Clinical Policy: Genetic Testing for Diagnosis and Treatment

Reference Number: WNC.CP.293 **Coding Implications**
Last Review Date: Revision Log

See Important Reminders at the end of this policy for important regulatory and legal information.

Note: When state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Description

Genetic testing is used to identify changes or abnormalities in chromosomes, genes, or proteins to confirm or rule out suspected genetic conditions. Testing samples include blood, amniotic fluid, or bodily tissues. A genetic test involves an analysis of human chromosomes, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), or gene products to establish a diagnosis of a genetic condition. In general, three categories of genetic testing—cytogenetic, biochemical, and molecular—are available to detect abnormalities in chromosome structure, protein function, and DNA sequence, respectively.

Policy/Criteria[1]

I. WellCare of North Carolina® **shall cover** Genetic Testing for Diagnosis and Treatment, when member meets **ALL** of the following specific criteria:

- **A.** Displays clinical features or is experiencing current signs and symptoms of a genetic condition; or there is documented reasonable expectation that the member is at high-risk based on family history, personal history, or ethnicity;
- **B.** The test yields results that can be used to develop a clinically useful approach or course of treatment, or to cease unnecessary treatments;
- **C.** The results of the test allow providers to treat current symptoms affecting the member's health, or manage the treatable progress of an established disease or alter recommended screening or monitoring;
- **D.** The ordering licensed provider shall obtain informed consent (indicating understanding of the testing procedure, the benefits and limitations of the test, and the possible consequences of the test results) from the member, parent, legal guardian, or authorized representative, prior to the genetic test;
- **E.** A clinically valid test, based on published peer-reviewed medical literature, is available for the suspected diagnosis; **AND**
- **F.** The test is proven to be scientifically valid for the identification of a specific genetically linked disease or clinical condition.

II. Specific Criteria Covered

- **A. Cystic Fibrosis (CF) and Spinal Muscular Atrophy (SMA)**

WellCare of North Carolina® **shall cover** genetic testing for diagnosis and treatment of cystic fibrosis (CF) and spinal muscular atrophy (SMA) when the criteria in **Criteria I., and ALL** of the following criteria are met:

1. The member has signs or symptoms of CF or SMA;
2. When the symptomatic member has a known familial variant, the test that is ordered for that specific variant;
3. If no mutation is found when testing for common variants and the member is symptomatic, full gene sequencing can be ordered; **AND**
4. After completing the full gene sequencing, if no mutation is found, testing may be done for duplication and deletion variants.

B. BRCA-Related Cancers

WellCare of North Carolina® **shall cover** genetic testing for diagnosis and treatment of BRCA-related cancers when the criteria in **Criteria I., and ONE OR MORE** of the following criteria are met:

1. The member has a personal history of breast cancer with one or more of the following:
    a. Diagnosed age 45 years and younger;
    b. Diagnosed age 50 years and younger with **one or more** of the following:
        1) A previous primary breast cancer diagnosis;
        2) One or more close blood relatives with breast cancer at any age;
        3) One or more relatives with pancreatic cancer;
        4) One or more relatives with prostate cancer; **OR**
        5) An unknown or limited family history;
    c. Diagnosed age less than or equal to 60 years with triple negative breast cancer;
    d. Diagnosed at any age with **one or more** of the following:
        1) Two (2) or more close blood relatives with breast cancer, pancreatic cancer or, prostate cancer at any age;
        2) One (1) or more close blood relative with breast cancer at age 50 years old or older;
        3) One (1) or more close blood relatives with ovarian carcinoma;
        4) Close male blood relative with breast cancer; **OR**
        5) Ethnicity associated with higher mutation frequency such as Ashkenazi Jewish;
2. The member has a personal history of epithelial ovarian, fallopian tube or primary peritoneal cancer;
3. The member has a personal history of male breast cancer;
4. The member has a personal history of prostate cancer at any age and one of the following:
    a. One (1) or more close blood relatives with ovarian cancer at any age or breast cancer at age 50 years old and younger; **OR**
    b. Two (2) relatives with breast, ovarian, or prostate cancer at any age;
5. The member has a personal history of metastatic prostate cancer (radiographic evidence);
6. The member has a personal history of pancreatic cancer at any age and **ONE OF** the following:

a. One (1) or more close blood relatives with ovarian carcinoma at any age or breast cancer at fifty years old and older;
b. Two (2) relatives with breast, ovarian, or prostate cancer at any age; **OR**
c. Ashkenazi Jewish heritage;

7. The member has a personal history of BRCA 1 and 2 mutation detected by tumor profiling on any tumor type in the absence of germline mutation analysis;
8. The member has a family history of known BRCA1 or BRCA2 gene mutation with **one** of the following:
   a. First or second-degree blood relative meeting any of the criteria under **Criteria III**.; **OR**
   b. Third-degree relative with breast cancer or ovarian carcinoma and who has two (2) or more close blood relatives with breast cancer (at least one (1) before 50 years old) or ovarian carcinoma;
9. The member has a family history of two (2) or more primary breast cancers (asynchronous, synchronous, bilateral, or metacentric) in a single-family member;
10. The member has a family history of two (2) or more relatives on the same side of the family with breast, prostate, or pancreatic cancer;
11. The member has a family history of epithelial ovarian, fallopian tube or primary peritoneal cancer;
12. The member has a family history of male breast cancer;
13. The member has a family history of known mutation carriers.

C. Lynch Syndrome Related Cancers

WellCare of North Carolina® **shall cover** genetic testing for diagnosis and treatment of Lynch syndrome related cancers when the criteria in **Criteria I., and ANY ONE** of the following criteria are met:

1. For a member with a diagnosis of any Lynch Syndrome (LS) related cancer, multi-gene panel testing is covered when **one** of the following conditions is met:
   a. Has a past personal medical history indicating a tumor with MMR deficiency, confirmed through polymerase chain reaction (PCR), next generation sequencing (NGS), immunohistochemistry (IHC) testing;
   b. Received their diagnosis before reaching 50 years of age;
   c. Experiences another LS-related cancer either simultaneously or at a different time, regardless of age;
   d. Has at least one (1) close relative (first or second-degree) diagnosed with LS-related cancer before reaching the age of 50 years; **OR**
   e. Has a minimum of two (2) close relatives (first or second-degree) diagnosed with LS-related cancers, regardless of their age.
2. For a member aged 18 years and older with a documented family history of LS-related cancer, multi-gene panel testing is covered when the specific family mutation is unknown (due to unavailability of family member testing or testing results) and **ONE** of the following conditions is met:
   a. Has at least one (1) first-degree relative diagnosed with LS-related cancer before the age of 50 years;
   b. Has at least one (1) first-degree relative affected by LS-related cancer and concurrently experiences another LS-related cancer or develops it at a different time;

c. Has a minimum of two (2) first or second-degree relatives with LS-related cancer, and at least one of these relatives was diagnosed before the age of 50 years;
d. Has three (3) or more first or second-degree relatives with LS-related cancers, regardless of the age at diagnosis; **OR**
e. Has a risk of having a pathogenic MMR gene variant is at least five (5) percent as determined by predictive models.

3. For members aged 18 years and older in a family with a harmful familial Lynch Syndrome (LS) gene mutation, the following testing is covered:
   a. Testing that is restricted to the known familial mutation; **OR**
   b. Full-scale genetic testing, which includes multi-gene panel testing, when the exact familial mutation remains unidentified.

D. Gene Mutation Testing for Cancer Susceptibility

WellCare of North Carolina® **shall cover** gene mutation testing for cancer susceptibility when the criteria in **Criteria I., and ALL** of the following criteria are met:

1. The genetic condition is linked to a potentially substantial risk of developing cancer;
2. Biochemical or other testing cannot identify the risk of the significant cancer linked to the genetic disorder;
3. Scientific literature has established a specific mutation, or set of mutations, as a dependable indicator of the risk of developing malignancy; **AND**
4. The outcomes of the genetic test may influence the medical approach (such as surveillance, lifestyle) for the member receiving the test.

E. Duchenne Muscular Dystrophy (DMD) and Becker Muscular Dystrophy (BMD)

WellCare of North Carolina® **shall cover** genetic testing for Diagnosis and treatment for Duchenne Muscular Dystrophy (DMD) and Becker Muscular Dystrophy (BMD)when the criteria in **Criteria I., and ALL** of the following criteria are met:

1. The member shows signs of DMD or BMD, such as gradually developing symmetric muscular weakness (with proximal muscles affected more than distal ones) and, in many cases, enlarged calf muscles. For those with DMD, reliance on a wheelchair usually occurs before the age of 13, while for those with BMD, it typically happens after the age of 16.; **AND**
2. The member's serum creatine kinase (CK) level is higher than normal.

F. Red Blood Cell Antigen Genotyping

WellCare of North Carolina® **shall cover** red cell genotyping for a member who meets **ANY ONE** of the following conditions:

1. Diagnosed with sickle cell disease, thalassemia syndromes, hemoglobinopathies, or other medical conditions necessitating frequent blood transfusions;
2. Experiencing post-transfusion hemolysis without detectable antibodies or identifiable alternate causes;
3. Has undergone a blood transfusion within the past three (3) months and expect to undergo further blood transfusions;
4. Has autoimmune hemolytic anemia;
5. Has received multiple blood transfusions or who test positive for direct antiglobulin test (DAT+);

6. Diagnosed with non-transfusion dependent thalassemia (NTDT) before receiving a transfusion in a pregnant member;
7. Assist in the management of hemolytic disease of the fetus and newborn (HDFN); **OR**
8. Reconcile inconsistent serological antibody findings.

NOTE: *Within Criteria I and II , it is essential to emphasize that any mention of prostate cancer pertains exclusively to cases with a Gleason score of 7 or higher (refer to Background, section J.).*

III. Additional Criteria Covered

In addition to the specific criteria covered in Criteria I, of this policy, WellCare of North Carolina® **shall cover** Genetic Testing for Diagnosis and Treatment when **ALL** of the following additional criteria are met:

A. A certified genetic counselor or ordering (licensed) provider shall evaluate and counsel the member pre- and post-test. Refer to Criteria IX and Background I;
B. The test must not be duplicative of another performed test; **AND**
C. The test must be performed by a certified Clinical Laboratories Improvement Amendment (CLIA) laboratory.

IV. WellCare of North Carolina® **shall NOT cover** Genetic Testing for Diagnosis and Treatment for **ALL** of the following:

A. The member does not meet the criteria listed in Criteria I or II;
B. The same test is being repeated after a negative result;
C. The test is repeated when limited to once in a lifetime testing;
D. The test is for member's family member(s);
E. A cell-free DNA based screening is performed in twin pregnancy in the setting of fetal demise, vanishing twin, or one (1) or more anomaly detected in one (1) or both twins; **OR**
F. The test is used to determine ancestry.

V. BRCA-Related Cancers

WellCare of North Carolina® **shall NOT cover** genetic testing for diagnosis and treatment for BRCA-related cancers for **ANY** of the following conditions:

A. The member does not meet the criteria in **CRITERIA II.B**.
B. Repeat testing for BRCA1 or BRCA2 before using Lynparza; **OR**
C. Testing of a member who is under 18 years of age.

VI. Red Blood Cell Antigen Genotyping

WellCare of North Carolina® **shall NOT cover** red cell genotyping for **ANY** of the following conditions:

A. For members who have undergone allogeneic hematopoietic stem cell transplants;
B. For diagnosing sickle cell disease;
C. For routine pre-transfusion testing; **OR**
D. For routine solid organ transplant screening.

VII. Testing Limitations

Refer to CPT Code Boxes below for testing limitations for CPT codes covered in this policy.

VIII. Documentation Requirements

When the provider requests additional units for the CPT Codes found in CPT Code Box below, then, in addition to the prior approval requirements found in Criteria I and II then the provider shall submit all of the following supporting documentation to justify the request:

- **A.** The reason for the test(s);
- **B.** Previous related lab results;
- **C.** How the test results contribute to improved health outcomes; **AND**
- **D.** How the test results alter the member's treatment and management.

IX. Provider Certifications

- **A.** Genetic counseling must be provided by a medical (licensed) provider or genetic counselor that is certified by the American Board of Genetic Counseling or has an Active Candidate Status. A genetic counselor shall be employed by or under contract to hospitals or other entities that employ licensed physicians. Licensed physicians shall be responsible for providing on-site clinical supervision and be directly involved in the care of an NC Medicaid member for whom the counseling service is billed. The services of the Genetic Counselor are billed by the supervising physician. See Definitions H. and I. for additional requirements for licensed providers and genetic counselors.
- **B.** Clinical laboratory services must be rendered only by medical care entities that are issued certifications that are in compliance with the Clinical Laboratories Improvement Amendment (CLIA) [Public Law 100-578, amended §353 of the Public Health Service Act (PHSA)].

Background[1]

I. Definitions:

A. BRCA-Related Cancers

Individuals with a genetic mutation in either BRCA1 or BRCA2 genes face an elevated susceptibility to certain types of cancer. In women, this includes an increased risk of breast, ovarian, and pancreatic cancers, while in men, it raises the likelihood of prostate, pancreatic, and breast cancers.

B. Breast Cancer

1. **Primary breast cancer** is the initial growth of malignant cells in the breast tissue, requiring early detection for effective treatment.
2. **Triple negative breast cancer** is an aggressive subtype without estrogen, progesterone, and HER2 receptors, requiring specialized treatment approaches like chemotherapy and immunotherapy.

C. Close Relatives (First-, Second- and Third-Degree Relatives)

1. A **first-degree relative** is a close blood relative which includes the member's parents, full siblings, and children.

2. A **second-degree relative** is a blood relative which includes the member's grandparents, grandchildren, aunts, uncles, nephews, nieces, and half-siblings.
3. A **third-degree relative** is a blood relative which includes the member's first cousins, great-grandparents, great-grandchildren on the same side of the family.

D. Cytogenetic Testing

Cytogenetic testing involves the examination of cells obtained from various sources such as tissue, blood, bone marrow, or amniotic fluid. Its purpose is to identify alterations in chromosomes, including fractures, absences, rearrangements, or additional chromosomes. Specific changes in chromosomes can indicate the presence of genetic disorders, certain types of cancer, or other medical conditions. This type of analysis aids in the diagnosis of diseases, treatment planning, and assessing treatment efficacy.

E. Direct Antiglobulin Test (DAT)

The direct antiglobulin test (DAT) is a clinical laboratory test used to identify the presence of immunoglobulin or complement on the outer surface of red blood cells. Its purpose is to determine whether homolysis is caused by an immune or non-immune factor. It is important to interpret the results of the DAT alongside clinical and other laboratory information, as with any diagnostic test.

F. Family History

Family medical history is information about the health conditions and diseases that have affected close relatives, helping healthcare professionals assess the member's risk and plan personalized care.

G. Genetic Testing

Genetic testing involves analyzing the genetic code of an individual to identify variations, irregularities, or mutations that could potentially indicate a pathological condition.

H. Genetic Counselor

Genetic counselors are health professionals with specialized education, training, and experience in medical genetics and counseling. They are certified by the American Board of Genetic Counseling or have an Active Candidate Status for certification. They help people understand and adapt to the implications of genetic contributions to disease.

I. Genetic Counseling

Genetic counseling is a process of communication that allows members and their families to make informed medical decisions. These services include obtaining a structured family medical and genetic history, constructing a multiple-generation genetic pedigree, performing an analysis of available medical information for genetic risk assessment, and counseling the member and family. This counseling includes natural history of disease, recurrence risk to family members, and availability of testing, screening, and monitoring options. (Refer to Criteria IX).

A licensed provider may provide genetic counseling when there is no access to a fellowship-trained genetic subspecialty physician or a certified genetic counselor. Similar to other genetic counselors, the licensed provider shall discuss and document in the member's health record the following:

1. Likelihood of developing disease;
2. Impact of the disease;

3. Possibility of modification of either the impact or likelihood of disease;
4. Anticipated future developments in diagnosis or treatment; **AND**
5. Informed consent to testing was obtained after the member verbalized understanding of the testing procedure, the benefits and limitations of the test, and the possible consequences of the test results.

J. Gleason Score

The Gleason score is a grading system used to assess the aggressiveness of prostate cancer based on the appearance of cancer cells. It ranges from 2 to 10 and helps determine treatment options and prognosis.

K. Lynch Syndrome (LS) Related Cancers

LS-related cancers comprise colorectal, endometrial, gastric, ovarian, pancreas, urothelial, brain (typically glioblastoma), biliary tract, small intestinal cancers, as well as sebaceous adenomas, sebaceous carcinomas, and keratoacanthomas as observed in Muir-Torre syndrome.

L. MMR Deficiency

Inadequate MMR (Mismatch Repair) function leads to an inability to rectify errors during DNA replication, consequently elevating the risk of cancer. Members with LS inherit mutations in genes encoding for MMR proteins, which predisposes them to colorectal and other cancer types.

M. Personal History

Personal medical history is a summary of the member's past and current health information, aiding healthcare professionals in understanding their medical needs and providing appropriate care.

N. Red Blood Cell (RBC) Antigen Genotyping

RBC antigen genotyping testing proves valuable in determining allelic variants that predict red blood cell antigen phenotypes for members who have recently received blood transfusions or have conflicting serological antibody results due to partial, variant, or weakly expressed antigens.

Coding Implications

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2025, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

BRCA RELATED CANCERS		
CPT®* Codes	Description	Unit Limitation
	SINGLE GENE	
81162	RCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (i.e., detection of large gene rearrangements)	Once in a lifetime
81163	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis	Once in a lifetime
81164	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (i.e., detection of large gene rearrangements)	Once in a lifetime
81165	BRCA1 (BRCA1, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis	Once in a lifetime
81166	BRCA1 (BRCA1, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (i.e., detection of large gene rearrangements)	Once in a lifetime
81167	BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (i.e., detection of large gene rearrangements)	Once in a lifetime
81212	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants	Once in a lifetime
81215	BRCA1 (BRCA1, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant	Once in a lifetime
81216	BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis	Once in a lifetime
81217	BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; known familial variant	Once in a lifetime
81309	PIK3CA (phosphatidylinositol-4, 5-biphosphate 3-kinase, catalytic subunit alpha) (e.g., colorectal and breast cancer) gene analysis, targeted sequence analysis (e.g., exons 7, 9, 20)	Once in a lifetime
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	Once in a lifetime
0138U	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) mRNA sequence analysis (List separately in addition to code for primary procedure)	Once in a lifetime

CPT®* Codes	BRCA RELATED CANCERS Description	Unit Limitation
	GENE PANELS	
81432	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 10 genes, always including BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PATEN, STK11, and TP53	Once in a lifetime
0102U	Hereditary breast cancer-related disorders (e.g., 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])	Once in a lifetime
0103U	Hereditary ovarian cancer (e.g., 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])	Once in a lifetime
0129U	Hereditary breast cancer-related disorders (e.g., 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)	Once in a lifetime
0131U	Hereditary breast cancer-related disorders (e.g., 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)	Once in a lifetime
0132U	Hereditary ovarian cancer-related disorders (e.g., 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)	Once in a lifetime
0133U	Hereditary prostate cancer-related disorders, targeted mRNA sequence analysis panel (11 genes) (List separately in addition to code for primary procedure)	Once in a lifetime
0134U	Hereditary pan cancer (e.g., 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)	Once in a lifetime
0135U	Hereditary gynecological cancer (e.g., hereditary breast and ovarian cancer, hereditary endometrial cancer, hereditary colorectal cancer),	Once in a lifetime

BRCA RELATED CANCERS		
CPT®* Codes	Description	Unit Limitation
	GENE PANELS	
	targeted mRNA sequence analysis panel (12 genes) (List separately in addition to code for primary procedure)	

Cystic Fibrosis and Spinal Muscular Atrophy		
CPT®* Codes	**Description**	**Unit Limitation**
81173	AR (androgen receptor) (e.g., spinal, and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; full gene sequence	Once in a lifetime
81174	AR (androgen receptor) (e.g., spinal, and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; known familial variant	Once in a lifetime
81204	AR (androgen receptor) (e.g., spinal, and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; characterization of alleles (e.g., expanded size or methylation status)	Once in a lifetime
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; common variants (e.g., ACMG/ACOG guidelines)	Once in a lifetime
81221	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; known familial variants	Once in a lifetime
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; duplication/deletion variants	Once in a lifetime
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; full gene sequence	Once in a lifetime
81224	CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; intron 8 poly-T analysis (e.g., male infertility)	Once in a lifetime
81329	SMN1 (survival of motor neuron 1, telomeric) (e.g., spinal muscular atrophy) gene analysis; dosage/deletion analysis (e.g., carrier testing), includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed	Once in a lifetime
81336	SMN1 (survival of motor neuron 1, telomeric) (e.g., spinal muscular atrophy) gene analysis; full gene sequence	Once in a lifetime
81337	SMN1 (survival of motor neuron 1, telomeric) (e.g., spinal muscular atrophy) gene analysis; known familial sequence variant(s)	Once in a lifetime

Cystic Fibrosis and Spinal Muscular Atrophy		
CPT®* Codes	**Description**	**Unit Limitation**
0230U	AR (androgen receptor) (e.g., 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	Once in a lifetime

Duchenne Muscular Dystrophy (DMD) and Becker Muscular Dystrophy (BMD)		
CPT®* Codes	**Description**	**Unit Limitation**
81161	DMD (dystrophin) (e.g., Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed	Once in a lifetime

Hereditary Colorectal Cancers (such as Lynch Syndrome related cancers)		
CPT®* Codes	**Description**	**Unit Limitation**
	SINGLE GENE	
81288	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis	Once in a lifetime
81292	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis	Once in a lifetime
81293	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants	Once in a lifetime
81294	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants	Once in a lifetime
81295	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis	Once in a lifetime
81296	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants	Once in a lifetime

CPT®* Codes	Description	Unit Limitation
	Hereditary Colorectal Cancers (such as Lynch Syndrome related cancers)	
	SINGLE GENE	
81297	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants	Once in a lifetime
81298	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis	Once in a lifetime
81299	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants	Once in a lifetime
81300	MSH6 (mutS homolog 6 [E. coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants	Once in a lifetime
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	Once in a lifetime
81317	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis	Once in a lifetime
81318	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants	Once in a lifetime
81319	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants	Once in a lifetime
81201	APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; full gene sequence	Once in a lifetime
81202	APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; known familial variants	Once in a lifetime
81203	APC (adenomatous polyposis coli) (e.g., familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; duplication/deletion variants	Once in a lifetime
0162U	Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2) (List separately in addition to code for primary procedure)	Once in a lifetime

Hereditary Colorectal Cancers (such as Lynch Syndrome related cancers)		
CPT®* Codes	**Description**	**Unit Limitation**
	GENE PANELS	
81435	Hereditary colon cancer disorders (e.g., Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include sequencing of at least 10 genes, including APC, BMPR1A, CDH1, MLH1, MSH2, MSH6, MUTYH, PTEN, SMAD4, and STK11	Once in a lifetime
0101U	Hereditary colon cancer disorders (e.g., 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])	Once in a lifetime
0130U	Hereditary colon cancer disorders (e.g., 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)	Once in a lifetime
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	Once in a lifetime

Red Blood Cell Antigen Genotyping		
CPT®* Codes	**Description**	**Unit Limitation**
81105	Human Platelet Antigen 1 genotyping (HPA-1), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa], antigen CD61 [GPIIIa]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-1a/b (L33P)	Once in a lifetime
81106	Human Platelet Antigen 2 genotyping (HPA-2), GP1BA (glycoprotein Ib [platelet], alpha polypeptide [GPIba]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-2a/b (T145M)	Once in a lifetime
81107	Human Platelet Antigen 3 genotyping (HPA-3), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex], antigen CD41 [GPIIb]) (e.g., neonatal alloimmune thrombocytopenia	Once in a lifetime

Red Blood Cell Antigen Genotyping		
CPT®* Codes	**Description**	**Unit Limitation**
	[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]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-4a/b (R143Q)	Once in a lifetime
81109	Human Platelet Antigen 5 genotyping (HPA-5), ITGA2 (integrin, alpha 2 [CD49B, alpha 2 subunit of VLA-2 receptor] [GPIa]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant (e.g., HPA-5a/b (K505E))	Once in a lifetime
81110	Human Platelet Antigen 6 genotyping (HPA-6w), ITGB3 (integrin, beta 3 [platelet glycoprotein IIIa, antigen CD61] [GPIIIa]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-6a/b (R489Q)	Once in a lifetime
81111	Human Platelet Antigen 9 genotyping (HPA-9w), ITGA2B (integrin, alpha 2b [platelet glycoprotein IIb of IIb/IIIa complex, antigen CD41] [GPIIb]) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-9a/b (V837M)	Once in a lifetime
81112	Human Platelet Antigen 15 genotyping (HPA-15), CD109 (CD109 molecule) (e.g., neonatal alloimmune thrombocytopenia [NAIT], post-transfusion purpura), gene analysis, common variant, HPA-15a/b (S682Y)	Once in a lifetime
0001U	Red blood cell antigen typing, DNA, human erythrocyte antigen gene analysis of 35 antigens from 11 blood groups, utilizing whole blood, common RBC alleles reported	Once in a lifetime

Other Gene Mutation Testing for Cancer Susceptibility		
CPT®* Codes	**Description** *SINGLE GENE*	**Unit Limitation**
81120	IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (e.g., glioma), common variants (e.g., R132H, R132C)	Once in a lifetime
81121	IDH2 (isocitrate dehydrogenase 2 [NADP+], mitochondrial) (e.g., glioma), common variants (e.g., R140W, R172M)	Once in a lifetime
81175	ASXL1 (additional sex combs like 1, transcriptional regulator) (e.g., myelodysplastic syndrome, myeloproliferative neoplasms,	Once in a lifetime

CPT®* Codes	Description	Unit Limitation
	Other Gene Mutation Testing for Cancer Susceptibility *SINGLE GENE*	
	chronic myelomonocytic leukemia), gene analysis; full gene sequence	
81176	ASXL1 (additional sex combs like 1, transcriptional regulator) (e.g., myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; targeted sequence analysis (e.g., exon 12)	Once in a lifetime
81191	NTRK1 (neurotrophic receptor tyrosine kinase 1) (e.g., solid tumors) translocation analysis	Once in a lifetime
81192	NTRK2 (neurotrophic receptor tyrosine kinase 2) (e.g., solid tumors) translocation analysis	Once in a lifetime
81193	NTRK3 (neurotrophic receptor tyrosine kinase 3) (e.g., solid tumors) translocation analysis	Once in a lifetime
81194	NTRK (neurotrophic receptor tyrosine kinase 1, 2, and 3) (e.g., solid tumors) translocation analysis	Once in a lifetime
81206	BCR/ABL1 (t(9;22)) (e.g., chronic myelogenous leukemia) translocation analysis; major breakpoint, qualitative or quantitative	Once in a lifetime
81207	BCR/ABL1 (t(9;22)) (e.g., chronic myelogenous leukemia) translocation analysis; minor breakpoint, qualitative or quantitative	Once in a lifetime
81208	BCR/ABL1 (t(9;22)) (e.g., chronic myelogenous leukemia) translocation analysis; other breakpoint, qualitative or quantitative	Once in a lifetime
81210	(B-Raf proto-oncogene, serine/threonine kinase) (e.g., colon cancer, melanoma), gene analysis, V600 variant(s)	Once in a lifetime
81218	CEBPA (CCAAT/enhancer binding protein [C/EBP], alpha) (e.g., acute myeloid leukemia), gene analysis, full gene sequence	Once in a lifetime
81219	CALR (calreticulin) (e.g., myeloproliferative disorders), gene analysis, common variants in exon 9	Once in a lifetime
81233	BTK (Bruton's tyrosine kinase) (e.g., chronic lymphocytic leukemia) gene analysis, common variants (e.g., C481S, C481R, C481F)	Once in a lifetime
81235	EGFR (epidermal growth factor receptor) (e.g., non-small cell lung cancer) gene analysis, common variants (e.g., exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)	Once in a lifetime
81236	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (e.g., myelodysplastic syndrome, myeloproliferative neoplasms) gene analysis, full gene sequence	Once in a lifetime
81237	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (e.g., diffuse large B-cell lymphoma) gene analysis, common variant(s) (e.g., codon 646)	Once in a lifetime

Other Gene Mutation Testing for Cancer Susceptibility		
CPT®* Codes	**Description** *SINGLE GENE*	**Unit Limitation**
81245	FLT3 (fms-related tyrosine kinase 3) (e.g., acute myeloid leukemia), gene analysis; internal tandem duplication (ITD) variants (i.e., exons 14, 15)	Once in a lifetime
81246	FLT3 (fms-related tyrosine kinase 3) (e.g., acute myeloid leukemia), gene analysis; tyrosine kinase domain (TKD) variants (e.g., D835, I836)	Once in a lifetime
81270	JAK2 (Janus kinase 2) (e.g., myeloproliferative disorder) gene analysis, p.Val617Phe (V617F) variant	Once in a lifetime
81272	JAK2 (Janus kinase 2) (e.g., myeloproliferative disorder) targeted sequence analysis (e.g., exons 12 and 13)	Once in a lifetime
81279	JAK2 (Janus kinase 2) (e.g., myeloproliferative disorder) targeted sequence analysis (e.g., exons 12 and 13)	Once in a lifetime
81287	MGMT (O-6-methylguanine-DNA methyltransferase) (e.g., glioblastoma multiforme) promoter methylation analysis	Once in a lifetime
81307	PALB2 (partner and localizer of BRCA2) (e.g., breast and pancreatic cancer) gene analysis; full gene sequence	Once in a lifetime
81308	PALB2 (partner and localizer of BRCA2) (e.g., breast and pancreatic cancer) gene analysis; known familial variant	Once in a lifetime
81309	PIK3CA (phosphatidylinositol-4, 5-biphosphate 3-kinase, catalytic subunit alpha) (e.g., colorectal and breast cancer) gene analysis, targeted sequence analysis (e.g., exons 7, 9, 20)	Once in a lifetime
81310	NPM1 (nucleophosmin) (e.g., acute myeloid leukemia) gene analysis, exon 12 variants	Once in a lifetime
81311	NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (e.g., colorectal carcinoma), gene analysis, variants in exon 2 (e.g., codons 12 and 13) and exon 3 (e.g., codon 61)	Once in a lifetime
81315	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (e.g., promyelocytic leukemia) translocation analysis; common breakpoints (e.g., intron 3 and intron 6), qualitative or quantitative	Once in a lifetime
81316	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (e.g., promyelocytic leukemia) translocation analysis; single breakpoint (e.g., intron 3, intron 6 or exon 6), qualitative or quantitative	Once in a lifetime
81320	PLCG2 (phospholipase C gamma 2) (e.g., chronic lymphocytic leukemia) gene analysis, common variants (e.g., R665W, S707F, L845F)	Once in a lifetime

Other Gene Mutation Testing for Cancer Susceptibility		
CPT®* Codes	**Description** *SINGLE GENE*	**Unit Limitation**
81334	RUNX1 (runt related transcription factor 1) (e.g., acute myeloid leukemia, familial platelet disorder with associated myeloid malignancy), gene analysis, targeted sequence analysis (e.g., exons 3-8)	Once in a lifetime
81338	MPL (MPL proto-oncogene, thrombopoietin receptor) (e.g., myeloproliferative disorder) gene analysis; common variants (e.g., W515A, W515K, W515L, W515R)	Once in a lifetime
81339	MPL (MPL proto-oncogene, thrombopoietin receptor) (e.g., myeloproliferative disorder) gene analysis; sequence analysis, exon 10	Once in a lifetime
81345	TERT (telomerase reverse transcriptase) (e.g., thyroid carcinoma, glioblastoma multiforme) gene analysis, targeted sequence analysis (e.g., promoter region)	Once in a lifetime
81347	SF3B1 (splicing factor [3b] subunit B1) (e.g., myelodysplastic syndrome/acute myeloid leukemia) gene analysis, common variants (e.g., A672T, E622D, L833F, R625C, R625L)	Once in a lifetime
81348	SRSF2 (serine and arginine-rich splicing factor 2) (e.g., myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variants (e.g., P95H, P95L)	Once in a lifetime
81351	TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome) gene analysis; full gene sequence	Once in a lifetime
81352	TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome) gene analysis; targeted sequence analysis (e.g., 4 oncology)	Once in a lifetime
81353	TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome) gene analysis; known familial variant	Once in a lifetime
81357	U2AF1 (U2 small nuclear RNA auxiliary factor 1) (e.g., myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variants (e.g., S34F, S34Y, Q157R, Q157P)	Once in a lifetime
81360	ZRSR2 (zinc finger CCCH-type, RNA binding motif and serine/arginine-rich 2) (e.g., myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variant(s) (e.g., E65fs, E122fs, R448fs)	Once in a lifetime

Other Gene Mutation Testing for Cancer Susceptibility		
CPT®* Codes	**Description**	**Unit Limitation**
	GENE PANELS	
81437	Hereditary neuroendocrine tumor disorders (e.g., 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	Once in a lifetime
0022U	Targeted genomic sequence analysis panel, non-small cell lung neoplasia, DNA and RNA analysis, 23 genes, interrogation for sequence variants and rearrangements, reported as presence or absence of variants and associated therapy(ies) to consider	Once in a lifetime

Other Single Gene Tests		
CPT®* Codes	**Description**	**Unit Limitation**
81171	AFF2 (ALF transcription elongation factor 2 [FMR2]) (e.g., fragile X intellectual disability 2 [FRAXE]) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles	Once in a lifetime
81172	AFF2 (ALF transcription elongation factor 2 [FMR2]) (e.g., fragile X intellectual disability 2 [FRAXE]) gene analysis; characterization of alleles (e.g., expanded size and methylation status)	Once in a lifetime
81200	ASPA (aspartoacylase) (e.g., Canavan disease) gene analysis, common variants (e.g., E285A, Y231X)	Once in a lifetime
81240	F2 (prothrombin, coagulation factor II) (e.g., hereditary hypercoagulability) gene analysis, 20210G>A variant	Once in a lifetime
81241	F5 (coagulation factor V) (e.g., hereditary hypercoagulability) gene analysis, Leiden variant	Once in a lifetime
81242	FANCC (Fanconi anemia, complementation group C) (e.g., Fanconi anemia, type C) gene analysis, common variant (e.g., IVS4+4A>T)	Once in a lifetime
81243	FMR1 (fragile X messenger ribonucleoprotein 1) (e.g., fragile X syndrome, X-linked intellectual disability [XLID]) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles	Once in a lifetime
81244	FMR1 (fragile X messenger ribonucleoprotein 1) (e.g., fragile X syndrome, X-linked intellectual disability [XLID]) gene analysis; characterization of alleles (e.g., expanded size and promoter methylation status)	Once in a lifetime
81251	GBA (glucosidase, beta, acid) (e.g., Gaucher disease) gene analysis, common variants (e.g., N370S, 84GG, L444P, IVS2+1G>A)	Once in a lifetime

Other Single Gene Tests		
CPT®* Codes	**Description**	**Unit Limitation**
81255	HEXA (hexosaminidase A [alpha polypeptide]) (e.g., Tay-Sachs disease) gene analysis, common variants (e.g., 1278insTATC, 1421+1G>C, G269S)	Once in a lifetime
81256	HFE (hemochromatosis) (e.g., hereditary hemochromatosis) gene analysis, common variants (e.g., C282Y, H63D)	Once in a lifetime
81257	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; common deletions or variant (e.g., Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, alpha4.2, alpha20.5, Constant Spring)	Once in a lifetime
81258	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; known familial variant	Once in a lifetime
81259	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; full gene sequence	Once in a lifetime
81269	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; duplication/deletion variants	Once in a lifetime
81271	HTT (huntingtin) (e.g., Huntington disease) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles	Once in a lifetime
81274	HTT (huntingtin) (e.g., Huntington disease) gene analysis; characterization of alleles (e.g., expanded size)	Once in a lifetime
81291	MTHFR (5,10-methylenetetrahydrofolate reductase) (e.g., hereditary hypercoagulability) gene analysis, common variants (e.g., 677T, 1298C)	Once in a lifetime
81302	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; full sequence analysis	Once in a lifetime
81303	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; known familial variant	Once in a lifetime
81304	MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; duplication/deletion variants	Once in a lifetime
81331	SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (e.g., Prader-Willi syndrome and/or Angelman syndrome), methylation analysis	Once in a lifetime
81332	SERPINA1 (serpin peptidase inhibitor, clade A, alpha-1 antiproteinase, antitrypsin, member 1) (e.g., alpha-1-antitrypsin deficiency), gene analysis, common variants (e.g., *S and *Z)	Once in a lifetime

Other Single Gene Tests		
CPT®* Codes	**Description**	**Unit Limitation**
81361	HBB (hemoglobin, subunit beta) (e.g., sickle cell anemia, beta thalassemia, hemoglobinopathy); common variant(s) (e.g., HbS, HbC, HbE)	Once in a lifetime
81362	HBB (hemoglobin, subunit beta) (e.g., sickle cell anemia, beta thalassemia, hemoglobinopathy); known familial variant(s)	Once in a lifetime
81363	HBB (hemoglobin, subunit beta) (e.g., sickle cell anemia, beta thalassemia, hemoglobinopathy); duplication/deletion variant(s)	Once in a lifetime
81364	HBB (hemoglobin, subunit beta) (e.g., sickle cell anemia, beta thalassemia, hemoglobinopathy); full gene sequence	Once in a lifetime
0234U	MECP2 (methyl CpG binding protein 2) (e.g., 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	Once in a lifetime

Other Gene Panels		
CPT®* Codes	**Description**	**Unit Limitation**
81412	Ashkenazi Jewish associated disorders (e.g., Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group C, Gaucher disease, Tay-Sachs disease), genomic sequence analysis panel, must include sequencing of at least 9 genes, including ASPA, BLM, CFTR, FANCC, GBA, HEXA, IKBKAP, MCOLN1, and SMPD1	Once in a lifetime
81441	Inherited bone marrow failure syndromes (IBMFS) (e.g., Fanconi anemia, dyskeratosis congenita, Diamond-Blackfan anemia, Shwachman-Diamond syndrome, GATA2 deficiency syndrome, congenital amegakaryocytic thrombocytopenia) sequence analysis panel, must include sequencing of at least 30 genes, including BRCA2, BRIP1, DKC1, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, GATA1, GATA2, MPL, NHP2, NOP10, PALB2, RAD51C, RPL11, RPL35A, RPL5, RPS10, RPS19, RPS24, RPS26, RPS7, SBDS, TERT, and TINF2	Once in a lifetime
81443	Genetic testing for severe inherited conditions (e.g., cystic fibrosis, Ashkenazi Jewish-associated disorders [e.g., Bloom syndrome, Canavan disease, Fanconi anemia type C, mucolipidosis type VI, Gaucher disease, Tay-Sachs disease], beta hemoglobinopathies, phenylketonuria, galactosemia), genomic sequence analysis panel,	Once in a lifetime

Other Gene Panels		
CPT®* Codes	**Description**	**Unit Limitation**
	must include sequencing of at least 15 genes (e.g., ACADM, ARSA, ASPA, ATP7B, BCKDHA, BCKDHB, BLM, CFTR, DHCR7, FANCC, G6PC, GAA, GALT, GBA, GBE1, HBB, HEXA, IKBKAP, MCOLN1, PAH)	

Genetic Counseling:		
CPT®* Codes	**Description**	**Unit Limitation**
96041	Medical genetics and genetic counseling services, each 30 minutes face-to-face with patient/family	3 units (1 unit = 30 minutes) 90 minutes total:

Reviews, Revisions, and Approvals	Reviewed Date	Approval Date
Original approval date	08/24	08/24
Title changed '/' to' for.' Criteria V/VI, changed "all" to "any." Criteria VIII. added text 'then, in addition to the prior approval requirements found in Criteria I and II.'	11/24	11/24
Annual Review. Added CPT 81194 96041 0172U Deleted 91194 81433 81436 81438 96040 0712U effective date 01/01/2025. Under NC Guidance/Claims related information, updated state web address.		

References

1. State of North Carolina Medicaid Clinical Coverage Policy No:1S-9 Genetic Testing - Diagnosis and Treatment. Program Specific Clinical Coverage Policies | NC Medicaid (ncdhhs.gov). Published February 1, 2025. Accessed March 11, 2025.

North Carolina Guidance

Eligibility Requirements

1. An eligible beneficiary shall be enrolled in the NC Medicaid Program (Medicaid is NC Medicaid program, unless context clearly indicates otherwise);
2. Provider(s) shall verify each Medicaid beneficiary's eligibility each time a service is rendered.
3. The Medicaid beneficiary may have service restrictions due to their eligibility category that would make them ineligible for this service.

EPSDT Special Provision: Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age

- 42 U.S.C. § 1396d(r) [1905(r) of the Social Security Act]

Early and Periodic Screening, Diagnostic, and Treatment (EPSDT) is a federal Medicaid requirement that requires the state Medicaid agency to cover services, products, or procedures for Medicaid beneficiary under 21 years of age if the service is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition [health problem] identified through a screening examination (includes any evaluation by a physician or other licensed practitioner).

This means EPSDT covers most of the medical or remedial care a child needs to improve or maintain his or her health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

Medically necessary services will be provided in the most economic mode, as long as the treatment made available is similarly efficacious to the service requested by the beneficiary's physician, therapist, or other licensed practitioner; the determination process does not delay the delivery of the needed service; and the determination does not limit the beneficiary's right to a free choice of providers.

EPSDT does not require the state Medicaid agency to provide any service, product, or procedure:

I. that is unsafe, ineffective, or experimental or investigational.
II. that is not medical in nature or not generally recognized as an accepted method of medical practice or treatment.

Service limitations on scope, amount, duration, frequency, location of service, and other specific criteria described in clinical coverage policies may be exceeded or may not apply as long as the provider's documentation shows that the requested service is medically necessary "to correct or ameliorate a defect, physical or mental illness, or a condition" [health problem]; that is, provider documentation shows how the service, product, or procedure meets all EPSDT criteria, including to correct or improve or maintain the beneficiary's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

EPSDT and Prior Approval Requirements

- If the service, product, or procedure requires prior approval, the fact that the beneficiary is under 21 years of age does NOT eliminate the requirement for prior approval.
- **IMPORTANT ADDITIONAL INFORMATION** about EPSDT and prior approval is found in the *NCTracks Provider Claims and Billing Assistance Guide*, and on the EPSDT provider page. The Web addresses are specified below:
  NCTracks Provider Claims and Billing Assistance Guide:
  https://www.nctracks.nc.gov/content/public/providers/provider-manuals.html

EPSDT provider page: https://medicaid.ncdhhs.gov/

Provider(s) Eligible to Bill for the Procedure, Product, or Service

To be eligible to bill for the procedure, product, or service related to this policy, the provider(s) shall:

i. meet Medicaid qualifications for participation;
ii. have a current and signed Department of Health and Human Services (DHHS) Provider Administrative Participation Agreement; and
iii. bill only for procedures, products, and services that are within the scope of their clinical practice, as defined by the appropriate licensing entity.

Compliance

Provider(s) shall comply with the following in effect at the time the service is rendered:

A. All applicable agreements, federal, state, and local laws and regulations including the Health Insurance Portability and Accountability Act (HIPAA) and record retention requirements; and
B. All NC Medicaid's clinical (medical) coverage policies, guidelines, policies, provider manuals, implementation updates, and bulletins published by the Centers for Medicare and Medicaid Services (CMS), DHHS, DHHS division(s) or fiscal contractor(s).

Claims-Related Information

Provider(s) shall comply with the NC Tracks Provider Claims and Billing Assistance Guide, Medicaid bulletins, fee schedules, NC Medicaid's clinical coverage policies and any other relevant documents for specific coverage and reimbursement for Medicaid:

- Claim Type - as applicable to the service provided:
  Professional (CMS-1500/837P transaction)
  Institutional (UB-04/837I transaction)
  Unless directed otherwise, Institutional Claims must be billed according to the National Uniform Billing Guidelines. All claims must comply with National Coding Guidelines.
- International Classification of Diseases and Related Health Problems, Tenth Revisions, Clinical Modification (ICD-10-CM) and Procedural Coding System (PCS) - Provider(s) shall report the ICD-10-CM and Procedural Coding System (PCS) to the highest level of specificity that supports medical necessity. Provider(s) shall use the current ICD-10 edition and any subsequent editions in effect at the time of service. Provider(s) shall refer to the applicable edition for code description, as it is no longer documented in the policy.
- Code(s) - Provider(s) shall report the most specific billing code that accurately and completely describes the procedure, product or service provided. Provider(s) shall use the Current Procedural Terminology (CPT), Health Care Procedure Coding System (HCPCS), and UB-04 Data Specifications Manual (for a complete listing of valid revenue codes) and any subsequent editions in effect at the time of service. Provider(s) shall refer

to the applicable edition for the code description, as it is no longer documented in the policy. If no such specific CPT or HCPCS code exists, then the provider(s) shall report the procedure, product or service using the appropriate unlisted procedure or service code.
Unlisted Procedure or Service
CPT: The provider(s) shall refer to and comply with the Instructions for Use of the CPT Codebook, Unlisted Procedure or Service, and Special Report as documented in the current CPT in effect at the time of service.
HCPCS: The provider(s) shall refer to and comply with the Instructions For Use of HCPCS National Level II codes, Unlisted Procedure or Service and Special Report as documented in the current HCPCS edition in effect at the time of service

- Modifiers - Providers shall follow applicable modifier guidelines.
- Billing Units - Provider(s) shall report the appropriate code(s) used which determines the billing unit(s).
- Co-payments -
  For Medicaid refer to Medicaid State Plan:
  https://medicaid.ncdhhs.gov/meetingsnotices/medicaid-state-plan-public-notices

- Reimbursement - Provider(s) shall bill their usual and customary charges. For a schedule of rates, refer to: https://medicaid.ncdhhs.gov/.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a

discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended to recommend treatment for members/enrollees. Members/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members/enrollees, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members/enrollees and their representatives agree to be bound by such terms and conditions by providing services to members/enrollees and/or submitting claims for payment for such services.