Pathology: Molecular Pathology

Page updated: August 2020

This section contains information to help providers bill for clinical laboratory tests or examinations related to molecular pathology and diagnostic services.

Molecular Pathology Code Chart

The chart included later in this section correlates molecular pathology CPT® and HCPCS Level II Codes with the following:

- *Treatment Authorization Request* (TAR) and claim documentation requirements
- Allowable diagnosis (ICD-10-CM) codes
- Once-in-a-lifetime and other frequency limitations for reimbursement
- Select modifier and split-billing information

Note: Policy for most molecular pathology codes fits within the chart; however, some policy was too lengthy or complex for the chart and is covered outside of the chart.

Modifiers

For a description of the modifiers billed with certain codes, refer to the *Modifiers: Approved List* section in this manual.

Tier 1, Molecular Pathology, Code Correlation Chart

Providers should refer to the CPT code book for full descriptions of the following codes.

‹‹**Molecular Pathology CPT Codes, TAR and Billing Information**››

CPT Code Description	**TAR Required**	**TAR and/or Billing Requirements**	**Frequency**
81120 IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble), common variants	No	One of the following ICD-10-CM codes is required on the claim (except with valid TAR): C71.0 thru C71.9 or C92.00 thru C92.02	Once-in-a-lifetime
81121 IDH2 (isocitrate dehydrogenase 2 [NADP+], mitochondrial), common variants	No	One of the following ICD-10-CM codes is required on the claim (except with valid TAR): C71.0 thru C71.9 or C92.00 thru C92.02	Once-in-a-lifetime
81161 DMD (dystrophin) deletion analysis, and duplication analysis, if performed	No	ICD-10-CM diagnosis code G71.0 (muscular dystrophy) is required on the claim.	Once-in-a-lifetime

‹‹**Molecular Pathology CPT Codes, TAR and Billing Information (continued)**››

CPT Code Description	**TAR Required**	**TAR and/or Billing Requirements**	**Frequency**
81162 BRCA1, BRCA2 gene analysis; full sequence analysis and full duplication/deletion analysis	Yes	A TAR for CPT code 81162 requires documentation of one *or more* of the following numbered criteria. Based on 2019 U.S. Preventive Services Task Force (USPSTF) recommendation: – The patient has personal or family history that suggests an inherited cancer susceptibility based on any one of the following familial risk assessment tools: ❖ The Ontario Family History Assessment Tool ❖ Manchester Scoring System ❖ Referral Screening Tool ❖ Pedigree Assessment Tool ❖ 7-Question Family History Screening Tool ❖ International Breast Cancer Intervention Study instrument ❖ Brief versions of BRCAPRO; and – The patient is willing to talk with a health professional who is suitably trained to provide genetic counseling and interpret test results; and *(continued on next page)*	Once-in-a-lifetime except with valid TAR override *

‹‹Molecular Pathology CPT Codes, TAR and Billing Information (continued)››

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81162 BRCA1, BRCA2 gene analysis; full sequence analysis and full duplication/deletion analysis	Yes	– The test results will aid in the decision-making; <u>or</u> An individual from a family member with a known deleterious BRCA mutation; <u>or</u> Personal history of breast cancer (invasive or ductal carcinoma in situ) plus one or more of the following: – Diagnosed at ≤45 years of age; <u>or</u> – Diagnosed at 46 to 50 years of age with: ❖ An additional breast cancer primary at any age ❖ One or more close blood relatives with breast cancer at any age ❖ One or more close blood relatives with prostate cancer (Gleason score ≥7) ❖ An unknown or limited family history; <u>or</u> – Diagnosed at ≤60 years of age with a triple negative breast cancer; <u>or</u> *(continued on next page)*	Once-in-a-lifetime except with valid TAR override *

‹‹Molecular Pathology CPT Codes, TAR and Billing Information (continued)››

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81162 BRCA1, BRCA2 gene analysis; full sequence analysis and full duplication/deletion analysis	Yes	– Diagnosed at any age with: ❖ One or more close blood relatives with: ▪ Breast cancer diagnosed at ≤50 years of age; or ▪ Ovarian carcinoma; or ▪ Male breast cancer; or ▪ Metastatic prostate cancer; or ▪ Pancreatic cancer ❖ Two or more additional diagnosis of breast cancer at any age in patient and/or in close blood relatives; or – Ashkenazi Jewish ancestry; or Personal history of ovarian carcinoma (includes fallopian tube and primary peritoneal cancers); or Personal history of male breast cancer; or *(continued on next page)*	Once-in-a-lifetime except with valid TAR override *

‹‹Molecular Pathology CPT Codes, TAR and Billing Information (continued)››

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81162 BRCA1, BRCA2 gene analysis; full sequence analysis and full duplication/deletion analysis	Yes	Personal history of pancreatic cancer; or Personal history of metastatic prostate cancer (biopsy-proven and/or with radiographic evidence; includes distant metastasis and regional bed or nodes; not biochemical recurrence); or Personal history of high-grade prostate cancer (Gleason score ≥7) at any age with: – One or more close blood relatives (first-, second- or third-degree) with ovarian carcinoma, pancreatic cancer or metastatic prostate cancer at any age or breast cancer under 50 years of age; or – Two or more close blood relatives (first-, second- or third-degree relatives on the same side of family) with breast or prostate cancer (any grade) at any age; or – Ashkenazi Jewish ancestry; or *(continued on next page)*	Once-in-a-lifetime except with valid TAR override *

‹‹Molecular Pathology CPT Codes, TAR and Billing Information (continued)››

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81162 BRCA1, BRCA2 gene analysis; full sequence analysis and full duplication/deletion analysis	Yes	BRCA1/2 pathogenic/likely pathogenic variant detected by tumor profiling on any tumor type in the absence of germline pathogenic/likely pathogenic variant analysis; or For an individual without history of breast or ovarian cancer, but with one or more first- or second-degree blood relative meeting any of the above criteria; or For BRACAnalysis CDx testing for breast cancer, all of the following TAR criteria must be met: – Patient has metastatic breast cancer. – Patient is human epidermal growth factor receptor 2 (HER2)-negative. – Patient has previously been treated with chemotherapy in the neoadjuvant, adjuvant or metastatic setting. – Patient's additional treatment is contingent on the test results.	Once-in-a-lifetime except with valid TAR override *

‹‹Molecular Pathology CPT Codes, TAR and Billing Information (continued)››

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81163 BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) gene analysis; full sequence analysis	Yes	See CPT code 81162 for TAR criteria and billing requirements.	See CPT code 81162
81164 BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) gene analysis; full duplication/deletion analysis	Yes	See CPT code 81162 for TAR criteria and billing requirements.	See CPT code 81162
81165 BRCA1 (BRCA1, DNA repair associated) gene analysis; full sequence analysis	Yes	See CPT code 81162 for TAR criteria and billing requirements.	See CPT code 81162
81166 BRCA1 (BRCA1, DNA repair associated) gene analysis; full duplication/deletion analysis	Yes	See CPT code 81162 for TAR criteria and billing requirements.	See CPT code 81162

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81167 BRCA2 (BRCA2, DNA repair associated) gene analysis; full duplication/deletion analysis	Yes	See CPT code 81162 for TAR criteria and billing requirements.	See CPT code 81162
‹‹81168 CCND1/IGH (t[11;14])(e.g., mantle cell lymphoma) translocation analysis, major breakpoint, qualitative and quantitative, if performed	No	One of the following ICD-10-CM diagnosis codes is required on the claim: C83.10 thru C83.19.	Once in a lifetime››
81170 ALB1 gene analysis, variants in the kinase domain	Yes	Requires documentation on the TAR that the recipient has chronic myeloid leukemia (CML) and failed tyrosine kinase inhibitor (TKI) therapy	Once-in-a-lifetime
81171 AFF2 (AF4/FMR2 family, member 2 [FMR2]) gene analysis evaluation to detect abnormal alleles	No	One of the following ICD-10-CM diagnosis codes is required on the claim (except with valid TAR): F70, F71, F80.0 thru F89, H93.25, R48.0, R62.0 thru R62.59, F82, F88, R48.2	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

81172 AFF2 (AF4/FMR2 family, member 2 [FMR2]) gene analysis; characterization of alleles	No	One of the following ICD-10-CM diagnosis codes is required on the claim (except with valid TAR): • F70, F71, F80.0 thru F89, H93.25, R48.0, R62.0 thru R62.59, F82, F88, R48.2	Once-in-a-lifetime except with valid TAR override
81173 AR (androgen receptor) gene analysis; full gene sequence	Yes	A TAR for CPT code 81173 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for bulbar muscular atrophy, and • The patient requires the service as a confirmatory test for spinal and bulbar muscular atrophy	Once-in-a-lifetime except with valid TAR override
81174 AR (androgen receptor) gene analysis; known familial variant	Yes	A TAR for CPT code 81174 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for bulbar muscular atrophy, and • The patient requires the service as a confirmatory test for spinal and bulbar muscular atrophy	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81175 ASXL gene analysis, full gene sequence	No	One of the following ICD-10-CM codes is required on the claim (except with valid TAR): C93.10 thru C93.12, D46.0 thru D46.C, D47.1	Once-in-a-lifetime
81176 ASXL gene analysis, targeted sequence analysis	No	One of the following ICD-10-CM codes is required on the claim (except with valid TAR): C93.10 thru C93.12, D46.0 thru D46.C, D47.1	Once-in-a-lifetime
81177 ATN1 (atrophin 1) gene analysis, evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81177 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for dentatorubral pallidoluysian atrophy, and • The patient requires the service as a confirmatory test for dentatorubral pallidoluysian atrophy	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81178 ATXN1 (ataxin 1) gene analysis, evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81178 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for spinocerebellar ataxia type 1 (SCA1), and • The patient requires the service as a confirmatory test for SCA1	Once-in-a-lifetime except with valid TAR override
81179 ATXN2 (ataxin 2) gene analysis, evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81179 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for spinocerebellar ataxia type 2 (SCA2), and • The patient requires the service as a confirmatory test for SCA2	Once-in-a-lifetime except with valid TAR override
81180 ATXN3 (ataxin 3) gene analysis, evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81180 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for spinocerebellar ataxia type 3 (SCA3), and • The patient requires the service as a confirmatory test for SCA3	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81181 ATXN7 (ataxin 7) gene analysis, evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81181 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for spinocerebellar ataxia type 7 (SCA7), and • The patient requires the service as a confirmatory test for SCA7	Once-in-a-lifetime except with valid TAR override
81182 ATXN8OS (ATXN8 opposite strand [non-protein coding]) gene analysis, evaluation to detect abnormal	Yes	A TAR for CPT code 81182 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for spinocerebellar ataxia type 8 (SCA8), and • The patient requires the service as a confirmatory test for SCA8	Once-in-a-lifetime except with valid TAR override
81183 ATXN10 (ataxin 10) gene analysis, evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81183 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for spinocerebellar ataxia type 10 (SCA10), and • The patient requires the service as a confirmatory test for SCA10	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81184 CACNA1A (calcium voltage-gated channel subunit alpha1 A) gene analysis; evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81184 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for Episodic ataxia type 2 (EA2), and • The patient requires the service as a confirmatory test for EA2	Once-in-a-lifetime except with valid TAR override
81185 CACNA1A (calcium voltage-gated channel subunit alpha1 A) gene analysis; full gene sequence	Yes	A TAR for CPT code 81185 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for Episodic ataxia type 2 (EA2), and • The patient requires the service as a confirmatory test for EA2	Once-in-a-lifetime except with valid TAR override
81186 CACNA1A (calcium voltage-gated channel subunit alpha1 A) gene analysis; known familial variant	Yes	A TAR for CPT code 81186 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for Episodic ataxia type 2 (EA2), and • The patient requires the service as a confirmatory test for EA2	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81187 CNBP (CCHC-type zinc finger nucleic acid binding protein) gene analysis, evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81187 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for Myotonic dystrophy type 2 (MD2), and • The patient requires the service as a confirmatory test for MD2	Once-in-a-lifetime except with valid TAR override
81188 CSTB (cystatin B) gene analysis; evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81188 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for myoclonic epilepsy type 1 and requires the service as a confirmatory test for myoclonic epilepsy type 1, and • Treatment will be contingent on test results	Once-in-a-lifetime except with valid TAR override
81189 CSTB (cystatin B) gene analysis; full gene sequence	Yes	A TAR for CPT code 81189 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for myoclonic epilepsy type 1 and requires the service as a confirmatory test for myoclonic epilepsy type 1, and • Treatment will be contingent on test results	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81190 CSTB (cystatin B) gene analysis; known familial variant(s)	Yes	A TAR for CPT code 81190 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for myoclonic epilepsy type 1 and requires the service as a confirmatory test for myoclonic epilepsy type 1, and Treatment will be contingent on test results	Once-in-a-lifetime except with valid TAR override
‹‹81191 NTRK1 (neurotrophic receptor tyrosine kinase 1) (e.g., solid tumors) translocation analysis	Yes	A TAR for CPT code 81191 requires documentation of the following criteria: Adult and pediatric patients with solid tumors with any one of the following clinical scenarios: • Metastatic tumor or where surgical resection is likely to result in severe morbidity, or • Have no satisfactory alternative treatments or have progressed following treatment	N/A››

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
‹‹81192 NTRK2 (neurotrophic receptor tyrosine kinase 2)(e.g., solid tumors) translocation analysis	Yes	See CPT code 81191 for TAR criteria and billing requirements.	N/A››
‹‹81193 NTRK3 (neurotrophic receptor tyrosine kinase 3)(e.g., solid tumors) translocation analysis	Yes	See CPT code 81191 for TAR criteria and billing requirements.	N/A››
‹‹81194 NTRK (neurotrophic-tropomyosin receptor tyrosine kinase 1, 2, and 3) (e.g., solid tumors) translocation analysis	Yes	See CPT code 81191 for TAR criteria and billing requirements.	N/A››

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81201 APC gene analysis; full gene sequence	No	One of the following ICD-10-CM codes is required on the claim: C18.0 thru C18.9, D12.0 thru D12.9, K63.5, Z86.010	Once-in-a-lifetime
81202 APC gene analysis; known familial variants	Yes	Requires documentation on the TAR of a family history of familial adenomatous polyposis that includes a relative with a known deleterious APC mutation	Once-in-a-lifetime
81203 APC gene analysis; duplication/deletion variants	No	One of the following ICD-10-CM codes is required on the claim: C18.0 thru C18.9, D12.0 thru D12.9, K63.5, Z86.010	Once-in-a-lifetime
81204 AR (androgen receptor) gene analysis; characterization of alleles	Yes	A TAR for CPT code 81204 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for bulbar muscular atrophy, and • The patient requires the service as a confirmatory test for spinal and bulbar muscular atrophy	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81206 BCR/ABL1 translocation analysis; major breakpoint	No	One of the following ICD-10-CM codes is required on the claim: C91.00 thru C91.02 or C92.10 thru C92.12	N/A
81207 BCR/ABL1 translocation analysis; minor breakpoint	No	One of the following ICD-10-CM codes is required on the claim: C91.00 thru C91.02 or C92.10 thru C92.12	N/A
81208 BCR/ABL1 translocation analysis; other breakpoint	No	One of the following ICD-10-CM codes is required on the claim: C91.00 thru C91.02 or C92.10 thru C92.12	N/A
81210 BRAF (B-Raf proto-oncogene, serine/threonine kinase), gene analysis, V600 variant(s)	No	One of the following ICD-10-CM codes is required on the claim: C18.0 thru C18.9, C19, C20, C33, C34.00 thru C34.92, C43.0 thru C43.9, C79.2 or D03.0 thru D03.9	Once-in-a-lifetime
81212 BRCA1, BRCA2 gene analysis; variants	Yes	Requires documentation on the TAR of the following: • An individual is of an ethnicity associated with the Ashkenazi Jewish population No additional family history may be required	Once-in-a-lifetime
81215 BRCA1 (breast cancer 1) gene analysis; known familial variant	Yes	See CPT code 81162 for TAR criteria and billing requirements.	See CPT code 81162

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81216 BRCA2 (breast cancer 2) gene analysis; full sequence analysis	Yes	See CPT code 81162 for TAR criteria and billing requirements.	See CPT code 81162
81217 BRCA2 (breast cancer 2) gene analysis; known familial variant	Yes	See CPT code 81162 for TAR criteria and billing requirements.	See CPT code 81162
81218 CEBPA (CCAAT/enhancer binding protein [C/EBP], alpha) gene analysis, full gene sequence	No	One of the following ICD-10-CM codes is required on the claim: C92.00 thru C92.02, C92.40 thru C92.42 or C92.50 thru C92.52	Once-in-a-lifetime
81219 CALR (calreticulin) gene analysis, common variants in exon 9	No	One of the following ICD-10-CM codes is required on the claim: C92.10 thru C92.12, D45, D47.3 or D75.81	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81220 CFTR (cystic fibrosis transmembrane conductance regulator) gene analysis; common variants	No	When used to bill for cystic-fibrosis screening requires ICD-10-CM diagnosis code O09.00 thru O09.93, Z31.430, Z31.440, ‹‹Z31.5,›› Z34.00 thru Z34.03, Z34.80 thru Z34.83, Z34.90 thru Z34.93 Not reimbursable with code 81224 for same date of service, recipient and provider May be billed separately with an appropriate National Correct Coding Initiative (NCCI) associated modifier Refer to the *Genetic Counseling and Screening* section for additional information	Once-in-a-lifetime
81221 CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; known familial variants	Yes	TAR requires documentation of the following criteria: • The Patient has a strong clinical presentation suspicious of CF, and • Family with known variant not included in the test for common variants	Once-in-a-lifetime
81222 CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; duplication/deletion variants	Yes	TAR requires a documentation of the following criteria: • The patient has a strong clinical presentation suspicious of CF, and • Gene test for common variants did not result in two disease-causing variants in CFTR	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81223 CFTR (cystic fibrosis transmembrane conductance regulator) (e.g., cystic fibrosis) gene analysis; full gene sequence	Yes	TAR requires documentation of the following criteria: • Patient has intermediate sweat chloride result, or • Patient with confirmed or suspected CF, with unknown genotype, and additional treatment or assessment of prognosis is contingent on the result of the test, or • Patient with normal sweat chloride results despite a strong clinical suspicion of CF	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)	No	When used to bill for cystic-fibrosis testing requires ICD-10-CM diagnosis code N46.9	Once-in-a-lifetime
81225 CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19), gene analysis, common variants	No	Billable with any valid ICD-10-CM diagnosis code	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81226 CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6), gene analysis, common variants	Yes	A TAR requires documentation that: • The patient is being treated with Tetrabenazine and requires a dose above 50 milligrams per day, or • The patient has Gaucher disease type 1 and is being considered for treatment with Eliglustat	Once-in-a-lifetime except with valid TAR override
81227 CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *5, *6)	Yes	A TAR requires documentation that the patient has a diagnosis of multiple sclerosis and is being considered for treatment with Siponimod	Once-in-a-lifetime except with valid TAR override
‹‹81232 DPYD (dihydropyrimidine dehydrogenase) gene analysis, common variant(s)	Yes	A TAR requires documentation of the following criteria: • Patient had severe and unexpected toxicity (such as myelosuppression, mucositis, diarrhea, neurotoxicity, cardiotoxicity) during treatment with Fluorouracil or Capecitabine chemotherapy.	Once-in-a-lifetime except with valid TAR override››
81233 BTK (Bruton's tyrosine kinase) gene analysis, common variants	No	One of the following ICD-10-CM codes is required on the claim (except with valid TAR): D80.0 thru D80.6, C91.10 thru C91.12, C83.00 thru C83.09	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81234 DMPK (DM1 protein kinase) gene analysis; evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81234 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for myotonic dystrophy type 1 (MD1), and • The patient requires the service as a diagnostic test for MD1	Once-in-a-lifetime except with valid TAR override
81235 EGFR (epidermal growth factor receptor) gene analysis, common variants	No	One of the following ICD-10-CM codes is required on the claim: C33, C34.00 thru C34.92	Once-in-a-lifetime
81236 EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) gene analysis, full gene sequence	No	One of the following ICD-10-CM codes is required on the claim (except with valid TAR): D47.1, D47.3, C83.30 thru C83.39	N/A
81237 EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) gene analysis, common variant(s)	No	One of the following ICD-10-CM codes is required on the claim (except with valid TAR): D47.1, D47.3, C83.30 thru C83.39	N/A
81238 F9 (coagulation factor IX) full gene analysis sequence	No	ICD-10-CM code D67 is required on the claim (except with valid TAR)	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81239 DMPK (DM1 protein kinase) gene analysis; characterization of alleles	Yes	A TAR for CPT code 81239 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for myotonic dystrophy type 1 (MD1), and The patient requires the service as a diagnostic test for MD1.	Once-in-a-lifetime except with valid TAR override
81243 FMR1 (fragile X mental retardation 1) gene analysis; evaluation to detect abnormal alleles	No	One of the following ICD-10-CM codes is required on the claim: F70, F71 thru F73, F78, F80.0 thru F84.2, F88, F89, H93.25, R48.2, R62.0, R62.50 thru R62.59	Once-in-a-lifetime
81244 FMR1 (fragile X mental retardation 1) gene analysis; characterization of alleles	No	One of the following ICD-10-CM codes is required on the claim: F70, F71 thru F73, F78, F80.0 thru F84.2, F88, F89, H93.25, R48.2, R62.0, R62.50 thru R62.59	Once-in-a-lifetime
81245 FLT3 (fms-related tyrosine kinase 3), gene analysis; internal tandem duplication (ITD) variants	No	One of the following ICD-10-CM codes is required on the claim: C92.00 thru C92.02, C92.60 thru C92.62 or C92.A0 thru C92.A2	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81246 FLT3 (fms-related tyrosine kinase 3), gene analysis; tyrosine kinase domain (TKD) variants	No	One of the following ICD-10-CM codes is required on the claim: C92.00 thru C92.02, C92.60 thru C92.62 or C92.A0 thru C92.A2	Once-in-a-lifetime
81250 G6PC (glucose-6-phosphatase, catalytic subunit) gene analysis, common variants	Yes	The patient has clinical features suspicious for, or requires the laboratory service as a diagnostic test for glycogen storage disease, type 1a	Once-in-a-lifetime
81256 HFE (hemochromatosis) gene analysis, common variants	No	One of the following ICD-10-CM codes is required on the claim: E83.10, E83.110 or E83.118 thru E83.119	Once-in-a-lifetime
81257 HBA1/HBA2 (alpha globin 1 and alpha globin 2), gene analysis; common deletions or variant	No	N/A	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81258 HBA1/HBA2 (alpha globin 1 and alpha globin 2), gene analysis; known familial variant	No	N/A	Once-in-a-lifetime
81259 HBA1/HBA2 (alpha globin 1 and alpha globin 2), gene analysis; full gene sequence	No	N/A	Once-in-a-lifetime
81260 IKBKAP (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinas complex-associated protein) gene analysis, common variants	Yes	Requires documentation on the TAR of: • Hypotonia in infancy • Decreased or absent deep tendon reflexes • Decreased taste and absence of fungiform papillae of the tongue • Absence of overflow tears with emotional crying (alacrima) • Absence of axon flare response after intradermal histamine injection • Pupillary hypersensitivity to parasympathomimetic agents	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81265 Comparative analysis using Short Tandem Repeat markers	No	One of the following ICD-10-CM codes is required on the claim: C81.00 thru C96.9, D45, T86.00 thru T86.09 or T86.5	Once-in-a-lifetime
81266 Comparative analysis using Short Tandem Repeat markers; each additional specimen	No	One of the following ICD-10-CM codes is required on the claim: C81.00 thru C96.9, D45, T86.00 thru T86.09 or T86.5	Once-in-a-lifetime
81267 Chimerism (engraftment) analysis, post transplantation specimen; without cell selection	No	One of the following ICD-10-CM codes is required on the claim: T86.01, T86.02, T86.09 or T86.5	N/A
81268 Chimerism (engraftment) analysis, post transplantation specimen; with cell selection	No	One of the following ICD-10-CM codes is required on the claim: T86.01, T86.02, T86.09 or T86.5	N/A
81269 HBA1/HBA2 (alpha globin 1 and alpha globin 2), gene analysis; duplication/deletion variants	No	N/A	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81270 JAK2 (Janus kinase 2) gene analysis, p. Val617Phe (V617F) variant	No	One of the following ICD-10-CM codes is required on the claim: C91.00 thru C91.02, D45, D47.1 or D47.3	Once-in-a-lifetime
81271 HTT (huntingtin) gene analysis; evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81271 requires documentation of the following criteria: • For adults, the patient has unequivocal motor signs of Huntington's disease (HD) and requires the service to confirm the diagnosis • For children, the patient has a family history of HD and develops symptoms that raise the suspicion for juvenile-onset HD as exemplified by two or more of the following: – Declining school performance – Seizures – Oral motor dysfunction – Rigidity – Gait disturbance	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81272 KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog), gene analysis, targeted sequence analysis	No	One of the following ICD-10-CM codes is required on the claim: C43.70, C92.00 thru C92.02, C92.40 thru C92.42, C92.50 thru C92.52, D03.70 thru D03.72 or D48.1	Once-in-a-lifetime
81273 KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog), gene analysis, D816 variant(s)	No	One of the following ICD-10-CM codes is required on the claim: C96.20 thru C96.29	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81274 HTT (huntingtin) gene analysis; characterization of alleles	Yes	A TAR for CPT code 81274 requires documentation of the following criteria: • For adults, the patient has unequivocal motor signs of Huntington's disease (HD) and requires the service to confirm the diagnosis • For children, the patient has a family history of HD and develops symptoms that raise the suspicion for juvenile-onset HD as exemplified by two or more of the following: – Declining school performance – Seizures – Oral motor dysfunction – Rigidity – Gait disturbance	Once-in-a-lifetime except with valid TAR override
81275 KRAS (Kirsten rat sarcoma viral oncogene homolog) gene analysis; variants in exon 2	No	One of the following ICD-10-CM codes is required on the claim: C18.0 thru C20, D01.1, D01.2, D01.40, D01.49, D37.4 or D37.5	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81276 KRAS (Kristen rat sarcoma viral oncogene homolog) gene analysis; additional variant(s)	No	One of the following ICD-10-CM codes is required on the claim: C18.0, C18.2 thru C20, D01.1, D01.2, D01.40, D01.49, D37.4 or D37.5	Once-in-a-lifetime
81278 IGH @/BLC2 (t[4; 18]) (e.g., follicular lymphoma)translocation analysis, major breakpoint region (MBR) and minor cluster region (mcr) breakpoints, qualitative or quantitative	Yes	A TAR for CPT code 81278 requires documentation of the following criteria: The patient has clinical features suspicious for, or requires the service as a diagnostic test for follicular lymphoma	Once in a lifetime
81279 JAK2 (Janus kinase 2) (e.g., myeloproliferative disorder) gene analysis, (e.g., exons 12 and 13)	No	One of the following ICD-10-CM codes is required on the claim: C91.00 thru C91.02, D45, D47.1 or D47.3	N/A

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81283 IFNL3 (interferon, lambda 3), gene analysis, rs12979860 variant	No	ICD-10-CM code B18.2 is required on the claim (except with valid TAR)	Once-in-a-lifetime
81284 FXN (frataxin) gene analysis; evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81284 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for Friedreich ataxia (FRDA), and • The patient requires the service as a confirmatory test for FRDA	Once-in-a-lifetime except with valid TAR override
81285 FXN (frataxin) gene analysis; characterization of alleles	Yes	A TAR for CPT code 81285 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for Friedreich ataxia (FRDA), and • The patient requires the service as a confirmatory test for FRDA	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81286 FXN (frataxin) gene analysis; full gene sequence	Yes	A TAR for CPT code 81286 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for Friedreich ataxia (FRDA), and The patient requires the service as a confirmatory test for FRDA	Once-in-a-lifetime except with valid TAR override
81287 MGMT (O-6 methylguanin-DNA methyltransferase) methylation analysis	Yes	Document on the TAR: • The patient has the diagnosis of glioblastoma multiforme, and • Treatment strategy will be contingent on the test results	Once-in-a-lifetime, any provider
81288 MLH1 gene analysis; promoter methylation analysis	Yes	Document the following criteria on the TAR: • Patient with cancer(s) associated with Lynch Syndrome, and • The tumor demonstrates microsatellite instability or immunohistochemistry results indicating loss of MLH1 protein expression	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81289 FXN (frataxin) gene analysis; known familial variant(s)	Yes	A TAR for CPT code 81289 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for Friedreich ataxia (FRDA), and • The patient requires the service as a confirmatory test for FRDA	Once-in-a-lifetime except with valid TAR override
81292 MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) gene analysis; full sequence analysis	No	One of the following ICD-10-CM codes is required on the claim: C17.0 thru C20, C24.0 thru C25.9, C54.0 thru C54.9, C65.1 thru C66.9, C71.0 thru C71.9, D23.0 thru D23.9, Z80.0, Z80.49, Z85.030, Z85.038, Z85.040, Z85.048, Z85.42	Once-in-a-lifetime
81293 MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) gene analysis; known familial variants	Yes	Document on the TAR family history of Lynch Syndrome that includes a relative with a known deleterious MLH1 mutation	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81294 MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) gene analysis; duplication/deletion variants	No	One of the following ICD-10-CM codes is required on the claim: C17.0 thru C20, C24.0 thru C25.9, C54.0 thru C54.9, C65.1 thru C66.9, C71.0 thru C71.9, D23.0 thru D23.9, Z80.0, Z80.49. Z85.030, Z85.038, Z85.040, Z85.048, Z85.42	Once-in-a-lifetime
81295 MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) gene analysis; full sequence analysis	No	One of the following ICD-10-CM codes is required on the claim: C17.0 thru C20, C24.0 thru C25.9, C54.0 thru C54.9, C65.1 thru C66.9, C71.0 thru C71.9, D23.0 thru D23.9, Z80.0, Z80.49, Z85.030, Z85.038, Z85.040, Z85.048, Z85.42	Once-in-a-lifetime
81296 MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) gene analysis; known familial variants	Yes	Document on the TAR family history of Lynch Syndrome that includes a relative with a known deleterious MSH2 mutation	Once-in-a-lifetime
81297 MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) gene analysis; duplication/deletion variants	No	One of the following ICD-10-CM codes is required on the claim: C17.0 thru C20, C24.0 thru C25.9, C54.0 thru C54.9, C65.1 thru C66.9, C71.0 thru C71.9, D23.0 thru D23.9, Z80.0, Z80.49. Z85.030, Z85.038, Z85.040, Z85.048, Z85.42	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81298 MSH6 (mutS homolog 6 [E. coli]) gene analysis; full sequence analysis	No	One of the following ICD-10-CM codes is required on the claim: C17.0 thru C20, C24.0 thru C25.9, C54.0 thru C54.9, C65.1 thru C66.9, C71.0 thru C71.9, D23.0 thru D23.9, Z80.0, Z80.49, Z85.030, Z85.038, Z85.040, Z85.048, Z85.42	Once-in-a-lifetime
81299 MSH6 (mutS homolog 6 [E. coli]) gene analysis; known familial variants	Yes	Document on the TAR family history of Lynch Syndrome that includes a relative with a known deleterious MSH6 mutation	Once-in-a-lifetime
81300 MSH6 (mutS homolog 6 [E. coli]) gene analysis; duplication/deletion variants	No	One of the following ICD-10-CM codes is required on the claim: C17.0 thru C20, C24.0 thru C25.9, C54.0 thru C54.9, C65.1 thru C66.9, C71.0 thru C71.9, D23.0 thru D23.9, Z80.0, Z80.49. Z85.030, Z85.038, Z85.040, Z85.048, Z85.42	Once-in-a-lifetime
81301 Microsatellite instability analysis of markers for mismatch repair deficiency, includes comparison of neoplastic and normal tissue, if performed	No	Reimbursable for patients who meet one of the following criteria: the patient is diagnosed with one of the Lynch syndrome-associated cancers; or, the patient is diagnosed with an unresectable or metastatic solid tumor and the treatment will be contingent on the test result.	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81305 MYD88 (myeloid differentiation primary response 88) (gene analysis, p.Leu265Pro (L265P) variant	No	The following ICD-10-CM code is required on the claim (except with valid TAR): C88.0	Once-in-a-lifetime except with valid TAR override
81306 NUDT15 (nudix hydrolase 15) gene analysis, common variant(s)	Yes	A TAR for CPT code 81306 requires documentation of the following criteria: • The patient is undergoing thiopurine therapy, and • The patient has severe or prolonged myelosuppression.	Once-in-a-lifetime except with valid TAR override
81309 PIK3CA gene analysis, targeted sequence analysis	Yes	A TAR/SAR for CPT code 81309 requires documentation of the following criteria: • The patient has confirmed diagnosis of breast cancer • Treatment is contingent on the result of the test	Once-in-a-lifetime
81310 NPM1 (nucleophosmin) gene analysis, exon 12 variants	No	One of the following ICD-10-CM codes is required on the claim: C92.00 thru C92.02	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81311 NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) gene analysis, variants in exon 2 and exon 3	No	One of the following ICD-10-CM codes is required on the claim: C18.0, C18.2 thru C20, D01.1, D01.2, D01.40, D01.49, D37.4 or D37.5	Once-in-a-lifetime
81312 PABPN1 (poly[A] binding protein nuclear 1) gene analysis, evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81312 requires documentation of the following criteria: • The patient has symptoms of ptosis and dysphagia, and • The patient requires the service as a confirmatory test for Oculopharyngeal Muscular Dystrophy	Once-in-a-lifetime except with valid TAR override
81314 PDGFRA (platelet-derived growth factor receptor, alpha polypeptide), gene analysis, targeted sequence analysis	No	ICD-10-CM code D48.1 is required on the claim.	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81315 PML/RAR-alpha (promyelocytic leukemia/retinoic acid receptor alpha) translocation analysis; common breakpoints	No	One of the following ICD-10-CM codes is required on the claim: C92.40 thru C92.42	N/A
81316 PML/RAR-alpha (promyelocytic leukemia/retinoic acid receptor alpha) translocation analysis; single breakpoint	No	One of the following ICD-10-CM codes is required on the claim: C92.40 thru C92.42	N/A
81317 PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) gene analysis; full sequence analysis	No	One of the following ICD-10-CM codes is required on the claim: C17.0 thru C20, C24.0 thru C25.9, thru C54.0 thru C54.9, C65.1 thru C66.9, C71.0 thru C71.9, D23.0 thru D23.9, Z80.0, Z80.49, Z85.030, Z85.038, Z85.040, Z85.048, Z85.42	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81318 PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) gene analysis; known familial variants	Yes	Document on the TAR family history of Lynch Syndrome that includes a relative with a known deleterious PMS2 mutation	Once-in-a-lifetime
81319 PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) gene analysis; duplication/deletion variants	No	One of the following ICD-10-CM codes is required on the claim: C17.0 thru C20, C24.0 thru C25.9, C54.0 thru C54.9, C65.1 thru C66.9, C71.0 thru C71.9, D23.0 thru D23.9, Z80.0, Z80.49. Z85.030, Z85.038, Z85.040, Z85.048, Z85.42	Once-in-a-lifetime
81320 PLCG2 (phospholipase C gamma 2) gene analysis, common variants	No	One of the following ICD-10-CM codes is required on the claim (except with valid TAR): C91.10 thru C91.12	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81321 PTEN (phosphatase and tensin homolog) gene analysis; full sequence analysis	Yes	A TAR for CPT code 81321 requires documentation of one or more of the following numbered criteria: 1. Individual with a personal history of: Bannayan-Riley-Ruvalcaba syndrome, or – Adult Lhermitte-Duclos disease, or – Autism spectrum disorder AND macrocephaly, or – Two or more biopsy-proven trichilemmomas, or – Two or more major criteria (one macrocephaly), or – Three major criteria without macrocephaly, or – One major and three or more minor criteria, or – Four or more minor criteria (please see list below) At-risk individual: With a relative who has a clinical diagnosis of Cowden syndrome or Bannayan-Riley-Ruvalcaba syndrome for whom testing has not been performed AND who has any one major criterion or two minor criteria *(continued on next page)*	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81321 PTEN gene analysis; full sequence analysis	Yes	Major Criteria • Breast cancer • Mucocutaneous lesions • One biopsy-proven trichilemmoma • Multiple palmoplantar keratosis • Multifocal or extensive oral mucosal papillomatosis • Multiple cutaneous facial papules (often verrucous) • Macular pigmentation of glans penis • Macroencephaly (megalocephaly, ie, ≥97th percentile) • Endometrial cancer • Non-medullary thyroid cancer • Multiple GI tract hamartomas or ganglioneuromas *(continued on next page)*	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81321 PTEN gene analysis; full sequence analysis	Yes	Minor Criteria • Other thyroid lesions (adenoma, nodule, goiter) • Mental retardation (IQ ≤75) • Autism spectrum disorder • Single GI tract hamartoma or ganglioneuroma • Fibrocystic disease of the breast • Lipomas • Fibromas • Renal cell carcinoma • Uterine fibroids	Once-in-a-lifetime
81322 PTEN gene analysis; known familial variant	Yes	Requires documentation on the TAR that patient is from a family with a known PTEN mutation	Once-in-a-lifetime
81323 PTEN gene analysis; duplication/deletion variant	Yes	Requires documentation on the TAR of a negative result in the full sequence analysis in PTEN (CPT code 81321), and that patient meets one or more criteria listed under code 81321	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81329 SMN1 (survival of motor neuron 1, telomeric) gene analysis; dosage/deletion analysis, includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed	No	One of the following ICD-10-CM diagnosis codes is required on the claim (except with valid TAR): O09.00 thru O09.93, Z31.430, Z31.440, Z31.5, Z34.00 thru Z34.03, Z34.80 thru Z34.83, Z34.90 thru Z34.93,	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81331 SNRPN/UBE3A methylation analysis	Yes	Document the following age-specific criteria on the TAR • Birth to two years: Hypotonia with poor suck • Two to six years: Hypotonia with history of poor suck and global development delay • Six to 13 years: History of hypotonia with poor suck (hypotonia often persists); global development delay; and excessive eating (hyperphagia; obsession with food) with central obesity if uncontrolled • 13 years to adult: Cognitive impairment – usually mild mental retardation; excessive eating (hyperphagia; obsession with food) with central obesity if uncontrolled; and hypothalamic hypogonadism and/or typical behavior problems (including temper tantrums and obsessive-compulsive features)	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81334 RUNX1 (runt related transcription factor 1), gene analysis, targeted sequence analysis	No	One of the following ICD-10-CM codes is required on the claim (except with valid TAR): C92.00 thru C92.02, C92.40 thru C92.A2	Once-in-a-lifetime
81335 TPMT (thiopurine S-methyltransferase), gene analysis, common variants	Yes	The service requires a TAR with documentation of the following criteria: • That the patient is undergoing thiopurine therapy, and • The patient has severe or prolonged myelosuppression.	Once-in-a-lifetime
81336 SMN1 (survival of motor neuron 1, telomeric) gene analysis; full gene sequence	Yes	A TAR for CPT code 81336 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for spinal muscular atrophy, and • The patient requires the service as a confirmatory test for spinal muscular atrophy	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81337 SMN1 (survival of motor neuron 1, telomeric) gene analysis; known familial sequence variant(s)	Yes	A TAR for CPT code 81337 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for spinal muscular atrophy, and The patient requires the service as a confirmatory test for spinal muscular atrophy	Once-in-a-lifetime except with valid TAR override
81338 MPL (MPL proto-oncogene, thrombopoietin receptor) (eg, myeloproliferative disorder) gene analysis; common variants (eg, W515A, W515K, W515L, W515R)	Yes	A TAR for CPT code 81338 requires documentation of the following criteria: • The patient has clinical features suspicious for, or requires the service as a diagnostic test for myeloproliferative disorder	N/A

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81339 MPL (MPL proto-oncogene, thrombopoietin receptor) (eg, myeloproliferative disorder) gene analysis; sequence analysis, exon 10	Yes	A TAR for CPT code 81339 requires documentation of the following criteria: The patient has clinical features suspicious for, or requires the service as a diagnostic test for myeloproliferative disorder	N/A
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)	Yes	A TAR for CPT code 81340 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for lymphoma and requires the service as a confirmatory test for lymphoma; or The test is used to aid in classification of lymphomas	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
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)	Yes	A TAR for CPT code 81341 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for lymphoma and requires the service as a confirmatory test for lymphoma; or The test is used to aid in classification of lymphomas	Once-in-a-lifetime
81342 TRG@ (T cell antigen receptor, gamma) (eg, leukemia and lymphoma), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)	Yes	A TAR for CPT code 81342 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for lymphoma and requires the service as a confirmatory test for lymphoma; or • The test is used to aid in classification of lymphomas	Once-in-a-lifetime

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81343 PPP2R2B (protein phosphatase 2 re.g.ulatory subunit Bbeta) gene analysis, evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81343 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for spinocerebellar ataxia type 12 (SCA12), and • The patient requires the service as a confirmatory test for SCA12	Once-in-a-lifetime except with valid TAR override
81344 TBP (TATA box binding protein) gene analysis, evaluation to detect abnormal alleles	Yes	A TAR for CPT code 81344 requires documentation of the following criteria: • The patient has clinical signs or symptoms suspicious for spinocerebellar ataxia type 17 (SCA17), and • The patient requires the service as a confirmatory test for SCA17	N/A
81345 TERT (telomerase reverse transcriptase) gene analysis, targeted sequence analysis	Yes	A TAR for CPT code 81345 requires documentation of the following criteria: • The patient has the diagnosis of grade II, III or IV glioma.	Once-in-a-lifetime except with valid TAR override

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
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)	No	One of the following ICD-10-CM codes is required on the claim C92.00 thru C92.02, D46.0, D46.1, D46.20, D46.21, D46.22, D46.A, D46.B, D46.C, D46.4, D46.Z, D46.9.	N/A
81348 SRSF2 (serine and arginine-rich splicing factor 2) (e.g., myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variants (e.g., P95H, P95L)	No	One of the following ICD-10-CM codes is required on the claim C92.00 thru C92.02, D46.0, D46.1, D46.20, D46.21, D46.22, D46.A, D46.B, D46.C, D46.4, D46.Z, D46.9.	N/A

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81351 TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome) gene analysis; full gene sequence	Yes	A TAR for CPT code 81351 requires documentation for one of the following numbered criteria: 1. All of the following conditions: • The patient has sarcoma diagnosed before 45 years of age, and • A first-degree relative with any cancer before 45 years of age, and • A first or second-degree relative with any cancer before 45 years of age, or a sarcoma at any age; or 2. All of the following conditions: • A tumor belonging to the Li-Fraumeni Syndrome (LFS) tumor spectrum (soft tissue sarcoma, osteosarcoma, pre-menopausal breast cancer, brain tumor, adrenocortical carcinoma, leukemia or lung bronchoalveolar cancer) before 46 years of age, and (continued)	N/A

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81351 TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome) gene analysis; full gene sequence (continued)	Yes	• At least one first or second-degree relative with an LFS tumor (except breast cancer if the patient has breast cancer) before 56 years of age or with multiple tumors; or 3. The patient has multiple tumors (except multiple breast tumors), two of which belong to the LFS tumor spectrum, and the first occurred before 46 years of age; or 4. The patient is diagnosed with adrenocortical carcinoma or choroid plexus tumor	N/A
81352 TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome) gene analysis; targeted sequence analysis (e.g., 4 oncology)	Yes	See CPT code 81351 for TAR criteria and billing requirements.	N/A

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81353 TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome) gene analysis; known familial variant	Yes	See CPT code 81351 for TAR criteria and billing requirements.	N/A
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)	No	One of the following ICD-10-CM codes is required on the claim C92.00 thru C92.02, D46.0, D46.1, D46.20, D46.21, D46.22, D46.A, D46.B, D46.C, D46.4, D46.Z, D46.9.	N/A
81360 ZRSR2 (zinc finger CCCH-type, RNA binding motif and serine/argine-rich 2) (e.g., myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variant(s) (e.g., E65fs, E122fs, R448fs)	No	One of the following ICD-10-CM codes is required on the claim C92.00 thru C92.02, D46.0, D46.1, D46.20, D46.21, D46.22, D46.A, D46.B, D46.C, D46.4, D46.Z, D46.9.	N/A

Molecular Pathology CPT Codes, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81361 HBB (hemoglobin, subunit beta); common variant(s) (e.g., HbS, HbC, HbE)	No	N/A	Once-in-a-lifetime
81362 HBB (hemoglobin, subunit beta); known familial variant(s)	No	N/A	Once-in-a-lifetime
81363 HBB (hemoglobin, subunit beta); duplication/deletion variant(s)	No	N/A	Once-in-a-lifetime
81364 HBB (hemoglobin, subunit beta); full gene sequence	No	N/A	Once-in-a-lifetime

Human Platelet Antigen Genotyping ICD-10-CM Diagnosis Codes

When billing for the following Tier 1 Molecular Pathology CPT codes, ICD-10-CM diagnosis codes D69.51 and P61.0 are required.

CPT Codes

81105	81109
81106	81110
81107	81111
81108	81112

Tier 2, Molecular Pathology Procedure, Level 1

Coverage for CPT code 81400 (molecular pathology procedure, Level 1) is limited to the listed services. Reimbursement for code 81400 requires an approved *Treatment Authorization Request* (TAR), is limited to once in a lifetime and requires providers to document one of the following on the TAR:

- CCR5 (chemokine C-C motif receptor 5):
  - Initial test:
    - The use of a CCR5 inhibitor is being considered, or
    - The patient exhibits virologic failure on a CCR5 inhibitor
  - Subsequent tests:
    - A previous Trofile test was performed including the test date and the results showing that the patient has a CCR5 virus, and,
    - The patient's previous Trofile test was not less than 90 days from subsequent request, and,
    - The patient has clinical scenario such as, but not limited to the following:
      - The treatment with CCR5 antagonist drug therapy was interrupted and the clinician wishes to reinstitute CCR5 antagonist drug therapy, or,
      - The patient had a Trofile test performed previously that showed that the patient had the CCR5 virus, but the CCR5 antagonist drug therapy was never initiated.

Tier 2, Molecular Pathology Procedure, Level 2

Coverage for CPT code 81401 (molecular pathology procedure, Level 2) is limited to the listed services. Reimbursement for code 81401 requires an approved TAR and requires providers to document one of the following on the TAR:

- ABCC8 (familial hyperinsulinism):
  - The patient has persistent hyperinsulinemic hypoglycemia of infancy (PHHI), failed medical therapy, and
  - The patient is under evaluation for surgical intervention
- ABL (c-abl oncogene 1, receptor tyrosine kinase) – The patient has chronic myeloid leukemia (CML) and failed tyrosine kinase inhibitor (TKI) therapy
- ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase) (e.g., acquired imatinib resistance), T315I variant – The patient has chronic myeloid leukemia (CML) and failed tyrosine kinase inhibitor (TKI) therapy.
- APOE (apolipoprotein E) (for example, hyperlipoproteinemia type III, cardiovascular disease, Alzheimer disease), common variants (for example, 2, 3, 4)
  - The patient has clinical signs and symptoms consistent with Alzheimer Disease, and
  - Medical treatment strategy will be contingent on the test results.
- DEK/NUP214 (t [6; 9])(for example:. acute myeloid leukemia), translocation analysis, qualitative, and quantitative, if performed – The patient has acute myeloid leukemia and the test is intended for the process of risk stratification
- E2A/PBX1 (acute lymphocytic leukemia):
  - The patient has the diagnosis of acute lymphocytic/lymphoblastic leukemia, and
  - Treatment or monitoring strategy will be contingent on the test results
- ETV6/RUNX1 (acute lymphocytic leukemia) – The patient has the diagnosis of acute lymphocytic or lymphoblastic leukemia and requires the test for assessment of cancer prognosis.
- H19 (Beckwith-Wiedemann syndrome) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for Beckwith-Wiedemann syndrome.
- KCNQ1OT1 (Beckwith-Wiedemann syndrome) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for Beckwith-Wiedemann syndrome.

- MLL/AFF1 (acute lymphoblastic leukemia):
  - The patient has the diagnosis of acute lymphoblastic leukemia, and
  - Treatment or monitoring strategy will be contingent on the test results
- MLL/MLLT3 (acute myeloid leukemia):
  - The patient has the diagnosis of acute myeloid leukemia, and
  - Treatment or monitoring strategy will be contingent on the test results
- MUTYH (MYH-associated polyposis) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for MUTYH-associated polyposis.
- MT-ATP6 (neuropathy with ataxia and retinitis pigmentosa [NARP], Leigh syndrome) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for NARP or Leigh syndrome.
- PRSS1 (hereditary pancreatitis):
  - An unexplained documented episode of acute pancreatitis in childhood, or
  - Recurrent acute attacks of pancreatitis of unknown cause, or
  - Chronic pancreatitis of unknown cause, particularly with onset younger than 25 years of age, or
  - A family history of recurrent acute pancreatitis, chronic pancreatitis of unknown cause, and/or childhood pancreatitis of unknown cause consistent with autosomal dominant inheritance
- PYGM (glycogen storage disease type V, McArdle disease) – The patient has clinical features suspicious for or requires the service as a confirmatory test for glycogen storage disease type V (McArdle disease).
- RUNX1/RUNX1T1 (t[8;21]) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for acute myeloid leukemia.

Tier 2, Molecular Pathology Procedure, Level 3

Coverage for CPT code 81402 (molecular pathology procedure, Level 3) is limited to the listed services. Reimbursement for code 81402 requires an approved TAR and requires providers to document one of the following on the TAR:

- Chromosome 1p-/19q- (e.g., glial tumors), deletion analysis – Patient with diagnosis of grade II, III or IV glioma
- MEFV (Mediterranean fever) (eg, familial Mediterranean fever), common variants:
  - The patient has clinical signs and symptoms suspicious for familial MEFV, and
  - The patient requires the service as a confirmatory test for familial MEFV

Tier 2, Molecular Pathology Procedure, Level 4

Coverage for CPT code 81403 (molecular pathology procedure, Level 4) is limited to the listed services. Reimbursement for code 81403 requires an approved TAR and requires providers to document one of the following on the TAR:

- DNMT3A (acute myeloid leukemia):
  - The patient has diagnosis of acute myeloid leukemia, and
  - The treatment strategy will be contingent on test results
- EPCAM (Lynch syndrome) – The patient has one of the following:
  - Colon cancer
  - Uterine cancer
  - Lynch syndrome
  - Family history of colorectal cancer, uterine cancer or Lynch syndrome
  - Presence of synchronous, metachronous colorectal or other Lynch-associated tumors
- KCNC3 (spinocerebellar ataxia) – The patient has clinical features suspicious for or requires the service as a confirmatory test for spinocerebellar ataxia.
- KCNJ11 (familial hyperinsulinism) – TAR may be approved based on one of the following criteria:
  - For persistent hyperinsulinemic hypoglycemia of infancy (PHHI):
    - ❖ The patient has PHHI and failed medical therapy, and
    - ❖ The patient is under evaluation for surgical intervention

  - For suspected developmental delay, epilepsy and neonatal diabetes (DEND) syndrome:
    - ❖ The patient has developmental delay, epilepsy and neonatal diabetes
    - ❖ The confirmation of the diagnosis and the treatment strategy is contingent on the test result
- KIR (killer cell immunoglobulin-like receptor for hematopoietic stem cell transplantation):
  - The patient has diagnosis of acute myeloid leukemia or multiple myeloma, and
  - The test is used for donor search process for patients considering hematopoietic stem cell transplantation
- Known family variant not otherwise specified, for gene listed in Tier 1 or Tier 2, or identified during a genomic sequencing procedure (GSP), DNA sequence analysis, each variant exon:
  - Documentation of the specific gene listed in Tier 1, Tier 2 or GSP for which further analysis is being requested
- MICA (solid organ transplantation):
  - The patient is undergoing evaluation for kidney transplantation, or
  - The patient is post kidney transplantation
- NDP (Norrie disease) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for Norrie disease
- SH2D1A (X-linked lymphoproliferative syndrome) – The patient is a male with the diagnosis of:
  - Common variable immune deficiency, or
  - Hypogammaglobulinemia, or
  - Hemophagocytic lymphohistiocytosis, or
  - Severe infectious mononucleosis, or
  - Lymphoma, or
  - Family history of X-linked lymphoproliferative syndrome
- VHL (von Hippel-Lindau tumor suppressor), deletion/duplication analysis – The patient has clinical features suspicious for, or requires the service as a diagnostic test for von Hippel-Lindau syndrome.

Tier 2, Molecular Pathology Procedure, Level 5

Coverage for CPT code 81404 (molecular pathology procedure, Level 5) is limited to the listed services. Reimbursement for code 81404 requires an approved *Treatment Authorization Request* (TAR) and requires providers to document one of the following on the TAR:

- ACADS (acyl-CoA dehydrogenase, C-2 to C-3 short chain), targeted sequence analysis:
  - The patient has elevated C4-C on newborn screening test, and
  - Confirmation (urine acylglycines or urine organic acids) that C4 (butyrylcarnitine) and/or ethylmalonic acid (EMA) are elevated
- CD40LG (X-linked hyper IgM syndrome) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for hyperimmunoglobulin M syndromes.
- EMD (Emery-Dreifuss muscular dystrophy) – The patient has clinical features suspicious for or requires the service as a confirmatory test for Emery-Dreifuss muscular dystrophy.
- EPM2A (progressive myoclonus epilepsy) – The patient has clinical features suspicious for or requires the service as a confirmatory test for progressive myoclonus epilepsy.
- FHL1 (Emery-Dreifuss muscular dystrophy) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for Emery-Dreifuss muscular dystrophy.
- MEFV (Mediterranean fever) (eg, familial Mediterranean fever), full gene sequence:
  - The patient has clinical signs and symptoms suspicious for familial MEFV, and
  - The patient requires the service as a confirmatory test for familial MEFV
- NDP (Norrie disease) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for Norrie disease.
- PDX1 (pancreatic and duodenal homeobox 1):
  - The patient requires the service as a diagnostic test for (maturity onset diabetes of the young) MODY, and
  - Is younger than 25 years of age, and
  - Has a family history of diabetes, and
  - Has negative islet of autoantibodies

- PRNP (genetic prion disease) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for genetic prion disease.
- PRSS1 (hereditary pancreatitis):
  - An unexplained documented episode of acute pancreatitis in childhood, or
  - Recurrent acute attacks of pancreatitis of unknown cause, or
  - Chronic pancreatitis of unknown cause, particularly with onset younger than 25 years of age, or
  - A family history of recurrent acute pancreatitis, chronic pancreatitis of unknown cause, and/or childhood pancreatitis of unknown cause consistent with autosomal dominant inheritance
- RET (ret proto-oncogen), common variants
  - The patient has a personal history of primary C cell hyperplasia, Medullary Thyroid Carcinoma (MTC), or Multiple Endocrine Neoplasia (MEN), type 2B, or
  - The patient has a family history consistent with MEN, type 2B or MTC, and at risk for autosomal dominant inheritance of the syndrome
- SH2D1A (X-linked lymphoproliferative syndrome) – The patient is a male with the diagnosis of:
  - Common variable immune deficiency, or
  - Hypogammaglobulinemia, or
  - Hemophagocytic lymphohistiocytosis, or
  - Severe infectious mononucleosis, or
  - Lymphoma, or
  - Family history of X-linked lymphoproliferative syndrome
- SOD1 (superoxide dismutase 1, soluble) (e.g., amyotrophic lateral sclerosis), full gene sequence:
  - The patient requires the service as a confirmatory test for Amyotrophic Lateral Sclerosis (ALS) when the diagnosis is not clear, or
  - The patient has a diagnosis of ALS and is being considered for treatment with Tofersen.

- SPINK1 (hereditary pancreatitis):
  - An unexplained documented episode of acute pancreatitis in childhood, or
  - Recurrent acute attacks of pancreatitis of unknown cause, or
  - Chronic pancreatitis of unknown cause, particularly with onset younger than 25 years of age, or
  - A family history of recurrent acute pancreatitis, chronic pancreatitis of unknown cause, and/or childhood pancreatitis of unknown cause consistent with autosomal dominant inheritance
- UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (e.g., hereditary unconjugated hyperbilirubinemia [Crigler-Najjar syndrome]) full gene sequence
  - The patient has clinical features suspicious for or requires the service as a confirmatory test for Crigler-Najjar syndrome
- VHL (von Hippel-Lindau tumor suppressor), full gene sequence – the patient has clinical features suspicious for or requires the service as a diagnostic test for von Hippel-Lindau syndrome.

Tier 2, Molecular Pathology Procedure, Level 6

Coverage for CPT code 81405 (molecular pathology procedure level 6) is limited to the listed services. Reimbursement for code 81405 requires an approved TAR and requires providers to document one of the following on the TAR:

- ABCD1 (adrenoleukodystrophy):
  - The patient has clinical features suspicious for adrenoleukodystrophy, and
  - The service is required as a confirmatory test for the diagnosis of adrenoleukodystrophy
- ACADS (acyl-CoA dehydrogenase, C-2 to C-3 short chain), full gene sequence:
  - The patient has elevated C4-C on newborn screening test, and
  - Confirmation (urine acylglycines or urine organic acids) that C4 (butyrylcarnitine) and/or ethylmalonic acid (EMA) are elevated
- CPOX (coproporphyrinogen oxidase), full gene sequence:
  - The patient has elevated urinary and fecal coproporphyrin III, and
  - The patient requires the service as a confirmatory test for hereditary coproporphyria
- CTRC (chymotrypsin C) (e.g, hereditary pancreatitis), full gene sequence:
  - The patient has an unexplained documented episode of acute pancreatitis in childhood, or
  - Recurrent acute attacks of pancreatitis of unknown cause, or
  - Chronic pancreatitis of unknown cause, particularly with onset younger than 25 years of age, or
  - A family history of recurrent acute pancreatitis, chronic pancreatitis of unknown cause, and/or childhood pancreatitis of unknown cause consistent with autosomal dominant inheritance
- EMD (Emery-Dreifuss muscular dystrophy) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for Emery-Dreifuss muscular dystrophy
- FH (fumarate hydratase) (for example., fumarate hydratase deficiency, hereditary leiomyomatosis with renal cell cancer), full gene sequence:
  - The patient presents with clinical symptoms and history suspicious for Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC), which may include one of the criteria below:

- ❖ Multiple cutaneous leiomyomas, with at least one histologically confirmed lesion
- ❖ Solitary cutaneous leiomyoma and family history of HLRCC
- ❖ Presentation of severely symptomatic uterine fibroids before age 40
- ❖ Presentation of Type II papillary renal cell cancer before age 40
- ❖ Family history of first-degree family member meeting one of the above-mentioned criteria; and

– The patient requires the service as a confirmatory test for HLRCC

- GLA (galactosidase alpha [for example, Fabry disease]), full gene sequence:
  - The patient has a family member with documented disease-causing mutation, and
  - The decision whether to initiate enzyme replacement therapy will be contingent on the results
- HNF1A (HNF1 homeobox A)
  - The patient requires the service as a diagnostic test for MODY, and
  - Is younger than 25 years of age, and
  - Has a family history of diabetes, and
  - Has negative islet of autoantibodies
- HNF1B (HNF1 homeobox B)
  - The patient requires the service as a diagnostic test for MODY, and
  - Is younger than 25 years of age, and
  - Has a family history of diabetes, and
  - Has negative islet of autoantibodies
- LAMP2 (Danon disease) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for glycogen storage disease IIb (Danon disease)
- NF2 (neurofibromatosis, type 2):
  - The patient has clinical features suspicious for, or requires the service as a confirmatory test for type 2 neurofibromatosis, OR
  - The patient is at high risk for neurofibromatosis with one or more of the following:
    - ❖ A first-degree relative with type 2 neurofibromatosis
    - ❖ Multiple spinal tumors (schwannomas, meningiomas)
    - ❖ Cutaneous schwannomas

- ❖ Sporadic vestibular schwannoma younger than 30 years of age, or spinal tumor or meningioma younger than 20 years of age

- NPHS2 (steroid resistant nephrotic syndrome [SRNS])
  - The patient has clinical diagnosis of SRNS, and
  - Treatment will be contingent on the test results
- OTC (ornithine transcarbamylase deficiency) – The patient has clinical signs and symptoms of urea cycle disorders with positive biochemical laboratory results and requires the service as a confirmatory test for ornithine transcarbamylase deficiency
- PKLR (pyruvate kinase, liver and RBC), full gene sequence – The patient has clinical features suspicious for, or requires the service as a confirmatory test for pyruvate kinase deficiency
- RET (multiple endocrine neoplasia [MEN], type 2A and familial medullary thyroid carcinoma [MTC]) – exons 10, 11, 13 - 16:
  - The patient has a personal history of MTC, or MEN, type 2A, or
  - The patient has pheochromocytoma and a family history of MTC or pheochromocytoma, or
  - The patient has sporadic MEN2-related tumors and is younger than 35 years of age, multicentric tumors in one organ, and/or two different organs affected, or
  - The patient has a family history consistent with MEN, type 2A
- RET (ret proto-oncogen), targeted sequence analysis:
  - The patient has a personal history of primary C cell hyperplasie, MTC, or MEN, type 2A, or
  - The patient has a family history consistent with MEN, type 2A or MTC, and at risk for autosomal dominant inheritance of the syndrome
- SLC2A1 (glucose transporter type 1 [GLUT 1] deficiency syndrome) – The patient has clinical features suspicious for or requires the service as a confirmatory test for GLUT 1 deficiency syndrome.

- SPRED1 (Legius syndrome) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for Legius syndrome.
- TCF4 (Pitt-Hopkins syndrome) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for Pitt-Hopkins syndrome.
- THRB (Thyroid Hormone Receptor, Beta) (e.g., thyroid hormone resistance, thyroid hormone beta receptor deficiency), full gene sequence or targeted sequence analysis of more than 5 exons
  - The patient has clinical presentation suspicious for Resistance to Thyroid Hormone-beta (RTH-beta) with any one of the following:
    - Elevated free T4 and/or free T3 with normal or mildly elevated TSH
    - Goiter or tachycardia regardless of other clinical signs and symptoms of thyroid dysfunction
    - Requiring high doses of T4 or T3 to reduce the TSH secretion or to induce the appropriate responses in peripheral tissues
    - No evidence of thyroid hormone binding abnormalities or pituitary adenoma
    - Family history of thyroid disease or RTH-beta
  - The test is needed to confirm the diagnosis of RTH-beta
- TSC1 (tuberous sclerosis complex 1) – duplication/deletion analysis – The patient has signs or symptoms of tuberous sclerosis complex but a diagnosis cannot be clinically confirmed.
- WT1 (Wilms tumor 1) – full gene sequence – The patient has suspected or confirmed acute myeloid leukemia, and the result of the test will influence the diagnosis, prognosis and/or therapeutic management.

Tier 2, Molecular Pathology Procedure, Level 7

Coverage for CPT code 81406 (molecular pathology procedure, Level 7) is limited to the listed services. Reimbursement for code 81406 requires an approved *Treatment Authorization Request* (TAR) and requires providers to document one of the following on the TAR:

- ACADVL (very long chain acyl-coenzyme A dehydrogenase deficiency) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for ACADVL.
- AFG3L2 (spinocerebellar ataxia) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for spinocerebellar ataxia.
- ATP7B (Wilson disease):
  - The patient has clinical features suspicious for Wilson disease, and
  - Diagnosis cannot be made based on the results of biochemical testing and liver biopsy, and
  - The patient requires the service as a confirmatory test for Wilson disease
- BTK (X-linked agammaglobulinemia):
  - The male patient has clinical features suspicious for X-linked agammaglobulinemia, and
  - The male patient has less than two percent CD19+ B cells
- CDH1 (hereditary diffuse gastric cancer):
  - Two gastric cancer cases in family, one confirmed diffuse gastric cancer younger than 50 years of age, or
  - Three confirmed diffuse gastric cancer cases in first or second degree relatives, regardless of age, or
  - Diffuse gastric cancer diagnosed younger than 40 years of age, or
  - Personal or family history of diffuse gastric cancer and lobular breast cancer, one diagnosed younger than 50 years of age
- CNTNAP2 (Pitt-Hopkins-like syndrome) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for Pitt-Hopkins syndrome.

- GCK (glucokinase [hexokinase 4]):
  - The patient requires the service as a diagnostic test for MODY and
  - Is younger than 25 years of age, and
  - Has a family history of diabetes, and
  - Has negative islet of autoantibodies
- GLUD1 (familial hyperinsulinism):
  - The patient has persistent hyperinsulinemic hypoglycemia of infancy (PHHI) and failed medical therapy, and
  - The patient is under evaluation for surgical intervention
- HMBS (hydroxymethylbilane synthase), full gene sequence – The patient has clinical features suspicious for, or requires the service as a confirmatory test for acute intermittent porphyria
- HNF4A (hepatocyte nuclear factor 4, alpha):
  - The patient requires the service as a diagnostic test for MODY, and
  - Is younger than 25 years of age, and
  - Has a family history of diabetes, and
  - Has negative islet of autoantibodies
- IDUA (iduronidase, alpha-L) (eg, mucopolysaccharidosis type I), full gene sequence:
  - The patient has clinical signs and symptoms consistent with mucopolysaccharidosis type I, and
  - Treatment option (allogeneic transplantation or gene therapy) will be contingent on the test results

- JAG1 (Alagille syndrome) – duplication/deletion – The patient has clinical features suspicious for, or requires the service as a confirmatory test for Alagille syndrome.
- KCNQ2 (potassium voltage-gated channel, KQT-like subfamily, member 2 [for example, epileptic encephalopathy], full gene sequence):
  - The patient has clinical symptoms and electroencephalogram (EEG) patterns consistent with early infantile epileptic encephalopathy, and
  - Treatment is contingent on test results
- MUTYH (MYH-associated polyposis) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for MUTYH-associated polyposis.
- NF2 (neurofibromatosis, type 2):
  - The patient has clinical features suspicious for, or requires the service as a confirmatory test for type 2 neurofibromatosis, or
  - The patient is at high risk for neurofibromatosis with one or more of the following:
    - ❖ A first-degree relative with type 2 neurofibromatosis
    - ❖ Multiple spinal tumors (schwannomas, meningiomas)
    - ❖ Cutaneous schwannomas
    - ❖ Sporadic vestibular schwannoma younger than 30 years of age, or spinal tumor or meningioma younger than 20 years of age
- PCSK9 (proprotein convertase subtilisin/kexin type 9) (e.g., familial hypercholesterolemia), full gene sequence:
  - Patient has coronary artery disease (CAD) or has risk factors for CAD
  - The intention to treat or not to treat with PCSK9 inhibitors will be contingent, at least in part, on the test results
- PHEX (phosphate-regulating endopeptidase homolog, X-Linked) (e.g., hypophosphatemic rickets), full gene sequence:
  1. The patient is undergoing evaluation for X-Linked Hypophosphatemia (XLH); and

     Diagnosis was not able to be established based on biochemical testing, which included the following tests:

     - ❖ Serum calcium, phosphate and alkaline phosphatase, and
     - ❖ PTH, 25 hydroxyvitamin D, and 1,25 dihydroxyvitamin D, and
     - ❖ Urinary calcium excretion; and

The confirmation of the diagnosis and the treatment strategy is contingent on the test result.

- POLG (polymerase [DNA directed], gamma [e.g., Alpers-Huttenlocher syndrome, autosomal dominant progressive external ophthalmoplegia], full gene sequence). TAR may be approved based on one of the following numbered criteria:
  - The patient is undergoing consideration for treatment using valproic acid, or
  - The patient is undergoing evaluation for potentially having any one of the following conditions:
    - Alpers-Huttenlocher syndrome
    - Ataxia neuropathy spectrum (ANS), previously known as mitochondrial recessive ataxia syndrome (MIRAS) and sensory ataxia neuropathy, dysarthria and ophthalmoplegia (SANDO)
    - Autosomal dominant progressive external ophthalmoplegia
    - Autosomal recessive progressive external ophthalmoplegia
    - Childhood myocerebrohepatopathy spectrum
    - Myoclonic epilepsy myopathy sensory ataxia
- PPOX (protoporphyrinogen oxidase), full gene sequence – The patient has clinical features suspicious for, or requires the service as a confirmatory test for acute variegate porphyria.
- PRKCG (spinocerebellar ataxia) – The patient has clinical features suspicious for or requires the service as a confirmatory test for spinocerebellar ataxia.
- PYGM (glycogen storage disease type V, McArdle disease) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for glycogen storage disease type V (McArdle disease).

- RPE65 (retinal pigment epithelium-specific protein 65kDa):
  - Patient has a clinical diagnosis of retinal dystrophy, and
  - The decision for gene therapy is contingent on the test results
- RYR1 (ryanodine receptor 1, skeletal) (e.g., malignant hyperthermia), targeted sequence analysis of exons with functionally-confirmed mutations:
  - The patient has a clinical history suspicious for malignant hyperthermia, or
  - The patient has a positive contracture test for malignant hyperthermia, or
  - The patient has a family member who had a positive contracture or genetic test for malignant hyperthermia
- SCNN1A (pseudohypoaldosteronism) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for pseudohypoaldosteronism.
- SCNN1B (Liddle syndrome, pseudohypoaldosteronism) – The patient has clinical features suspicious for or requires the service as a confirmatory test for Liddle syndrome, pseudohypoaldosteronism.
- SCNN1G (Liddle syndrome, pseudohypoaldosteronism) – The patient has clinical features suspicious for or requires the service as a confirmatory test for Liddle syndrome, pseudohypoaldosteronism.
- SLC37A4 (glycogen storage disease, type Ib) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for glycogen storage disease, type Ib.
- TCF4 (Pitt-Hopkins syndrome) – The patient has clinical features suspicious for or requires the service as a confirmatory test for Pitt-Hopkins syndrome.
- TSC1 (tuberous sclerosis complex 1) – full gene sequence – The patient has signs or symptoms of tuberous sclerosis complex but a diagnosis cannot be clinically confirmed.
- TSC2 (tuberous sclerosis complex 2) – duplication/deletion analysis – The patient has signs or symptoms of tuberous sclerosis complex but a diagnosis cannot be clinically confirmed.
- UMOD (glomerulocystic kidney disease with hyperuricemia and isosthenuria) – The patient has clinical features suspicious for or requires the service as a confirmatory test for glomerulocystic kidney disease with hyperuricemia and isosthenuria.
- WAS (Wiskott-Aldrich syndrome) – The patient has clinical features suspicious for or requires the service as a confirmatory test for Wiskott-Aldrich syndrome.

Tier 2, Molecular Pathology Procedure, Level 8

Coverage for CPT code 81407 (molecular pathology procedure, Level 8) is limited to the listed services. Reimbursement for code 81407 requires an approved TAR and requires providers to document one of the following on the TAR:

- ABCC8 (familial hyperinsulinism):
  - The patient has persistent hyperinsulinemic hypoglycemia of infancy (PHHI) who failed medical therapy, and
  - The patient is under evaluation for surgical intervention
- AGL (glycogen storage disease type III) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for glycogen storage disease type III
- JAG1 (Alagille syndrome) – full gene sequence – The patient has clinical features suspicious for, or requires the service as a confirmatory test for Alagille syndrome
- NOTCH (notch 1) – full gene sequence – The patient has suspected or confirmed acute lymphoblastic leukemia, and the result of the test will influence the diagnosis, prognosis and/or therapeutic management
- NPHS1 (congenital Finnish nephrosis):
  - The patient has clinical diagnosis of steroid-resistant nephritic syndrome (SRNS)/congenital Finnish nephrosis, and
  - Treatment will be contingent on the test results

- SCN1A – The patient has clinical features suspicious for, or requires the service as a confirmatory test for Dravet syndrome.
- SPTBN2 (spinocerebellar ataxia) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for spinocrebellar ataxia.
- TSC2 (tuberous sclerosis complex 2) – full gene sequence – The patient has signs or symptoms of tuberous sclerosis complex but a diagnosis cannot be clinically confirmed.

Tier 2, Molecular Pathology Procedure, Level 9

Coverage for CPT code 81408 (molecular pathology procedure, Level 9) is limited to the listed services. Reimbursement for code 81408 requires an approved *Treatment Authorization Request* (TAR) explaining that the following criteria have been met:

- ITPR1 (spinocerebellar ataxia) – The patient has clinical features suspicious for, or requires the service as a confirmatory test for spinocerebellar ataxia.
- DMD (dsytophin), full gene analysis:
  - Patient has a clinical diagnosis of dystrophinopathy based on the history, physical examination and elevated creatine kinase (CK) level
  - Result of the DMD (dystrophin) deletion or duplication is negative
- RYR1 (ryanodine receptor 1, skeletal) (e.g., malignant hyperthermia), full gene sequence:
  - The patient has a clinical history suspicious for malignant hyperthermia, or
  - The patient has a positive contracture test for malignant hyperthermia, or
  - The patient has a family member who had a positive contracture or genetic test for malignant hyperthermia

Human Leukocyte Antigen Typing

CPT codes 81370 thru 81380, 81382 and 81383 (human leukocyte antigen typing) are reimbursable only with an ICD-10-CM diagnosis in the range of Z94.0 thru Z94.9.

CPT code 81381 (HLA Class I typing, high resolution, one allele or allele group, each) is only reimbursable with an ICD-10-CM diagnosis of B20, F31.0 thru F31.9, G40.001 thru G40.919, G50.0, R75, Z01.812, Z21, Z94.0 thru Z94.9.

Genomic Sequencing Procedures and Other Molecular Multianalyte Assays

Providers should refer to the CPT code book for full descriptions of the following codes:

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81413 Cardiac ion channelopathies; genomic sequence analysis panel, must include sequencing of at least 10 genes	Yes	The required TAR must document a copy of the report of the physician-interpreted 12-lead electrocardiogram (ECG) with pattern consistent with or suspicious for prolonged QT interval. The TAR must also have clinical documentation of one or more of the following: 1. Torsade de pointes in the absence of drugs known to prolong QT interval 2. T-wave alternans 3. Notched T-wave in three leads 4. Syncope 5. Family members with long QT syndrome 6. Sudden death in family members less than 30 years of age without defined cause	Once-in-a-lifetime for any provider A TAR may override the frequency limit.

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81414 Cardiac ion channelopathies; genomic sequence analysis panel, must include sequencing of at least 2 genes	Yes	The required TAR must document a copy of the report of the physician-interpreted 12-lead electrocardiogram (ECG) with pattern consistent with or suspicious for prolonged QT interval. The TAR must also have clinical documentation of one or more of the following: 7. Torsade de pointes in the absence of drugs known to prolong QT interval 8. T-wave alternans 9. Notched T-wave in three leads 10. Syncope 11. Family members with long QT syndrome 12. Sudden death in family members less than 30 years of age without defined cause	Once-in-a-lifetime for any provider A TAR may override the frequency limit.

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
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, SLC9AG, STXBP1, SYNGAP1, TCF4, TPP1, TSC1, TSC2, and ZEB2	Yes	The required TAR must document the following: • Patient has specific epilepsy syndrome of unknown cause for which a number of genetic etiologies exist. • The test is needed for identifying the underlying diagnosis • The diagnostic or treatment strategy will be contingent on test results	N/A

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81420 Fetal chromosomal aneuploidy genomic sequence analysis panel, must include analysis of chromosomes 13, 18, and 21	No	N/A	‹‹Reimbursement will be limited to one of the following Noninvasive Prenatal Tests per pregnancy: PLA code 0327U or CPT code 81420 or CPT code 81507. Concurrent or repeat use of these services during the same pregnancy is not covered unless there is documentation of medical necessity.››

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
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	Yes	A TAR with documentation of one or more the following criteria is required: 1. An individual from a family member with a known deleterious BRCA mutation; or 2. Personal history of breast cancer (invasive or ductal carcinoma in situ) plus one of more of the following: ❖ Diagnosed at ≤45 years of age, or ❖ Diagnosed at 46 to 50 years of age with: ❖ An additional breast cancer primary at any age ❖ One or more close blood relatives with breast cancer at any age ❖ One or more close blood relatives with prostate cancer (Gleason score ≥7) ❖ An unknown or limited family history; or – Diagnosed at ≤60 years of age with a triple negative breast cancer; or *(continued on next page)*	Once-in-a-lifetime except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
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	Yes	– Diagnosed at any age with: – One or more close relatives with: – Breast cancer diagnosed at ≤50 years of age; – Ovarian carcinoma; or – Male Breast cancer; or – Metastatic prostate cancer; or – Pancreatic cancer – Two or more additional diagnosis of breast cancer at any age in patient and/or in close blood relatives; or – Ashkenazi Jewish ancestry: or 3. Personal history of ovarian carcinoma (includes fallopian tube and primary peritoneal cancers); or 4. Personal history of male breast cancer; or 5. Personal history of pancreatic cancer, or *(continued on next page)*	Once-in-a-lifetime except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
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	Yes	6. Personal history of metastatic prostate cancer (biopsy-proven and/or with radiographic evidence; includes distant metastasis and regional bed or nodes; not biochemical recurrence); or 7. Personal history of high-grade prostate cancer (Gleason score ≥7) at any age with: – One or more close blood relatives (first, second or third-degree) with ovarian carcinoma, pancreatic cancer or metastatic prostate cancer at any age or breast cancer under 50 years of age; or – Two or more close blood relatives (first, second, or third-degree relatives on the same side of family) with breast or prostate cancer (any grade) at any age; or – Ashkenazi Jewish ancestry; or 8. BRCA1/2 pathogenic/likely pathogenic variant detected by tumor profiling on any tumor type in the absence of germline pathogenic/likely pathogenic variant analysis; or *(continued on next page)*	Once-in-a-lifetime except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
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	Yes	9. For an individual without history of breast or ovarian cancer, but with one or more first or second-degree blood relative meeting any of the above criteria	Once-in-a-lifetime except with valid TAR override
81434 Hereditary retinal disorders (e.g., 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	Yes	A TAR is required with the following documentation: • Patient has a clinical diagnosis of retinal dystrophy (retinitis pigmentosa, Leber congenital amaurosis, cone-rod dystrophy) and • The decision for gene therapy is contingent on the test results	Once-in-a-lifetime for any provider, without TAR/SAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81435 Hereditary colon cancer disorders; genomic sequence analysis panel, must include sequencing of at least 10 genes	No	Reimbursable only when billed in conjunction with one of the following ICD-10-CM diagnosis codes: C17.0 thru C20, C24.0 thru C25.9, C54.0 thru C54.9, C65.1 thru C66.9, C71.0 thru C71.9, D23.0 thru D23.9, Z80.0, Z80.49, Z85.030 thru Z85.038, Z85.040 thru Z85.048, Z85.42 or Z86.010	Once-in-a-lifetime
81436 Hereditary colon cancer disorders; genomic sequence analysis panel, must include sequencing of at least 5 genes	No	Reimbursable only when billed in conjunction with one of the following ICD-10-CM diagnosis codes: C17.0 thru C20, C24.0 thru C25.9, C54.0 thru C54.9, C65.1 thru C66.9, C71.0 thru C71.9, D23.0 thru D23.9, Z80.0, Z80.49, Z85.030 thru Z85.038, Z85.040 thru Z85.048, Z85.42 or Z86.010	Once-in-a-lifetime
81439 Inherited cardiomyopathy genomic sequence analysis panel, must include sequencing of at least 5 genes	No	Reimbursable only when billed in conjunction with ICD-10-CM diagnosis codes: I42.0 thru I42.5 or Z82.41 thru Z82.49 A TAR may override the required ICD-10-CM diagnosis codes	Once-in-a-lifetime for any provider A TAR may override the frequency limit

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81445 Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, 5 to 50 genes	Yes	A TAR for CPT code 81445 requires documentation of the following criteria: • For Somatic Testing: – The patient has either recurrent, relapsed, refractory, metastatic or advanced stages III or IV cancer, and – The patient either has not been previously tested using the same Next Generation Sequencing (NGS) test for the same primary diagnosis of cancer or repeat testing using the same NGS test only when a new primary cancer diagnosis is made by the treating physician, and – The decision for additional cancer treatment is contingent on the test results. TAR criteria continued on next page.	Once-in-a-lifetime for any provider except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81445 Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, 5 to 50 genes	Yes	• For Germline Testing: – Ovarian or breast cancer, and – Clinical indication for germline (inherited) testing for hereditary breast or ovarian cancer (i.e., American College of Obstetrician Gynecologists' criteria for further genetic evaluation for hereditary [germline] breast and ovarian cancer), and – A risk factor for germline (inherited) breast or ovarian cancer, and (BRCAPRO, Myriad, Claus, Boadicea, or Tyrer Cuzick), and – Has not been previously tested with the same germline test using NGS for the same germline genetic content. • Independent of the above criteria, either Somatic or Germline testing may be approved if the test is approved by the U.S. Food and Drug Administration (FDA) as a Companion Diagnostic Device, and the decision for additional treatment is contingent on the test results.	Once-in-a-lifetime for any provider except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81448 Hereditary peripheral neuropathies, genomic sequence analysis panel, must include sequencing of at least 5 neuropathy-related genes	No	One of the following ICD-10-CM diagnosis codes is required on the claim (except with valid TAR): • G11.4 or G60.0	Once-in-a-lifetime for any provider
81455 Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes	Yes	A TAR for CPT code 81455 requires documentation of the following criteria: • For Somatic Testing: – The patient has either recurrent, relapsed, refractory, metastatic or advanced stages III or IV cancer, and – The patient either has not been previously tested using the same Next Generation Sequencing (NGS) test for the same primary diagnosis of cancer or repeat testing using the same NGS test only when a new primary cancer diagnosis is made by the treating physician, and – The decision for additional cancer treatment is contingent on the test results. TAR criteria continued on next page.	Once-in-a-lifetime for any provider except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81455 Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes	Yes	• For Germline Testing: – Ovarian or breast cancer, and – Clinical indication for germline (inherited) testing for hereditary breast or ovarian cancer (i.e., American College of Obstetrician Gynecologists' criteria for further genetic evaluation for hereditary [germline] breast and ovarian cancer), and – A risk factor for germline (inherited) breast or ovarian cancer, and (BRCAPRO, Myriad, Claus, Boadicea, or Tyrer Cuzick), and – Has not been previously tested with the same germline test using NGS for the same germline genetic content. • Independent of the above criteria, either Somatic or Germline testing may be approved if the test is FDA-approved as a Companion Diagnostic Device, and the decision for additional treatment is contingent on the test results.	Once-in-a-lifetime for any provider except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81457 Solid organ neoplasm, genomic sequence analysis panel, interrogation for sequence variants; DNA analysis, microsatellite instability	Yes	A TAR for CPT code 81457 requires documentation of the following criteria: <u>For Somatic Testing</u> • The patient has recurrent, relapsed, refractory, metastatic or advanced stage III or IV cancer, and • The patient either has not been previously tested using the same next-generation sequencing (NGS) test for the same primary diagnosis of cancer or repeat testing using the same NGS test only occurs when a new primary cancer diagnosis is made by the treating physician, and • The decision for additional cancer treatment is contingent on the test results. TAR criteria continued on next page.	Once-in-a-lifetime for any provider except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81457 Solid organ neoplasm, genomic sequence analysis panel, interrogation for sequence variants; DNA analysis, microsatellite instability	Yes	<u>For Germline Testing</u> • The patient has ovarian or breast cancer, and • The patient has a clinical indication for germline (inherited) testing for inherited breast or ovarian cancer, and • The patient has a risk factor for germline (inherited) breast or ovarian cancer, and • The patient has not been previously tested with the same germline test using NGS for the same germline genetic content. • Independent of the above criteria, either Somatic or Germline testing may be approved if the test is approved by the U.S. Food and Drug Administration (FDA) as a companion diagnostic device, and the decision for additional treatment is contingent on the test results.	Once-in-a-lifetime for any provider except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81458 Solid organ neoplasm, genomic sequence analysis panel, interrogation for sequence variants; DNA analysis, copy number variants and microsatellite instability	Yes	A TAR for CPT code 81458 requires documentation of the following criteria: <u>For Somatic Testing</u> • The patient has recurrent, relapsed, refractory, metastatic or advanced stage III or IV cancer, and • The patient either has not been previously tested using the same next-generation sequencing (NGS) test for the same primary diagnosis of cancer or repeat testing using the same NGS test only occurs when a new primary cancer diagnosis is made by the treating physician, and • The decision for additional cancer treatment is contingent on the test results. TAR criteria continued on next page.	Once-in-a-lifetime for any provider except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81458 Solid organ neoplasm, genomic sequence analysis panel, interrogation for sequence variants; DNA analysis, copy number variants and microsatellite instability	Yes	<u>For Germline Testing</u> • The patient has ovarian or breast cancer, and • The patient has a clinical indication for germline (inherited) testing for inherited breast or ovarian cancer, and • The patient has a risk factor for germline (inherited) breast or ovarian cancer, and • The patient has not been previously tested with the same germline test using NGS for the same germline genetic content. • Independent of the above criteria, either Somatic or Germline testing may be approved if the test is approved by the U.S. Food and Drug Administration (FDA) as a companion diagnostic device, and the decision for additional treatment is contingent on the test results.	Once-in-a-lifetime for any provider except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81459 Solid organ neoplasm, genomic sequence analysis panel, interrogation for sequence variants; DNA analysis or combined DNA and RNA analysis, copy number variants, microsatellite instability, tumor mutation burden, and rearrangements	Yes	A TAR for CPT code 81459 requires documentation of the following criteria: <u>For Somatic Testing</u> • The patient has recurrent, relapsed, refractory, metastatic or advanced stage III or IV cancer, and • The patient either has not been previously tested using the same next-generation sequencing (NGS) test for the same primary diagnosis of cancer or repeat testing using the same NGS test only occurs when a new primary cancer diagnosis is made by the treating physician, and • The decision for additional cancer treatment is contingent on the test results. TAR criteria continued on next page.	Once-in-a-lifetime for any provider except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81459 Solid organ neoplasm, genomic sequence analysis panel, interrogation for sequence variants; DNA analysis or combined DNA and RNA analysis, copy number variants, microsatellite instability, tumor mutation burden, and rearrangements	Yes	<u>For Germline Testing</u> • The patient has ovarian or breast cancer, and • The patient has a clinical indication for germline (inherited) testing for inherited breast or ovarian cancer, and • The patient has a risk factor for germline (inherited) breast or ovarian cancer, and • The patient has not been previously tested with the same germline test using NGS for the same germline genetic content. • Independent of the above criteria, either Somatic or Germline testing may be approved if the test is approved by the U.S. Food and Drug Administration (FDA) as a companion diagnostic device, and the decision for additional treatment is contingent on the test results.	Once-in-a-lifetime for any provider except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81462 Solid organ neoplasm, genomic sequence analysis panel, cell-free nucleic acid (e.g., plasma), interrogation for sequence variants; DNA analysis or combined DNA and RNA analysis, copy number variants and rearrangements	Yes	A TAR for CPT code 81462 requires documentation of the following criteria: 1. The patient has a diagnosis of non-small cell lung cancer, and 2. The patient is medically unable to undergo invasive biopsy or tumor tissue testing is not feasible, and 3. Management is contingent on the test results	Once-in-a-lifetime for any provider except with valid TAR override

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81500 Oncology (ovarian), biochemical assays of two proteins	No	Reimbursable for females who meet the following criteria: • 18 years of age or older • Ovarian adnexal mass present for which surgery is planned, and not yet referred to an oncologist ICD-10-CM diagnosis code R19.09 is required for reimbursement	81500 Oncology (ovarian), biochemical assays of two proteins
81503 Oncology (ovarian), biochemical assays of five proteins	No	Reimbursable for females who meet the following criteria: • 18 years of age or older • Ovarian adnexal mass present for which surgery is planned, and not yet referred to an oncologist CPT code 81503 is reimbursable only when billed in conjunction with at least one of the following ICD-10-CM diagnosis codes: D39.10 thru D39.12, N83.00 thru N83.02, N83.10 thru N83.12, N83.201, N83.202, N83.209, N83.291, N83.292, N83.299, R19.00, R19.03 thru R19.05, R19.07 or R19.09.	81503 Oncology (ovarian), biochemical assays of five proteins

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81507 Fetal aneuploidy (trisomy 21, 18 and 13) DNA sequence analysis of selected regions	No	N/A	‹‹Reimbursement will be limited to one of the following Noninvasive Prenatal Tests per pregnancy: PLA code 0327U or CPT code 81420 or CPT code 81507. Concurrent or repeat use of these services during the same pregnancy is not covered unless there is documentation of medical necessity.››

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81508 Fetal congenital abnormalities, biochemical assays of two proteins	No	Reimbursable only when billed in conjunction with one of the following ICD-10-CM diagnosis codes: O09.00 thru O09.73, Z34.00 thru Z34.93, Z36.0, Z36.81, or Z36.83 thru Z36.89. Reimbursable for females only	N/A
81509 Fetal congenital abnormalities, biochemical assays of three proteins	No	Reimbursable only when billed in conjunction with one of the following ICD-10-CM diagnosis codes: O09.00 thru O09.73, Z34.00 thru Z34.93, Z36.0, Z36.81, or Z36.83 thru Z36.89. Reimbursable for females only	N/A
81510 Fetal congenital abnormalities, biochemical assays of three analytes	No	Reimbursable only when billed in conjunction with one of the following ICD-10-CM diagnosis codes: O09.00 thru O09.73, Z34.00 thru Z34.93, Z36.0, Z36.81, or Z36.83 thru Z36.89. Reimbursable for females only	N/A
81511 Fetal congenital abnormalities, biochemical assays of four analytes	No	Reimbursable only when billed in conjunction with one of the following ICD-10-CM diagnosis codes: O09.00 thru O09.73, Z34.00 thru Z34.93, Z36.0, Z36.81, or Z36.83 thru Z36.89. Reimbursable for females only	N/A

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81512 Fetal congenital abnormalities, biochemical assays of five analytes	No	Reimbursable only when billed in conjunction with one of the following ICD-10-CM diagnosis codes: O09.00 thru O09.73, Z34.00 thru Z34.93, Z36.0, Z36.81, or Z36.83 thru Z36.89. Reimbursable for females only	N/A
81517 Liver disease, analysis of 3 biomarkers (hyaluronic acid [HA], procollagen III amino terminal peptide [PIIINP], tissue inhibitor of metalloproteinase 1 [TIMP-1]), using immunoassays, utilizing serum, prognostic algorithm reported as a risk score and risk of liver fibrosis and liver-related clinical events within 5 years	No	N/A	N/A

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81518‡ Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 11 genes	Yes	Requires a *Treatment Authorization Request* (TAR) with documentation of the following criteria: • The recipient is estrogen and/or progesterone receptor (ER/PgR)-positive. • The recipient is HER2-receptor negative. • The recipient is lymph node negative or lymph node positive with up to three positive nodes. • The recipient has stage I or stage II breast cancer. • The recipient is disease-free (or no evidence of metastasis). • Test results will be used in determining treatment management of the patient for chemotherapy and/or extended endocrine therapy. Use CPT code 81518 when billing for Breast Cancer Index.	Once-in-a-lifetime

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81519‡ Oncology (breast), mRNA, gene expression profiling by real time RT-PCR of 21 genes	Yes	Requires a TAR with documentation of the following criteria: • The recipient is estrogen and progesterone receptor (ER/PgR)-positive • The recipient is HER2-receptor negative • The recipient is lymph node negative; or has one to three positive lymph nodes • The recipient has stage I or stage II breast cancer • The recipient is a candidate for chemotherapy • The assay is used within six months of diagnosis • The recipient is under consideration for adjuvant systemic therapy Use CPT code 81519 when billing for Oncotype Dx.	Once-in-a-lifetime

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81520‡ Oncology (breast), mRNA gene expression profiling by hybrid capture of 58 genes	Yes	Requires a TAR with documentation of the following criteria: • The recipient is estrogen and progesterone receptor (ER/PgR)-positive. • The recipient is HER2-receptor negative. • The recipient is lymph node negative. • The recipient has stage I or stage II breast cancer. • The recipient is a candidate for chemotherapy. • The assay is used within six months of diagnosis. • The recipient is under consideration for adjuvant systemic therapy. Use CPT code 81520 when billing for Prosigna.	Once-in-a-lifetime

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81521‡ Oncology (breast), mRNA, microarray gene expression profiling of 70 content genes and 465 housekeeping genes	Yes	Requires a TAR with documentation of the following criteria: • The recipient has high clinical risk per MINDACT categorization. • The recipient is estrogen and progesterone receptor (ER/PgR)-positive. • The recipient is HER2-receptor negative. • The recipient is lymph node negative or lymph node positive. • The recipient is a candidate for chemotherapy. • The assay is used within six months of diagnosis. • The recipient is under consideration for adjuvant systemic therapy. Use CPT code 81521 when billing for MammaPrint. As noted in the 2017 ASCO guideline, the Adjuvant! Online website was not functional. As an alternative, clinicians can determine a patient's clinical risk status by using the printed version of the Adjuvant! Online clinical risk criteria found in the Data Supplement of the MINDACT publication.	Once-in-a-lifetime

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81522‡ Oncology (breast), mRNA, gene expression profiling by RT-PCR of 12 genes	Yes	Requires a TAR with documentation of the following criteria: • The recipient is estrogen and progesterone receptor (ER/PgR)-positive. • The recipient is HER2-receptor negative. • The recipient is lymph node negative. • The recipient has stage I or stage II breast cancer. • The recipient is a candidate for chemotherapy. • The assay is used within six months of diagnosis. • The recipient is under consideration for adjuvant systemic therapy. Use CPT 81522 when billing for EndoPredict.	Once-in-a-lifetime

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81523‡ Oncology (breast), mRNA, next-generation sequencing gene expression profiling of 70 content genes and 31 housekeeping genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk to distant metastasis	Yes	Requires a TAR with documentation of the following criteria: • The recipient has high clinical risk per MINDACT categorization. • The recipient is estrogen and progesterone receptor (ER/PgR)-positive. • The recipient is HER2-receptor negative. • The recipient is lymph node negative or lymph node positive. • The recipient is a candidate for chemotherapy. • The assay is used within six months of diagnosis. • The recipient is under consideration for adjuvant systemic therapy. Use CPT code 81523 when billing for MammaPrint. As noted in the 2017 ASCO guideline, the Adjuvant! Online website was not functional. As an alternative, clinicians can determine a patient's clinical risk status by using the printed version of the Adjuvant! Online clinical risk criteria found in the Data Supplement of the MINDACT publication.	N/A

enomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81528 Oncology (colorectal) screening, quantitative real-time target and signal amplification of 10 DNA markers	No	Reimbursable for recipients 45 thru 75 years of age. For recipients outside this age range, providers must submit a TAR documenting medical necessity.	Once per year For recipients requiring additional tests within a year, providers must submit a TAR documenting medical necessity.
81541 Oncology (prostate), mRNA gene expression profiling by real-time RT-PCR of 46 genes (31 content and 15 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a disease-specific mortality risk score	Yes	The following criteria must be documented on the TAR: 1. For identification of patients with Prostate Cancer who are most likely to benefit from active surveillance or treatment. – Coverage is limited to Decipher®, Prolaris® and ProMark. Gene expression profiling for prostate cancer may be billed as follows: ❖ Decipher® Prostate – Use CPT code 81542 ❖ Prolaris® – Use CPT code 81541 ❖ ProMark – Use CPT code 81599 *(continued on next page)*	Once-in-a-lifetime

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81541 oncology (prostate), mRNA gene expression profiling by real-time RT-PCR of 46 genes (31 content and 15 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a disease-specific mortality risk score	Yes	– The patient must have one of the following: ❖ Higher volume Grade Group 1 ❖ Favorable intermediate risk (e.g., Grade Group 2, percentage of positive biopsy scores, 50 percent and no more than on NCCN intermediate-risk factor) ❖ Discordant features in their risk stratification (e.g., palpable mass with Grade Group 1) ❖ Other features associated with progression while on active surveillance (e.g., high PSA density and certain germline or somatic mutations) ❖ Unfavorable intermediate-risk when considering decisions to proceed with treatment (i.e. add androgen deprivation therapy to radiation) – Result of the test, when considered as a whole with routine clinical factors, is likely to influence the decision to proceed with surveillance or treatment *(continued on next page)*	Once-in-a-lifetime

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81541	Yes	2. For post-prostatectomy patients who seek guidance on adjuvant vs. salvage radiation: – Coverage is limited to Decipher Genomic Classifier – Result of the test, when considered as a whole with routine clinical factors, is likely to affect treatment	Once-in-a-lifetime
81542 oncology (prostate), mRNA, microarray gene expression profiling of 22 content genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as metastasis risk score	Yes	See CPT code 81541 for TAR criteria and billing requirements.	Once-in-a-lifetime

Genomic Sequencing and Other Molecular Multianalyte Assay Code, TAR and Billing Information (continued)

CPT Code Description	TAR Required	TAR and/or Billing Requirements	Frequency
81546 Oncology (thyroid), mRNA, gene expression analysis of 10,196 genes, utilizing fine needle aspirate, algorithm reported as a categorical result (e.g., benign or suspicious)	Yes	The following numbered criteria must be documented on the TAR: 1. The patient is under evaluation for thyroid nodule(s) 2. The cytopathology result from fine needle aspiration is indeterminate, defined as one of the following: • Follicular lesion of undetermined significance (FLUS), Bethesda III, or • Atypia of undetermined significance (AUS), Bethesda III, or • Follicular neoplasm, Bethesda IV. 3. The diagnostic or treatment strategy will be contingent on test results	N/A
81552 Oncology (uveal melanoma), mRNA, gene expression profiling by real-time RT-PCR of 15 genes	No	An ICD-10-CD diagnosis code from the following ranges must be documented: C69.30 thru C69.32 or C69.40 thru C69.42	Once-in-a-lifetime
81596 Infectious disease, chronic hepatitis C virus (HCV) infection, six biochemical assays	No	The following ICD-10-CM code is required on the claim (except with valid TAR): B18.2	N/A

Legend

Symbols used in the document above are explained in the following table.

Symbol	Description
‹‹	This is a change mark symbol. It is used to indicate where on the page the most recent change begins.
››	This is a change mark symbol. It is used to indicate where on the page the most recent change ends.
*	An approved TAR that meets the necessary criteria listed below to override the once-in-a-lifetime frequency is required: For patients with previous BRCA test other than BRACAnalysis CDx, repeat BRCA testing with BRACAnalysis CDx may be necessary when treatment with Lynparza™ (olaparib) is contingent on the test results.
‡	These benefits are limited to EndoPredict, Oncotype Dx, Prosigna (PAM50 risk of recurrence score) and Breast Cancer Index. Use CPT code 81518 when billing for Breast Cancer Index. Use CPT code 81519 when billing for Oncotype Dx. Use CPT code 81520 when billing for Prosigna. Use CPT code 81521 when billing for MammaPrint. Use CPT code 81522 when billing for EndoPredict. These once-in-a-lifetime benefits may be billed for the same recipient and any provider. Providers need an approved TAR and documentation showing that the recipient has a new second primary breast cancer that meets the necessary criteria as listed above to override the once-in-a-lifetime frequency. Concurrent use of more than one test is not recommended as there is no data to support that ordering multiple assays in an individual patient would be beneficial in guiding treatment decisions.