivity analysis), RNA gene expression profile, 238 genes by next-generation sequencing, endometrial tissue, predictive algorithm reported as

Not Covered

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	endometrial window of implantation (eg, pre-receptive, receptive, post-receptive) *(ERA® (Endometrial Receptivity Analysis), by Igenomix; Florida)*
0254U	Reproductive medicine (preimplantation genetic assessment), analysis of 24 chromosomes using embryonic DNA genomic sequence analysis for aneuploidy, and a mitochondrial DNA score in euploid embryos, results reported as normal (euploidy), monosomy, trisomy, or partial deletion/duplication, mosaicism, and segmental aneuploidy, per embryo tested *(SMART PGT-A (Preimplantation Genetic Testing - Aneuploidy), by Igenomix; Florida)*
0278U	Hematology (genetic thrombosis), genomic sequence analysis of 12 genes, blood, buccal swab, or amniotic fluid *(Versiti™ Thrombosis Panel, by Versiti™ Diagnostic Laboratories; Wisconsin)*
0286U	CEP72 (centrosomal protein, 72-KDa), NUDT15 (nudix hydrolase 15) and TPMT (thiopurine S-methyltransferase) (eg, drug metabolism) gene analysis, common variants *(CNT (CEP72, TPMT and NUDT15) genotyping panel, by RPRD Diagnostics; Wisconsin)*
0289U	Neurology (Alzheimer disease), mRNA, gene expression profiling by RNA sequencing of 24 genes, whole blood, algorithm reported as predictive risk score *(MindX Blood Test™ - Memory/Alzheimer's, by MindX Sciences™ Inc.; Indiana)*
0290U	Pain management, mRNA, gene expression profiling by RNA sequencing of 36 genes, whole blood, algorithm reported as predictive risk score *(MindX Blood Test™ - Pain, by MindX Sciences™ Inc.; Indiana)*
0291U	Psychiatry (mood disorders), mRNA, gene expression profiling by RNA sequencing of 144 genes, whole blood, algorithm reported as predictive risk score *(MindX Blood Test™ - Mood, by MindX Sciences™ Inc.; Indiana)*
0292U	Psychiatry (stress disorders), mRNA, gene expression profiling by RNA sequencing of 72 genes, whole blood, algorithm reported as predictive risk score *(MindX Blood Test™ - Stress, by MindX Sciences™ Inc.; Indiana)*
0293U	Psychiatry (suicidal ideation), mRNA, gene expression profiling by RNA sequencing of 54 genes, whole blood, algorithm reported as predictive risk score *(MindX Blood Test™ - Suicidality, by MindX Sciences™ Inc.; Indiana)*
0294U	Longevity and mortality risk, mRNA, gene expression profiling by RNA sequencing of 18 genes, whole blood, algorithm reported as predictive risk score *(MindX Blood Test™ - Longevity, by MindX Sciences™ Inc.; Indiana)*
0296U	Oncology (oral and/or oropharyngeal cancer), gene expression profiling by RNA sequencing at least 20 molecular features (eg, human and/or microbial mRNA), saliva, algorithm reported as positive or negative for signature associated with malignancy *(mRNA CancerDetect™, by Viome Life Sciences, Inc.; Washington)*
0297U	Oncology (pan tumor), whole genome sequencing of paired malignant and normal DNA specimens, fresh or formalinfixed paraffin-embedded (FFPE) tissue, blood or bone marrow, comparative sequence analyses and variant identification *(Praxis Somatic Whole Genome Sequencing, by Praxis Genomics, LLC.; Georgia)*
0298U	Oncology (pan tumor), whole transcriptome sequencing of paired malignant and normal RNA specimens, fresh or formalin-fixed paraffin-embedded (FFPE) tissue, blood or bone

Not Covered

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	marrow, comparative sequence analyses and expression level and chimeric transcript identification *(Praxis Somatic Transcriptome, by Praxis Genomics, LLC.; Georgia)*
0299U	Oncology (pan tumor), whole genome optical genome mapping of paired malignant and normal DNA specimens, fresh frozen tissue, blood, or bone marrow, comparative structural variant identification *(Praxis Somatic Optical Genome Mapping, by Praxis Genomics, LLC.; Georgia)*
0300U	Oncology (pan tumor), whole genome sequencing and optical genome mapping of paired malignant and normal DNA specimens, fresh tissue, blood, or bone marrow, comparative sequence analyses and variant identification *(Praxis Somatic Combined Whole Genome Sequencing and Optical Genome Mapping, by Praxis Genomics, LLC.; Georgia)*
0313U	Oncology (pancreas), DNA and mRNA next-generation sequencing analysis of 74 genes and analysis of CEA (CEACAM5) gene expression, pancreatic cyst fluid, algorithm reported as a categorical result (ie, negative, low probability of neoplasia or positive, high probability of neoplasia)
0315U	Oncology (cutaneous squamous cell carcinoma), mRNA gene expression profiling by RT-PCR of 40 genes (34 content and 6 housekeeping), utilizing formalin-fixed paraffin-embedded (FFPE) tissue, algorithm reported as a categorical risk result (ie, Class 1, Class 2A, Class 2B)
0318U	Pediatrics (congenital epigenetic disorders), whole genome methylation analysis by microarray for 50 or more genes, blood
0319U	Nephrology (renal transplant), RNA expression by select transcriptome sequencing, using pretransplant peripheral blood, algorithm reported as a risk score for early acute rejection
0320U	Nephrology (renal transplant), RNA expression by select transcriptome sequencing, using posttransplant peripheral blood, algorithm reported as a risk score for acute cellular rejection
0321U	Infectious agent detection by nucleic acid (DNA or RNA), genitourinary pathogens, identification of 20 bacterial and fungal organisms and identification of 16 associated antibiotic-resistance genes, multiplex amplified probe technique
81200	ASPA (aspartoacylase) (eg, Canavan disease) gene analysis, common variants (eg, E285A, Y231X)
81205	BCKDHB (branched-chain keto acid dehyrogenase E1, beta polypeptide) (e.g., Maple syrup urine disease) gene analysis, common variants (e.g., R183P, G278s, E422X)
81209	BLM (Bloom syndrome, RecQ helicase-like) (e.g., Bloom syndrome) gene analysis 2281 del6ins7 variant
81228	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number variants, comparative genomic hybridization [CGH] microarray analysis
81229	Cytogenomic (genome-wide) analysis for constitutional chromosomal abnormalities; interrogation of genomic regions for copy number and single nucleotide polymorphism variants, comparative genomic hybridization [CGH] microarray analysis
81240	F2 (prothrombin, coagulation factor II) (eg, hereditary hypercoagulability) gene analysis, 20210G>A variant
81241	F5 (coagulation factor V) (eg, hereditary hypercoagulability) gene analysis, Leiden variant

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81242	FANCC (Fanconi anemia, complementation group C) (e.g., Fanconi Anemia, type C) gene analysis, common variant (e.g., IVS4=4A>T)
81243	FMR1 (Fragile X mental retardation 1) (e.g., fragile x mental retardation) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles
81244	FMR1 (Fragile X mental retardation 1) (e.g., fragile X mental retardation) gene analysis; characterization of alleles (e.g., expanded size and methylation status)
81251	GBA (glucosidase, bets, acid) (e.g., Gaucher disease) gene analysis, common variants (e.g., N370S, 84GG, L444P, IVS2=1G>A)
81252	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; full gene sequence
81253	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; known familial variants
81254	GJB6 (gap junction protein, beta 6, 30kDa, connexin 30) (eg, nonsyndromic hearing loss) gene analysis, common variants (eg, 309kb [del(GJB6-D13S1830)] and 232kb [del(GJB6-D13S1854)])
81255	HEXA (hexosaminidase A [alpha polypeptide]) (e.g. Tay-Sachs disease) gene analysis common variants (e.g., 1278insTATC, 1421+1G>C, G269S)
81260	IKBKAP (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein)(e.g. familial dysautonomia) gene analysis, common variants
81290	MCOLN1 (mucolipin 1) (e.g., Mucolipidosis, Type IV) gene analysis, common variants (e.g. IVS3-2A>G, del6.4b)
81291	MTHFR (5,10-methylenetetrahydrofolate reductase) (e.g., hereditary hypercoagulability) gene analysis, common variants (e.g., 677T, 1298C)
81302	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; full sequence analysis
81303	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; known familial variant
81304	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; duplication/deletion variants 6 or exon 6), qualitative or quantitative
81330	SMPD1 (sphingomyelin phosphodiesterase 1, acid lysomal) (e.g., Niemann-Pick disease Type A) gene analysis, common variants (e.g., R496L, L302P, fsP330)
81361	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); common variant(s) (eg, HbS, HbC, HbE)
81362	HBB (hemoglobin, subunit beta) (eg, sickle cell anemia, beta thalassemia, hemoglobinopathy); known familial variant(s)
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
81412	Ashkenazi Jewish associated disorders (eg, Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group C, Gaucher disease, Tay-Sachs

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	disease), genomic sequence analysis panel, must include sequencing of at least 9 genes, including ASPA, BLM, CFTR, FANCC, GBA, HEXA, IKBKAP, MCOLN1, and SMPD1
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
S3844	DNA analysis of the connexin 26 gene (GJB2) for susceptibility to congenital, profound deafness
S3870	Comparative genomic hybridization (cgh) microarray testing for developmental delay, autism spectrum disorder and/or intellectual disability
Unlisted Codes All unlisted codes will be reviewed for medical necessity, correct coding, and pricing. If an unlisted code is billed related to services addressed in this policy then **prior-authorization is required.**	
81479	Unlisted Molecular Pathology
81599	Unlisted multianalyte assay with algorithmic analysis
84999	Unlisted chemistry procedure
88299	Unlisted cytogenetic study
89398	Unlisted reproductive medicine laboratory procedure

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature. The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

MEDICAL POLICY CROSS REFERENCES

- Genetic Testing: CADASIL Disease, MP# 238
- Genetic Testing: Cytochrome P450 and VKORC1 Polymorphisms (Medicare Only), MP314
- Genetic Testing: Diagnostic Evaluation of Interstitial Lung Disease (Medicare Only), MP177
- Genetic Testing: Gene Expression Profile Testing for Breast Cancer (Medicare Only), MP48
- Genetic Testing: Gene Expression Profile Testing for Melanoma (Medicare Only), MP253
- Genetic Testing: Hereditary Breast and Ovarian Cancer (Medicare Only), MP144
- Genetic Testing: Inherited Susceptibility to Colorectal Cancer (Medicare Only), MP117
- Genetic Testing: *JAK2*, *CALR*, and *MPL* (Medicare Only), MP71
- Genetic Testing: Non-Covered Genetic Panel Tests (All Lines of Business except Medicare), MP213
- Genetic Testing: Pharmacogenetic Testing (Medicare Only), MP217
- Genetic Testing: Thyroid Nodules (Medicare Only), MP40
- PHA Medicare Medical Policy Development and Application, MP50

REFERENCES

1. *Medicare Claims Processing Manual, Chapter 16 - Laboratory Services, §120.1 - Negotiated Rulemaking Implementation* (See section titled, "Clarification of the Use of the Term “Screening” or “Screen""); Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/clm104c16.pdf [Cited 09/02/2021]
2. Medicare Coverage Determination Process; Available at: https://www.cms.gov/medicare/coverage/determinationprocess [Cited 09/02/2021]
3. Medicare Managed Care Manual, Ch. 4 - Benefits and Beneficiary Protections, §10.2 - Basic Rule; Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/mc86c04.pdf [Cited 09/02/2021]
4. Title XVIII of the Social Security Act, §1862(a)(1)(A); Available at: https://www.ssa.gov/OP_Home/ssact/title18/1862.htm [Cited 09/02/2021]
5. Medicare Benefit Policy Manual, Chapter 16 - General Exclusions From Coverage, §20 - Services Not Reasonable and Necessary; Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c16.pdf [Cited 09/02/2021]
6. Medicare Claims Processing Manual, Chapter 23 - Fee Schedule Administration and Coding Requirements, §30 - Services Paid Under the Medicare Physician’s Fee Schedule, Subsection A;

Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/clm104c23.pdf [Cited 09/02/2021]
7. 42 CFR §410.32(a); Available at: https://www.govinfo.gov/content/pkg/CFR-2011-title42-vol2/pdf/CFR-2011-title42-vol2-sec410-32.pdf [Cited 09/02/2021]
8. Medicare Benefit Policy Manual, Ch. 15 – Covered Medical and Other Health Services, §80.1 - Clinical Laboratory Services; Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf [Cited 09/02/2021]
9. Federal Register / Vol. 66, No. 226 / Friday, November 23, 2001; Available at: https://www.cms.gov/Medicare/Coverage/CoverageGenInfo/downloads/lab2.pdf [Cited 09/02/2021]
10. Medicare Claims Processing Manual, Chapter 16 - Laboratory Services, §50.5 - Jurisdiction of Laboratory Claims; Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/clm104C16.pdf [Cited 09/02/2021]
11. Medicare Program Integrity Manual, Chapter 13 – Local Coverage Determinations, §13.5.4 - Reasonable and Necessary Provision in an LCD; Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/pim83c13.pdf [Cited 09/02/2021]
12. Palmetto GBA MolDX Manual; Available at: https://www.palmettogba.com/Palmetto/moldx.Nsf/files/MolDX_Manual.pdf/$File/MolDX_Manual.pdf?Open& [Cited 09/29/2021]
13. Healthcare Fraud Prevention Partnership (HFPP) White Paper for Genetic Testing Fraud, Waste, and Abuse; Available at: https://www.cms.gov/hfpp/hfpp-white-papers [Cited 09/29/2021]
14. Noridian web page for Molecular Diagnostic Services (MolDX); Last Updated: 9/23/2021; Available at: https://med.noridianmedicare.com/web/jfb/policies/moldx
15. Medicare Managed Care Manual, Ch. 4 - Benefits and Beneficiary Protections, §90.4.1 - MACS with Exclusive Jurisdiction over a Medicare Item or Service; Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/mc86c04.pdf
16. Medicare Claims Processing Manual, Chapter 1 - General Billing Requirements, §10.1.5.4 - Independent Laboratories; Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/clm104c01.pdf
17. Noridian LCA for *Billing and Coding: MolDX: Targeted and Comprehensive Genomic Profile Next-Generation Sequencing Testing in Cancer* (A56518)
18. Medicare Claims Processing Manual, Ch. 1 - General Billing Requirements, §10.1.5.4.1 - Cases Involving Referral Laboratory Services; Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/clm104c01.pdf
19. Medicare Claims Processing Manual, Chapter 16 - Laboratory Services, §40.1 - Laboratories Billing for Referred Tests; Available at: https://www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/clm104c16.pdf
20. Medicare Claims Processing Manual, Chapter 16 - Laboratory Services, §50.5.1 - Jurisdiction Of Referral Laboratory Services; Available at: https://www.cms.gov/regulations-and-guidance/guidance/manuals/downloads/clm104c16.pdf