Chapter 18 Section 3

Defense Health Agency (DHA) Evaluation Of Non-United States (U.S.) Food and Drug Administration (FDA) Approved Laboratory Developed Tests (LDTs) Demonstration Project

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1.0 PURPOSE

The purpose of this demonstration project is to improve the quality of health care services for TRICARE beneficiaries. This demonstration is intended to evaluate whether it is feasible for the Department of Defense (DoD) to review LDTs which have not received U.S. FDA medical device 510(k) clearance or premarket approval (therefore considered non-FDA approved) to determine if they meet TRICARE requirements for safety and effectiveness according to the hierarchy of reliable evidence (32 CFR 199.4(g)(15)(i)(C)) and 32 CFR 199.2(b)), or TRICARE's rare disease policy (32 CFR 199.4(g)(15)(ii)) in the case of LDTs used in the diagnosis or medical management of a rare disease, and otherwise meet TRICARE criteria for coverage. Those that do will be covered as a benefit under this demonstration. The demonstration project will evaluate feasible alternatives to FDA approval to support modifications to 32 CFR 199.4(g)(15)(i)(A) to allow coverage for non-FDA approved LDTs that otherwise meet the TRICARE requirements for safety and effectiveness. The DoD currently has an ongoing demonstration project to test this same provision for LDTs with a Centers for Medicare and Medicaid Services (CMS) national or local coverage determination that were submitted by laboratories for consideration for coverage under TRICARE. However, this new demonstration is being conducted in order to evaluate the feasibility of establishing a cost-effective and efficient way to review an expanded pool of non-FDA approved LDTs prioritized based on their potential high utilization and clinical utility within the TRICARE population. This new demonstration project will also extend coverage for preconception and prenatal Cystic Fibrosis (CF) carrier screening, when provided in accordance with the most current American College of Obstetricians and Gynecologists (ACOG) guidelines in order to allow the DoD to establish whether there is a benefit to offering such testing to TRICARE beneficiaries. The demonstration project will operate throughout the Continental United States (CONUS), and in the TRICARE overseas regions.

2.0 BACKGROUND

2.1 On June 18, 2014, a notice was published in the **Federal Register** (79 FR 34726) announcing the start of a demonstration project in which the DHA will review LDTs which have not received FDA clearance or approval to determine if they meet TRICARE requirements for safety and effectiveness according to the hierarchy of reliable evidence or TRICARE's rare disease policy as stated above and approve those that do for cost-sharing under this demonstration. An annual evaluation will be

conducted to determine how many of these non-FDA approved LDTs were provided to beneficiaries across all TRICARE regions. The evaluation will also include a review of the LDT examination and recommendation process to assess feasibility, resource requirements, and cost-effectiveness of the DHA establishing an internal safety and efficacy review process for these LDTs for TRICARE cost-sharing purposes. These results will provide an evaluation of the potential improvement of the quality of health care services for beneficiaries who would not otherwise have access to these safe and effective tests. Based on the results, a recommendation will be made on whether to modify 32 CFR 199.4(g)(15)(i)(A) to remove the restriction for non-FDA approved LDTs and permit TRICARE cost-sharing of LDTs that are found to otherwise meet TRICARE requirements for safety and effectiveness.

2.2 This demonstration project also extends coverage for preconception and prenatal CF carrier screening, when provided in accordance with the most current ACOG guidelines. This demonstration project will allow the DoD to establish whether there is a benefit to offering such testing as part of the family planning genetic testing benefit at 32 CFR 199.4(e)(3)(ii), the maternity benefit at 32 CFR 199.4(e)(16), or otherwise as a special benefit. By extending coverage for CF carrier screening in accordance with the most current ACOG guidelines under this demonstration project, the DoD will be able to gather the necessary data to evaluate whether there is a benefit to offering such screening, including evaluating the impact on follow-on care that a patient is given based on testing results and any other identified benefits of the testing. The Director, DHA, or designee, shall issue guidelines for the collection of data involving individual cases of CF carrier screening covered under this demonstration, as necessary, for evaluation of the benefits resulting from such screening.

2.3 According to 32 CFR 199.4(g)(15)(i)(A), the DHA may not cost-share medical devices, including LDTs, if the tests are non-FDA approved, that is, they have not received FDA marketing 510(k) clearance or premarket approval. LDTs with FDA approval are available for cost-sharing under the TRICARE Basic Program as long as they otherwise meet TRICARE criteria for coverage.

2.4 An LDT is an In Vitro Diagnostic (IVD) that is designed, manufactured, and used within a single laboratory. In the past, these were relatively simple tests used within a single laboratory, usually at a local large hospital or academic medical center, to diagnose rare diseases or for other uses to meet the needs of a local patient population. Today, these tests may be highly complex. LDTs range from identifying one specific gene to identifying just a variant of the gene, while others can assess a person's risk of developing specific cancers or diseases. For purposes of this demonstration, LDTs approved for coverage under the TRICARE Program will be identified by the specific gene they test for as detailed in Figure 18.3-1.

2.5 Laboratories are assessed and accredited under minimum quality standards set by CMS under the Clinical Laboratory Improvement Amendments (CLIA) of 1988. CMS regulates laboratories that use non-FDA approved LDTs as well as FDA approved tests. Laboratories performing moderate or high complexity tests are subject to specific regulatory standards governing certification, personnel, proficiency testing, patient test management, quality assurance, quality control, and inspections. CLIA certification and periodic inspections evaluate whether the laboratory has determined the analytical validity of the tests they offer, including LDTs. Analytical validity refers to how well a test performs in the laboratory; that is, how well the test measures the properties or characteristics it is intended to measure. CLIA certification does not, however, assure a device is safe and effective for its intended use, or impose any type of post-market surveillance or adverse event reporting requirements.

2.6 On December 27, 2011, the DoD published a notice in the **Federal Register** (76 FR 80905-80907), announcing the TRICARE Evaluation of Centers for Medicare and Medicaid Services (CMS) Approved Laboratory Developed Tests (LDTs) Demonstration Project. LDTs for this demonstration were limited to only those that had a CMS national or local coverage determination and significantly informed clinical decision making for surveillance, surgical interventions, chemotherapy, or radiation therapy for cancer. The demonstration project was based on interested laboratories submitting their LDTs for consideration. Limited participation from industry in the demonstration served as a constraining factor and did not provide sufficient data for the DoD to make an affirmative decision regarding the feasibility of developing a cost-effective and efficient method of reviewing non-FDA approved LDTs for safety and efficacy. This three year demonstration will continue until it expires or is terminated via separate notice and LDTs covered under the current demonstration will continue to be covered.

3.0 POLICY

3.1 A new and expanded demonstration project was initiated by the DHA to review non-FDA approved LDTs to determine if they meet TRICARE requirements for safety and effectiveness according to the hierarchy of reliable evidence (32 CFR 199.4(g)(15)(i)(C) and 32 CFR 199.2(b)), or TRICARE's rare disease policy (32 CFR 199.4(g)(15)(ii)) in the case of LDTs used in the diagnosis or medical management of a rare disease, and otherwise meet TRICARE criteria for coverage and approve those that do for cost-sharing under this demonstration. The demonstration will evaluate an expanded pool of non-FDA approved LDTs. For example, LDTs evaluated under the new demonstration are not limited to those associated with cancer and do not require a CMS national or local coverage determination. Further, consideration of specific gene testing as part of the ongoing demonstration, discussed above, does not also prevent consideration under the new demonstration.

3.2 Non-FDA approved LDTs will be prioritized and reviewed for analytical validity, clinical validity, and clinical utility. LDT reviews will be based on the TRICARE hierarchy of reliable evidence to determine whether the specific test is proven safe and effective.

3.3 Reliable evidence is defined in 32 CFR 199.2(b) and includes:

3.3.1 Well-controlled studies of clinically meaningful endpoints, published in refereed medical literature;

3.3.2 Published formal technology assessments;

3.3.3 The published reports of national professional medical associations;

3.3.4 Published national medical policy organization positions; and

3.3.5 The published reports of national expert opinion organizations.

3.3.6 The hierarchy of reliable evidence of proven medical effectiveness, established by paragraphs 3.3.1 through 3.3.5, is the order of the relative weight to be given to any particular source. With respect to clinical studies, only those reports and articles containing scientifically valid data and published in the refereed medical and scientific literature shall be considered as meeting the

requirements of reliable evidence. Specifically not included in the meaning of reliable evidence are reports, articles, or statements by providers or groups of providers containing only abstracts, anecdotal evidence, or personal professional opinions. Also not included in the meaning of reliable evidence is the fact that a provider or a number of providers have elected to adopt a drug, device, or medical treatment or procedure as their personal treatment or procedure of choice or standard of practice.

3.4 There may also be non-FDA approved LDTs reviewed under the new demonstration project for use in the diagnosis or medical management of a rare disease. TRICARE defines a rare disease as any disease or condition that has a prevalence of less than 200,000 persons in the U.S. Due to the rare nature of the condition and lack of clinical research, the hierarchy of reliable evidence may not be met. In accordance with 32 CFR 199.4(g)(15)(ii), benefits for rare diseases are reviewed on a case-by-case basis. In reviewing proposed benefits for rare diseases under the new demonstration, consistent with TRICARE's rare disease policy, any or all of the following sources may be consulted to determine if the proposed non-FDA approved LDT for a rare disease is considered safe and effective:

- Trials published in refereed medical literature;
- Formal technology assessments;
- National medical policy organization positions;
- National professional associations; and
- National expert opinion organizations.

3.5 Cystic Fibrosis (CF) Carrier Screening

3.5.1 This new demonstration project will also extend coverage for preconception and prenatal CF carrier screening, as well as the follow-on prenatal CF diagnostic genetic testing, such as amniocentesis, chorionic villus sampling, or chordocentesis, when provided in accordance with the most current ACOG guidelines, in order to allow the DoD to establish whether there is a benefit to offering such testing to TRICARE beneficiaries. CF carrier screening will be covered from January 1, 2013, through the end of the demonstration in order to obtain sufficient data to be able to conduct a cost benefit analysis of providing this screening for our beneficiary population. Additionally, the CF screening test is exempt from the preauthorization requirements of this demonstration. Due to the volume of CF screening tests performed in the TRICARE population, it is not practicable or cost-effective for these tests to be preauthorized. Instead, the contractors shall ensure the test is provided in accordance with the most current ACOG guidelines, e.g. if a patient has been screened previously, CF screening results should be documented but the test should not be repeated.

3.5.2 Preconception and prenatal CF carrier screening is excluded from the TRICARE Basic Program regardless of whether an FDA approved kit or non-FDA approved test is utilized.

3.6 Non-FDA approved LDTs approved by the Director, DHA, or designee, during the demonstration period, as outlined in Figure 18.3-1, will become available for cost-sharing for qualified TRICARE beneficiaries during the demonstration period when performed by CLIA certified labs.

3.7 Non-FDA approved LDTs that lack sufficient reliable evidence for safety and efficacy based on the TRICARE hierarchy of reliable evidence will remain excluded from TRICARE coverage.

3.8 Notification to the contractors of non-FDA approved LDT eligibility for cost-sharing shall be published, periodically, to this Chapter of the TRICARE Operations Manual (TOM), as detailed in Figure 18.3-1. The codes listed in Figure 18.3-1 which are on the No Government Pay Procedure Code List (NGPL) but payable under this demonstration project will remain on the NGPL, since these non-FDA approved LDTs are not covered under the TRICARE Basic Program. Non-FDA approved LDTs listed in Figure 18.3-1 may be covered only as part of the demonstration project as denoted with the Special Processing Code (SPC) which shall be associated with each claim (see the TRICARE Systems Manual (TSM), Chapter 2. The TRICARE Encounter Data (TED) SPC for the new LDT demonstration is "L2 Non-FDA Approved Laboratory Developed Tests (LDTs) Demonstration."

3.9 The DHA shall cost-share all medical care and treatment associated with the LDT approved under the demonstration in the same manner it would any other care or treatment associated with the provision of medically necessary and appropriate care if the following conditions are met:

3.9.1 The specific non-FDA approved LDT has been approved by the Director, DHA, or designee, for cost-sharing to eligible TRICARE beneficiaries; and

3.9.2 The contractor has preauthorized the LDT approved under the demonstration, when required, and verified that the TRICARE authorized provider has determined the eligible patient's medical need for the LDT in accordance with all indications detailed in Figure 18.3-1; and

3.9.3 The contractor has verified that the patient's clinical diagnoses support the medical need and are fully documented according to and consistent with all indications detailed in Figure 18.3-1; and

3.9.4 The contractor has, as noted in TRICARE Policy Manual (TPM), Chapter 1, Section 6.1, paragraph 2.0, for dual eligible beneficiaries, applied all requirements when TRICARE is primary payer. As secondary payer under the TRICARE Dual Eligible Fiscal Intermediary Contract (TDEFIC), TRICARE will rely on and not replicate Medicare's determination of medical necessity and appropriateness in all circumstances where Medicare is primary payer. In the event that TRICARE is primary payer for these services and preauthorization, when required, was not obtained, the contractor shall obtain the necessary information and perform a retrospective review.

3.10 Genetic counseling may only be provided by TRICARE-authorized providers and must precede the actual LDT, in accordance with the TPM, Chapter 6, Section 3.1. There is no requirement to utilize the LDT SPC for claims for genetic counseling.

3.11 BRCA1 or BRCA2 Genetic Counseling and Testing

3.11.1 Genetic counseling rendered by a TRICARE-authorized provider that precedes BRCA1 or BRCA2 gene testing is covered with no copayment or cost-share as a preventive service for women who are identified as high risk for breast cancer by their primary care clinician.

3.11.2 BRCA1 or BRCA2 gene testing is covered with no copayment or cost-share as a preventive service for women who meet the coverage guidelines outlined in Figure 18.3-1.

Note: For men, applicable copayments or cost-shares will apply to medically necessary and appropriate BRCA1 or BRCA2 genetic counseling and testing.

3.12 The demonstration will expire on July 18, 2017. Requirements of this Chapter as related to this demonstration cease at midnight on July 18, 2017. Only TRICARE beneficiaries with current eligibility, as defined in paragraph 7.0, may participate in this demonstration project. Claims shall not be paid for individuals who are not eligible for TRICARE benefits. All medical care, treatments, or testing, with the exception of the LDT which has approval during the demonstration period only, must be a TRICARE covered benefit provided to TRICARE eligible beneficiaries. This applies to all care rendered during or after the end date of this demonstration project.

3.13 The records management requirements described in Chapter 9 apply to this demonstration project.

4.0 APPLICABILITY

4.1 This demonstration applies to all TRICARE-eligible beneficiaries, except for TRICARE dual-eligible beneficiaries. Additionally, for purposes of Chapter 17, Section 3, LDTs are covered for Service members as specified in the demonstration and no Supplemental Health Care Program (SHCP) waiver is required. The SPC **L2** shall accompany Service member claims.

4.2 The benefit for LDTs approved under this demonstration project differs from the TRICARE Basic Program benefit. Coverage inquiries shall be submitted to, and resolved by the appropriate contractor (referencing the DHA Evaluation of Non-FDA Approved LDTs Demonstration Project). Regarding a beneficiary with other insurance that provides primary coverage, any medical necessity reviews the contractor believes are necessary, to act as a secondary payer, shall be performed on a retrospective basis.

4.3 The DoD has no authority to cost-share non-FDA approved medical devices such as LDTs, under the TRICARE Basic Program. While the non-FDA approved LDTs may be covered under the demonstration, appeal rights do not apply. Denials under the new demonstration are not appealable. Further, the inclusion or exclusion of LDTs under the new demonstration is not appealable.

5.0 GENERAL DESCRIPTION OF THE ADMINISTRATIVE PROCESS

5.1 With the exception of the CF carrier screening test which must be provided in accordance with the most current ACOG guidelines, the contractor shall preauthorize all other demonstration approved LDTs, to verify that the TRICARE authorized provider has determined the eligible beneficiary's medical need based on the beneficiary's clinical diagnoses which support the medical need and, the contractor shall document these facts according to and consistent with the American Medical Association (AMA) Current Procedural Terminology (CPT), International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes, and according to all indications detailed in Figure 18.3-1. Following the contractor's identification of an appropriate request for an approved LDT, as identified within the terms of the demonstration, the TRICARE authorized provider requesting/ordering the LDT shall be notified that they are authorized to utilize the LDT for the beneficiary. The contractor shall issue the notification of decision to authorize use of the demonstration approved LDT in writing to both the applicant provider and the beneficiary receiving the LDT. The contractor shall identify each claim with the SPC **L2**.

5.2 For LDTs which must be performed on an emergency basis, contractors shall perform a retrospective authorization review and approval prior to payment (e.g., PML/RaRalpha testing

performed in an emergency room or inpatient hospital setting for acute promyelocytic leukemia patients where results are urgently needed and will immediately impact medical management/ treatment decisions).

5.3 All claims for approved care under the demonstration will be submitted to the contractor for adjudication.

5.4 Because some provisions of this demonstration are retroactive to January 1, 2013, exceptions may be granted to the time limitations on filing claims as outlined in Chapter 8, Section 3.

6.0 DHA RESPONSIBILITIES

6.1 The DHA Evaluation of Non-FDA Approved LDTs Demonstration Project will be paid by the DHA as non-financially underwritten transactions in accordance with each respective contractor's agreement and shall follow vouchering rules in Chapter 3 or Section G of the contract.

6.2 Perform periodic review and evaluation of the demonstration claims adjudication process.

6.3 Provide specific written guidance to the contractor or other contractor with jurisdiction for the claim regarding laboratory services and claims adjudication services to be provided by the claims processor under the terms of the demonstration.

7.0 CONTRACTOR RESPONSIBILITIES

The contractor shall:

- Verify the beneficiary's eligibility on the Defense Enrollment Eligibility Reporting System (DEERS).
- Correctly voucher the TED records for payment.
- Issue an authorization or denial letter to the applicant provider and beneficiary once a determination is made.
- Preauthorize the demonstration approved LDTs as required and verify medical necessity according to all indications detailed in Figure 18.3-1. Only the indications listed in the Coverage Guidelines may be considered for cost-sharing. The contractor shall issue the notification of decision to authorize use of the LDT in writing to both the applicant provider and the beneficiary receiving the LDT.
- Manage and resolve all inquiries related to the demonstration, including claims inquiries related to LDTs approved for cost-sharing during the LDT demonstration.

8.0 CLAIMS PROCESSING REQUIREMENTS

8.1 Both laboratory and professional charges shall be reimbursed based on existing TRICARE reimbursement rules. In the absence of a CHAMPUS Maximum Allowable Charge (CMAC) for the

specific test, the contractor shall develop a prevailing charge following the procedures in the TRICARE Reimbursement Manual (TRM), Chapter 5, Section 1.

8.2 The contractor shall assure that the laboratories submit all charges on the basis of fully itemized bills. Each service and supply shall be individually identified and submitted on the appropriate claim form. If a claim associated with the demonstration has missing information, Chapter 8, Section 6 guidelines shall be followed to either return or develop the claim and request the missing information.

8.3 All claims for the demonstration approved LDT shall meet the requirements outlined in Figure 18.3-1. All other covered care associated with treatment will be provided in accordance with the respective provisions of the TPM or TRM. Care associated with the LDT must be medically necessary and appropriate medical care and not otherwise excluded as a TRICARE benefit.

8.4 Cost-shares and deductibles applicable to TRICARE shall also apply under the demonstration.

8.5 Normal double coverage provisions apply to LDTs approved under the demonstration. Acceptable evidence of processing by the double coverage plan is outlined in Chapter 4.

8.6 Claims for this demonstration shall be paid from the applicable non-underwritten bank account (see Chapter 3), and submitted through normal TED processing as required in the TSM and in accordance with each respective contractor's agreement if claims data is not submitted through the TED system.

8.7 SPC **L2** shall be assigned to identify all claims paid under the new demonstration. The intent of this policy is to process claims for the demonstration approved LDTs with the SPC and the associated technical and professional components associated with the LDT-related CPTs. Medical care, treatments, and associated testing based on medical necessity as a consequence of the demonstration approved LDT's results are to be processed under the TRICARE Basic Program benefit.

8.8 Claims for this demonstration shall be submitted either by Electronic Media Claim (EMC) or by paper claim using the dedicated demonstration mailing address or using the appropriate regional claims processing address(es).

9.0 EFFECTIVE DATES

9.1 The effective date for coverage of LDTs approved under this demonstration project will be the later of:

9.1.1 January 1, 2013; or

9.1.2 The date on which there is sufficient reliable evidence to determine that the non-FDA approved LDT is proven safe and effective for TRICARE cost-sharing purposes. Effective dates of coverage for specific testing are included in Figure 18.3-1.

9.2 Effective January 1, 2017, no cost-share or copayment shall apply for genetic counseling rendered by a TRICARE-authorized provider that precedes BRCA1 or BRCA2 gene testing for women who are identified as high risk for breast cancer by their primary care clinician.

9.3 Effective January 1, 2017, no cost-share or copayment shall apply for BRCA1 or BRCA2 gene testing for women who meet the coverage guidelines outlined in Figure 18.3-1.

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED

GENE:	**ALK**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	ALK gene testing is covered for the following indication: • To determine response to Tyrosine Kinase Inhibitor (TKI) therapy in patients with adenocarcinoma of the lung or mixed lung cancer with adenocarcinoma component of the lung.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	88271 Molecular cytogenetics; DNA probe, each (e.g., FISH) Polyposis 88291 Cytogenetics and molecular cytogenetics, interpretation and report

GENE:	**APC**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	APC gene testing is covered for the following indications: • Testing for APC variants in individuals with clinical symptoms consistent with Familial Adenomatous Polyposis (FAP). • Testing for APC variants in individuals with clinical symptoms consistent with Attenuated Familial Adenomatous Polyposis (AFAP). • Testing for APC variants in individuals with clinical symptoms consistent with Turcot's or Gardner's syndromes. • Testing individuals with an APC-associated polyposis syndrome for the purpose of identifying a variant that may be used to screen at-risk relatives. • For the presymptomatic testing of at-risk relatives for a known familial variant.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81201 APC (Adenomatous Polyposis Coli) (e.g., Familial Adenomatosis Polyposis [FAP], attenuated FAP) gene analysis; full gene sequence 81202 known familial variants 81203 duplication/deletion variants

GENE:	**ATXN1**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	ATXN1 gene testing is covered for the following indications: • Diagnosis of Spinocerebellar Ataxia Type 1 (SCA1) in patients with cerebellar ataxia of unknown etiology, along with extracerebellar symptoms associated with SCA1 and/or a family history consistent with autosomal dominant inheritance. • Diagnosis of SCA1 in symptomatic family members of known SCA1 patients.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81401 ATXN1 (ataxin1) (e.g., spinocerebellar ataxia), evaluation to detect abnormal (e.g., expanded) alleles

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**ATXN2**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	ATXN2 gene testing is covered for the following indications: • Diagnosis of Spinocerebellar Ataxia Type 2 (SCA2) in patients with cerebellar ataxia of unknown etiology, along with extracerebellar symptoms associated with SCA2 and/or a family history consistent with autosomal dominant inheritance. • Diagnosis of SCA2 in symptomatic family members of known SCA2 patients.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81401 ATXN2 (ataxin2) (e.g., spinocerebellar ataxia), evaluation to detect abnormal (e.g., expanded) alleles

GENE:	**ATXN3**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	ATXN3 gene testing is covered for the following indications: • Diagnosis of Spinocerebellar Ataxia Type 3 (SCA3) in patients with cerebellar ataxia of unknown etiology, along with extracerebellar symptoms associated with SCA3 and/or a family history consistent with autosomal dominant inheritance. • Diagnosis of SCA3 in symptomatic family members of known SCA3 patients.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81401 ATXN3 (ataxin3) (e.g., spinocerebellar ataxia, Machado-Joseph disease), evaluation to detect abnormal (e.g., expanded) alleles

GENE:	**ATXN7**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	ATXN7 gene testing is covered for the following indications: • Diagnosis of Spinocerebellar Ataxia Type 7 (SCA7) in patients with cerebellar ataxia and visual disturbance. • Diagnosis of SCA7 in symptomatic family members of known SCA7 patients.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81401 ATXN7 (ataxin7) (e.g., spinocerebellar ataxia), evaluation to detect abnormal (e.g., expanded) alleles

GENE:	**ATXN10**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	ATXN10 gene testing is covered for the following indications: • Diagnosis of Spinocerebellar Ataxia Type 10 (SCA10) in ataxia patients whose ancestry is of American Indian origin, and whose family history is consistent with autosomal dominant inheritance. • Diagnosis of SCA10 in symptomatic family members of known SCA10 patients.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81401 ATXN10 (ataxin10) (e.g., spinocerebellar ataxia), evaluation to detect abnormal (e.g., expanded) alleles

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**BCR/ABL1**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	BCR/ABL1 gene testing is covered for the following indications: • Diagnostic assessment of individuals with suspected Chronic Myelogenous Leukemia (CML) by quantitative RT-PCR (RQ-PCR). • Diagnostic assessment of individuals with suspected CML by qualitative RT-PCR. • Monitoring response to TKI therapy, such as imatinib, in individuals with CML by RQ-PCR. • Testing for the presence of the BCR/ABL1 p.Thr315Ile variant in CML patients to guide treatment selection following resistance to first-line imatinib therapy. • Testing for the presence of BCR/ABL1 variants other than p.Thr315Ile in CML patients to guide treatment selection following resistance to first-line imatinib therapy.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81170 ABL1 81206 BCR/ABL1 gene major bp 81207 BCR/ABL1 gene major bp 81208 BCR/ABL1 gene major bp

GENE:	**BMPR1A**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	BMPR1A gene testing is covered for the following indications: • To clarify the diagnosis of individuals with Juvenile Polyposis Syndrome (JPS). • If a known SMAD4 mutation is in the family, genetic testing should be performed in the first six months of life due to hereditary hemorrhagic telangiectasia risk.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81479 Unlisted molecular pathology procedure

GENE:	**BRAF**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	BRAF gene testing is covered for the following indications: • To predict response to vemurafenib therapy in patients with a positive cobas 4800 BRAF mutation test result. • To predict response to trametinib monotherapy in advanced melanoma patients with a positive BRAF p.Val600GLu and/or p.Val600Lys test result. • To predict response to dabrafenib monotherapy in advanced melanoma patients with a positive BRAF p.Val600Glu test result. • To predict response to trametinib and dabrafenib combination therapy in advanced melanoma patients with a positive BRAF p.Val600Glu and/or p.Val600Lys test result. • For individuals with indeterminate thyroid Fine-Needle Aspiration (FNA) biopsy cytology for diagnosis of papillary thyroid carcinoma.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81210 BRAF gene

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**BRCA1/BRCA2**	
Effective Date:	January 1, 2013	

Coverage Guidelines:	BRCA1/BRCA2 gene testing is covered for the following indications:
	• For individuals from families transmitting a known BRCA1/2 variant.
	• For individuals with a history of breast cancer and at least one of the following:
	  • Breast cancer diagnosed ≤ 45 years of age.
	  • Breast cancer diagnosed ≤ 50 years of age and a close family member with breast cancer.
	  • Two breast primaries with one diagnosed at or before age 50.
	  • A diagnosis of triple negative breast cancer at or before age 60.
	  • Breast cancer diagnosed at any age and at least one close relative with breast cancer before age 50 and/or epithelial ovarian cancer at any age.
	  • Breast cancer diagnosed at any age and at least two close relatives diagnosed with breast, pancreatic, and/or prostate (Gleason ≥ 7) cancer at any age.
	  • A close male relative, which includes first-, second-, and third-degree relatives, with breast cancer.
	  • An ethnic background associated with a higher frequency of BRCA1/2 variants (i.e., Ashkenazi Jewish).
	• For individuals with a personal history of epithelial ovarian cancer.
	• For individuals with male breast cancer.
	• For individuals with a personal history of pancreatic cancer or prostate (Gleason ≥ 7) and at least two close relatives with breast, ovarian, prostate (Gleason ≥ 7), and/or pancreatic cancer.
	• For unaffected individuals (with no personal history of cancer) who have one of the following:
	  • A first- or second-degree relative satisfying the above criteria.
	  • A third-degree relative with breast and/or ovarian cancer and at least two more relatives with breast cancer (at least one diagnosed before age 50) and/or ovarian cancer.	

CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81162 BRCA1&2 seq & full dup/del 81211 BRCA1&2 seq & com dup/del 81212 BRCA1&2 185&538&6174 var 81213 BRCA1&2 uncom dup/del var 81214 BRCA1 full seq & com dup/del 81215 BRCA1 gene known fam variant 81216 BRCA2 gene full sequence 81217 BRCA2 gene known fam variant

GENE:	**CACNA1A**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	CACNA1A gene testing is covered for the following indications: • Diagnosis of Spinocerebellar Ataxia Type 6 (SCA6) in patients with cerebellar ataxia with dysarthria and/or nystagmus. • Diagnosis of SCA6 in symptomatic family members of known SCA6 patients.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81401 CACNA1A (calcium channel, voltage-dependent, P/Q type, alpha 1A subunit) (e.g., spinocerebellar ataxia), evaluation to detect abnormal (e.g., expanded) alleles

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**CALM1, CASQ2, RYR2, and TRDN**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	CALM1, CASQ2, RYR2, and TRDN gene testing is covered for the following indication: • To confirm a diagnosis of Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) in patients with clinically diagnosed or suspected CPVT.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81405 Mopath procedure level 6 81408 Mopath procedure level 9 81479 Unlisted molecular pathology

GENE:	**CDH1**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	CDH1 gene testing is covered for the following indication: • For large rearrangements in the CDH1 gene for the treatment of Hereditary Diffuse Gastric Cancer (HDGC).	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81406 Mopath procedure level 7

GENE:	**CEBPA**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	CEBPA gene testing is covered for the following indication: • To guide the treatment decisions for individuals with Acute Myeloid Leukemia (AML).	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81218 CEBPA gene full sequence

GENE:	**CFTR**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	CFTR gene testing is covered for the following indications: • Confirmation of diagnosis in individuals showing clinical symptoms of Cystic Fibrosis (CF) or having a high sweat chloride level. • Identification of newborns who are affected with CF. • Identification of individuals with the p.Gly551Asp variant who will respond to treatment with ivacaftor. • Male infertility testing and treatment. • Preconception and prenatal carrier screening in accordance with the most current ACOG guidelines.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81220 CFTR (cystic fibrosis transmembrane conductance regulator) (e.g. cystic fibrosis) gene analysis, common variants 81221 known familial variants 81222 duplication/deletion variants 81223 full gene sequence 81224 intron 8 poly-T analysis (e.g. male infertility)

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**Chimerism Analysis**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	Chimerism analysis is covered for the following indication: • For the management and treatment of stem cell transplant patients.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81265 81266 81267 81268	Str markers specimen anal Str markers spec anal addl Chimerism anal no cell selec Chimerism anal w/cell select

GENE:	**Chromosome 22q11.2**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	Chromosome 22q11.2 gene testing is covered for the following indication: • Confirmation of diagnosis in an individual suspected of chromosome 22q11.2 deletion syndrome based on clinical findings.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	88271 88291	Molecular cytogenetics; DNA probe, each (e.g., FISH)cystic fibrosis) Cytogenetics and molecular cytogenetics, interpretation and report

GENE:	**COL1A1/COL1A2**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	COL1A1/COL1A2 gene testing is covered for the following indication: • For sequence variants in the COL1A1/COL1A2 genes for the diagnosis of Osteogenesis Imperfecta (OI) when clinical and radiological examination and family history provide inadequate information for diagnosis of OI.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81408	Mopath procedure level 9

GENE:	**COL3A1**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	COL3A1 gene testing is covered for the following indication: • To confirm or establish a diagnosis of Ehlers-Danlos Syndrome Type 4 (EDS IV), also known as vascular EDS, in patients with clinical symptoms or features of EDS IV.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81479	Unlisted molecular pathology procedure

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**CYP2C9**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	CYP2C9 gene testing is covered for the following indication: • For the initiation and management of warfarin treatment	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81227 CYP2C9 gene com variants

GENE:	**CYP2C19**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	CYP2C19 gene testing is covered for the following indication: • To manage dosing of clopidogrel.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81225 CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *4, *8, *17)

GENE:	**Cytogenomic Constitutional Microarray Analysis**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	Cytogenomic Constitutional Microarray Analysis gene testing is covered for the following indications: • Diagnostic evaluation of patients suspected of having a genetic syndrome (i.e., have congenital anomalies, dysmorphic features, Developmental Delay (DD), and/or intellectual disability). • Diagnostic evaluation of individuals with Autism Spectrum Disorder (ASD), including autism, Asperger syndrome, and pervasive developmental disorder.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81228 Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (e.g., Bacterial Artificial Chromosome [BAC] or oligo-based Comparative Genomic Hybridization [CGH] microarray analysis 81229 interrogation of genomic regions for copy number and Single Nucleotide Polymorphism (SNP) variants for chromosomal abnormalities 81406 Cytogenomic microarray analysis, neoplasia (e.g., interrogation of copy number, and loss-of-heterozygosity via Single Nucleotide Polymorphism [SNP]-based Comparative Genomic Hybridization [CGH] microarray analysis)

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**DAZ/SRY**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	DAZ/SRY gene testing is covered for the following indication: • To detect submicroscopic deletions involving the Y chromosome in the evaluation of men with infertility secondary to azoospermia, oligozoospermia, or teratozoospermia.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81403 DAZ/SRY (deleted in azoospermia and sex determining region Y) (e.g., male infertility), common deletions (e.g., AZFa, AZFb, AZFc, AZFd)

GENE:	**DMD**	
Effective Date:	November 20, 2014	
Coverage Guidelines:	DMD gene testing is covered for the following indication: • For diagnostic DMD testing (deletion and duplication analysis with reflex to complete gene sequencing) in males or females exhibiting symptoms of Duchenne Muscular Dystrophy (DMD) or Becker Muscular Dystrophy (BMD).	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81161 DMD dup/delet analysis 81408 Mopath procedure level 9

GENE:	**DMPK**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	DMPK gene testing is covered for the following indications: • Confirmation of a diagnosis of Myotonic Dystrophy Type 1 (DM1) or Type 2 (DM2) in symptomatic patients. • Diagnosis of DM1 or DM2 in asymptomatic adults who are at an increased risk of DM1 or DM2 through a positive family history.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81401 DMPK (dystrophia myotonica-protein kinase) (e.g., myotonic dystrophy, type 1), evaluation to detect abnormal (e.g., expanded) alleles 81404 DMPK (dystrophia myotonica-protein kinase) (e.g., myotonic dystrophy type 1), characterization of abnormal (e.g., expanded) alleles

GENE:	**DSC2, DSG2, DSP, JUP, PKP2, RYR2, TGFB3, and TMEM43**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	DSC2, DSG2, DSP, JUP, PKP2, RYR2, TGFB3, and TMEM43 gene testing is covered for the following indications: • For sequence variants in the DSC2, DSG2, DSP, JUP, PKP2, RYR2, TGFB3, and TMEM43 genes to confirm a diagnosis of Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy (ARVD/C) in probands. • For a known familial sequence variant in the DSC2, DSG2, DSP, PKP2, or TMEM43 gene for at-risk relatives of probands with International Task Force (ITF)-confirmed ARVD/C to confirm a diagnosis of ARVD/C in those whose symptoms meet the ITF-diagnostic criteria.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81406 Mopath procedure level 7 81408 Mopath procedure level 9

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**EGFR**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	EGFR gene testing is covered for the following indication: • To help guide administration of Epidermal Growth Factor Receptor (EGFR) TKIs in the first-line treatment of non-small cell lung cancer.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81235	EGFR (epidermal growth factor receptor) (e.g. non-small cell lung cancer) gene analysis, common variants (e.g. exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)

GENE:	**F2**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	Prothrombin (Factor II) related thrombophilia gene testing is covered for the following indications: • Diagnostic evaluation of individuals with a prior Venous Thromboembolism (VTE) during pregnancy or puerperium. • For patients with VTE with a personal or family history of recurrent VTE (more than two in the same person). • For patients with their first VTE before age 50 with no precipitating factors. • For venous thrombosis at unusual sites such as the cerebral, mesenteric, portal, or hepatic veins. • For VTE associated with the use of estrogen-containing oral contraceptives, Selective Estrogen Receptor Modulators (SERMs), or Hormone Replacement Therapy (HRT). • To diagnose an inherited thrombophilia in female family members of individuals with an inherited thrombophilia if the female family member is pregnant or considering pregnancy or oral contraceptive use.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81240	F2 (prothrombin, coagulation factor II) (e.g., hereditary hypercoagulability) gene analysis, 20210G>A variant
		81400	F2 (coagulation factor 2) (e.g., hereditary hypercoagulability), 1199G>A variant

GENE:	**F5**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	Factor V Leiden thrombophilia gene testing is covered for the following indications: • Diagnostic evaluation of individuals with a prior VTE during pregnancy or puerperium. • For patients with VTE with a personal or family history of recurrent VTE (more than two in the same person). • For patients with their first VTE before age 50 with no precipitating factors. • For venous thrombosis at unusual sites such as the cerebral, mesenteric, portal, or hepatic veins. • For VTE associated with the use of estrogen-containing oral contraceptives, Selective Estrogen Receptor Modulators (SERMs), or Hormone Replacement Therapy (HRT). • To diagnose an inherited thrombophilia in female family members of individuals with an inherited thrombophilia if the female family member is pregnant or considering pregnancy or oral contraceptive use.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81241	F5 (coagulation factor V) (e.g., hereditary hypercoagulability) gene analysis, Leiden variant
		81400	F5 (coagulation factor V) (e.g., hereditary hypercoagulability), HR2 variant

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**FBN1**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	FBN1 gene testing is covered for the following indications: • To facilitate the diagnosis of Marfan syndrome in patients who do not fulfill the Ghent diagnostic criteria, but have at least one major feature of the condition. • To facilitate the diagnosis of Marfan syndrome in the at-risk relatives of patients carrying known disease-causing variants.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81408 FBN1 (fibrillin 1) (e.g., Marfan syndrome), full gene sequence

GENE:	**FLCN**	
Effective Date:	July 31, 2014	
Coverage Guidelines:	FLCN gene testing is covered for the following indication: • To confirm a diagnosis of Birt-Hogg-Dubé Syndrome (BHD) in patients with suspected BHD.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81479 Unlisted molecular pathology

GENE:	**FLT3**	
Effective Date:	October 7, 2013	
Coverage Guidelines:	FLT3 gene testing is covered for the following indication: • For diagnosis and prognosis in AML.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81245 FLT3 gene 81246 FLT3 gene analysis

GENE:	**FMR1**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	FMR1 gene testing is covered for the following indications: • Testing for CGG repeat length for diagnosis of patients of either sex with mental retardation, intellectual disability, developmental delay, or autism. FMR1 gene testing for Fragile X-Associated Tremor/Ataxia Syndrome is covered for the following individuals: • Males and females older than age 50 years who have progressive cerebellar ataxia and intention tremor with or without a positive family history of FMR1-related disorders in whom other common causes of ataxia have been excluded. • Women with unexplained Premature Ovarian Insufficiency (POI).	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81243 FMR1 (fragile X mental retardation 1) (e.g., fragile X mental retardation) gene analysis; evaluation to detect abnormal (e.g., expanded) alleles 81244 characterization of alleles (e.g., expanded size and methylation status)

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**GCK**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	GCK gene testing is covered for the following indication: • Diagnosis of Maturity-Onset Diabetes of the Young Type 2 (MODY2) in patients with hyperglycemia or non-insulin-dependent diabetes who have a family history of abnormal glucose metabolism in at least two consecutive generations, with the patient or ≥ 1 family member(s) diagnosed before age 25.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81406 GCK (glucokinase [hexokinase 4]) (e.g., maturity-onset diabetes of the young [MODY]), full gene sequence

GENE:	**GJB2**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	GJB2 gene testing is covered for the following indication: • Diagnosis of DFNB1 or DFNA3 in individuals with nonsyndromic hearing loss to aid in treatment.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81252 GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (e.g., nonsyndromic hearing loss) gene analysis; full gene sequence 81253 known familial variants

GENE:	**GJB6**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	GJB6 gene testing is covered for the following indication: • Diagnosis of DFNB1 or DFNA3 in individuals with nonsyndromic hearing loss to aid in treatment.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81254 GJB6 (gap junction protein, beta 6, 30kDa, connexin 30) (e.g., nonsyndromic hearing loss) gene analysis, common variants (e.g., 309kb [del(GJB6-D13S1830)] and 232kb [del(GJB6-D13S1854)])

GENE:	**HBA1/HBA2**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	HBA1/HBA2 gene testing is covered for the following indications: • To confirm the diagnosis of alpha-thalassemia in a symptomatic individual. • To confirm the diagnosis in a pregnant woman with low hemoglobin when alpha-thalassemia is suspected.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81257 HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis, for common deletions or variant (e.g., Southeast Asian, Thai, Filipino, Mediterranean, alpha3.7, alpha4.2, alpha20.5, and Constant Spring) 81404 HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia), duplication/deletion analysis 81405 HBA1/HBA2 (alpha globin 1 and alpha globin 2) (e.g., alpha thalassemia), full gene sequence

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**HEXA**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	HEXA gene testing is covered for the following indication: • As an adjunct to biochemical testing in patients with low hexosaminidase A levels in blood. When individuals are identified with apparent deficiency of hexosaminidase A enzymatic activity, targeted mutation analysis can then be used to distinguish pseudodeficiency alleles from disease-causing alleles.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81255	HEXA (hexosaminidase A [alpha polypeptide]) (e.g., Tay-Sachs disease) gene analysis, common variants (e.g., 1278insTATC, 1421+1G>C, G269S)
		81406	HEXA (hexosaminidase A, alpha polypeptide) (e.g., Tay-Sachs disease), full gene sequence

GENE:	**HFE**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	HFE-associated hereditary hemochromatosis gene testing is covered for the following indication: • Diagnosis of patients with or without symptoms of iron overload with a serum transferrin saturation >45% and/or elevated serum ferritin.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81256	HFE (hemochromatosis) (e.g., hereditary hemochromatosis) gene analysis, common variants (e.g., C282Y, H63D)

GENE:	**HLA**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	HLA gene testing is covered for the following indications: • To determine histocompatibility of tissue between organ and bone marrow donors and recipients prior to transplant. • For platelet transfusion for patients refractory to treatment due to alloimmunization. • Diagnosis of celiac disease in symptomatic patients with equivocal results on small bowel biopsy and serology, or in previously symptomatic patients who are asymptomatic while on a gluten-free diet. • Testing for the HLA-B*1502 allele prior to initiating treatment with carbamazepine in patients from high-risk ethnic groups. • Testing for the HLA-B*5701 allele for hypersensitivity reactions in patients prior to initiation or reinitiation with treatments containing abacavir. • Testing for the HLA-B*58:01 allele in patients prior to initiating treatment with allopurinol.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81370	HLA Class I and II typing, low resolution (e.g. antigen equivalents); HLA-A, -B, -C, -DRB1/3/4/5, and -DQB1
		81371	HLA-A, -B, and -DRB1 (e.g., verification typing)
		81372	HLA Class I typing, low resolution (e.g. antigen equivalents); complete (i.e., HLA-A, -B, and -C)
		81373	one locus (e.g., HLA-A, -B, or -C) each
		81374	one antigen equivalent (e.g. B*27), each

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

		81375	HLA Class II typing, low resolution (e.g. antigen equivalents); HLA-DRB1/3/4/5 and -DQB1
		81376	one locus (e.g., HLA-DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each
		81377	one antigen equivalent, each
		81378	HLA Class I and II typing, high resolution (i.e., alleles or allele groups), HLA-A, -B, -C, and -DRB1
		81379	HLA Class I typing, high resolution (i.e., alleles or allele groups); complete (i.e., HLA-A, -B, and –C)
		81380	one locus (e.g., HLA-A, -B, or –C), each
		81381	one allele or allele group (e.g., B*57:01P), each
		81382	HLA Class II typing, high resolution (i.e., alleles or allele groups); one locus (e.g., HLA-DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each
		81383	one allele or allele group (e.g., HLA- DQB1*06:02P), each

GENE:	**HNF1A**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	HNF1A gene testing is covered for the following indication: • Diagnosis of Maturity-Onset Diabetes of the Young Type 3 (MODY3) in patients with hyperglycemia or non-insulin-dependent diabetes who have a family history of abnormal glucose metabolism in at least two consecutive generations, with the patient or ≥ 1 family member(s) diagnosed before age 25.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81405	HNF1A (HNF1 homeobox A) (e.g., maturity-onset diabetes of the young [MODY]), full gene sequence

GENE:	**HTT**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	HTT gene testing is covered for the following indication: • To test for CAG repeat length for diagnosis of Huntington Chorea/Disease (HD) in patients suspected of having HD in the absence of a family history of HD.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81401	HTT (huntington) (e.g., Huntington disease), evaluation to detect abnormal (e.g., expanded) alleles

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**IGH**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	IGH gene testing is covered for the following indications: • For medical management of patients with Acute Lymphoblastic Leukemia (ALL) through analysis of rearrangements in the IGH gene to estimate Minimal Residual Disease (MRD) levels. • For diagnostic evaluation of rearrangements in the IGH gene in patients with suspected B-cell Non-Hodgkin's Lymphoma (NHL), but in whom clinical, immunophenotypic, and histologic evaluation have provided inconclusive results	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81261 IGH gene rearrange amp meth 81262 IGH gene rearrang dir probe 81263 IGH vari regional mutation

GENE:	**IGK**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	IGK gene testing is covered for the following indications: • For medical management of patients with ALL through analysis of rearrangements in the IGK gene to estimate MRD levels. • For diagnostic evaluation of rearrangements in the IGK gene in patients with suspected B-cell NHL, but in whom clinical, immunophenotypic, and histologic evaluations have provided inconclusive results.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81264 IGK rearrangeabn clonal pop

GENE:	**JAK2**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	JAK2 gene testing is covered for the following indications: • Diagnostic evaluation of individuals presenting with clinical, laboratory, or pathological findings suggesting classic forms of myeloproliferative neoplasms (MPN), that is, Polycythemia Vera (PV), Essential Thrombocythemia (ET), or Primary Myelofibrosis (PMF). • Diagnostic evaluation of PV through JAK2 Exon 12 variant detection in JAK2 p.Val617Phe negative individuals.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81270 JAK2 (Janus kinase 2) (e.g., myeloproliferative disorder) gene analysis, p.Val617Phe (V617F) variant 81403 JAK2 (Janus kinase 2) (e.g., myeloproliferative disorder), exon 12 sequence and exon 13 sequence, if performed

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**KCNQ1, KCNH2, SCN5A, KCNE1, and KCNE2**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	KCNQ1, KCNH2, SCN5A, KCNE1, and KCNE2 gene testing is covered for the following indication: • For patients with suspected familial Long QT Syndrome for confirmation of diagnosis and treatment.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81280 Long QT syndrome gene analysis (e.g., KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); full gene sequence 81281 known familial variant 81282 duplication/deletion variants

GENE:	**KIT**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	KIT gene testing is covered for the following indications: • To confirm a diagnosis of a gastrointestinal stromal tumor (GIST) in patients who are negative by immunostaining. • To determine primary resistance to treatment with TKIs in patients with an advanced metastatic or unresectable GIST. • To determine primary resistance to preoperative or postoperative treatment of a GIST with TKIs.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81272 Kit gene targeted seq analysis 81273 Kit gene analysis d816 variant

GENE:	**KRAS**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	KRAS gene testing is covered for the following indication: • To help guide administration of anti-EGFR monoclonal antibodies.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81275 KRAS gene variants exon 2 81276 KRAS gene addl variants

GENE:	**MECP2**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	MECP2 gene testing is covered for the following indications: • Testing for MECP2 sequence variants in patients who meet established clinical diagnostic criteria for classic or variant Rett Syndrome (RS). • Testing for MECP2 sequence variants in patients who have symptoms of RS, but do not meet established clinical diagnostic criteria.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81302 MECP2 (methyl CpG binding protein 2) (e.g., Rett syndrome) gene analysis; full sequence analysis 81303 known familial variant 81304 duplication/deletion variants

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**MLH1, MSH2, MSH6, MSI, PMS2, and EPCAM**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	Genetic testing for Lynch syndrome is covered for a symptomatic or asymptomatic beneficiary who meets one of the following criteria: 1. Amsterdam II criteria for Lynch syndrome genetic testing. At least three relatives of the affected beneficiary must have a cancer associated with Lynch syndrome; and all of the following criteria must be present: • One must be a first-degree relative of the other two; • At least two successive generations must be affected; • At least one relative with cancer associated with Lynch syndrome should be diagnosed before age 50 years; • FAP should be excluded in the colorectal cancer case(s) (if any); and • Tumors should be verified whenever possible. 2. Revised Bethesda guidelines: • Colorectal cancer diagnosed in a beneficiary at less than 50 years of age. • Presence of synchronous or metachronous Lynch syndrome-associated cancers, regardless of age. Lynch syndrome-associated cancers include colorectal, endometrial, ovarian, gastric, pancreas, ureter and renal pelvis, biliary tract, brain (usually glioblastoma), and small intestine cancers, as well as sebaceous gland adenomas/ carcinomas and keratoacanthomas. • Colorectal cancer with the MSI-H histology diagnosed in a beneficiary who is less than 60 years of age. • Colorectal cancer diagnosed in a beneficiary with one or more first-degree relatives with a Lynch syndrome-associated cancer, with one of the cancers being diagnosed under age 50 years. • Colorectal cancer diagnosed in a beneficiary with two or more first- or second-degree relatives with Lynch syndrome-associated cancers, regardless of age. 3. Has a known Lynch syndrome mutation in the family. 4. Endometrial cancer diagnosed in a beneficiary at less than 50 years of age. 5. If any of the revised Bethesda guidelines are met, Microsatellite Instability (MSI) and/or Immunohistochemistry (IHC) testing on the colon cancer tissue may be clinically appropriate. If the tumor is MSI positive or mutation of one of the mismatch repair genes is indicated by failure of IHC staining, then genetic testing should be undertaken. Further unnecessary testing can often be avoided by performance of IHC prior to any MSI testing. • Genetic testing is covered for symptomatic or asymptomatic patients > 18 years of age who are at risk of having a known familial sequence variant in a Mismatch Repair (MMR) gene.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81288 MLH1 gene 81292 MLH1 gene full seq 81293 MLH1 gene known variants 81294 MLH1 gene dup/delete variant 81295 MSH2 gene full seq 81296 MSH2 gene known variants 81297 MSH2 gene dup/delete variant

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

		81298 MSH6 gene full seq 81299 MSH6 gene known variants 81300 MSH6 gene dup/delete variant 81301 Microsatellite instability 81317 PMS2 gene full seq 81318 PMS2 gene known familial variants 81319 PMS2 gene dup /delete variants 81403 Mopath procedure level 4

GENE:	**MPL**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	MPL gene testing is covered for the following indication: • Diagnostic evaluation of Myeloproliferative Leukemia (MPL) variants to include Trp515Leu and Trp515Lys in JAK2 p.Val617Phe-negative individuals showing symptoms.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81402 MPL (myeloproliferative leukemia virus oncogene, thrombopoietin receptor, TPOR) (e.g., myeloproliferative disorder), common variants (e.g., W515A, W515K, W515L, W515R) 81403 MPL (myeloproliferative leukemia virus oncogene, thrombopoietin receptor, TPOR) (e.g., myeloproliferative disorder), exon 10 sequence

GENE:	**MUTYH**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	MUTYH or MYH gene testing is covered for the following indications: • Diagnosis of MYH-Associated Polyposis (MAP) in APC-negative colorectal polyposis patients, or in polyposis patients who have a family history consistent with autosomal recessive inheritance. • Diagnosis of MAP in asymptomatic siblings of patients with known MYH variants.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81401 MUTYH (mutY homolog [E. coli]) (e.g., MYH-associated polyposis), common variants (e.g., Y165C, G382D) 81406 MUTYH (mutY homolog [E. coli]) (e.g., MYH-associated polyposis), full gene sequence

GENE:	**Noninvasive Prenatal Screening for Trisomies 13, 18, 21, X & Y**	
Effective Date:	March 5, 2015	
Coverage Guidelines:	Nonivasive Prenatal Screening for Trisomies 13, 18, 21, X & Y is covered for the following indication: • In singleton pregnancies with a high risk of fetal aneuploidy.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81420 Fetal chrmoml aneuploidy 81479 Unlisted molecular pathology 81507 Fetal aneuploidy trisom risk 81599 Unlisted maaa

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**NPM1**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	NPM1 gene testing is covered for the following indication: • To guide treatment decisions for individuals with AML.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81310 NPM1 (nucleophosmin) (e.g., acute myeloid leukemia) gene analysis, exon 12 variants

GENE:	**NRAS**	
Effective Date:	October 3, 2014	
Coverage Guidelines:	NRAS gene testing is covered for the following indication: • For patients with metastatic colorectal cancer who are being considered for treatment with anti-EGFR monoclonal antibodies, and who have had negative KRAS gene testing.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81311 NRAS gene variants exon 2&3

GENE:	**Oncotype DX® Breast Cancer Assay (Oncotype DX®)**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	Oncotype DX® gene testing is covered for the following indications: • Estrogen Receptor (ER) positive (+), lymph node (LN) negative (-), human EGFR 2 negative (HER2-) breast cancer patients who are considering whether to use adjuvant chemotherapy in addition to standard hormone therapy. • ER+, HER2- breast cancer patients with 1-3 involved ipsilateral axillary lymph nodes who are considering whether to use adjuvant chemotherapy in addition to hormonal therapy.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81519 Oncology breast maa

GENE:	**PAX8**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	PAX8 gene testing is covered for the following indication: • For individuals with indeterminate thyroid FNA biopsy cytology for diagnosis of papillary thyroid carcinoma.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81401 PAX8/PPARG (t(2;3) (q13;p25)) (e.g., follicular thyroid carcinoma), translocation analysis

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**PDGFRA**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	PDGFRA gene testing is covered for the following indications: • To confirm a diagnosis of a GIST in patients who are negative by immunostaining. • To determine primary resistance to treatment with TKIs in patients with an advanced metastatic or unresectable GIST. • To determine primary resistance to preoperative or postoperative treatment of a GIST with TKIs.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81314 PDGFRA gene

GENE:	**PML/RARalpha**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	PML/RARalpha gene testing is covered for the following indications: • Diagnostic assessment of individuals with suspected acute promyelocytic leukemia (APL) by quantitative RT-PCR (RQ-PCR). • Diagnostic assessment of individuals with suspected APL by qualitative RT-PCR. • Monitoring response to treatment and disease progression in individuals with APL by RQ-PCR.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81315 PML/RARalpha, (t(15;17)), promyelocytic leukemia/retinoic acid receptor alpha (e.g., promyelocytic leukemia) translocation analysis; common breakpoints (e.g. intron 3 and intron 6), qualitative or quantitative 81316 single breakpoint (e.g., intron 3, intron 6 or exon 6), qualitative or quantitative

GENE:	**PMP22**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	PMP22 gene testing is covered for the following indication: • For the accurate diagnosis and classification of hereditary polyneuropathies.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81324 PMP22 (peripheral myelin protein 22) (e.g. Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; duplication/deletion analysis 81325 full sequence analysis 81326 known familial variant

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**PPP2R2B**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	PPP2R2B gene testing is covered for the following indications: • Diagnosis of Spinocerebellar Ataxia Type 12 (SCA12) in patients with action tremor of the upper extremities and signs of cerebellar and cortical dysfunction, in addition to Indian ancestry and a family history consistent with autosomal dominant inheritance. • Diagnosis of SCA12 in symptomatic family members of known SCA12 patients.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81401	PPP2R2B (protein phosphatase 2, regulatory subunit B, beta) (e.g., spinocerebellar ataxia), evaluation to detect abnormal (e.g., expanded) alleles

GENE:	**PRSS1**		
Effective Date:	January 1, 2013		

Coverage Guidelines:	PRSS1 gene testing is covered for the following indications:
	• To confirm a diagnosis of hereditary pancreatitis in symptomatic patients with any of the following:
	  • A family history of pancreatitis in a first-degree (parent, sibling, child) or second-degree (aunt, uncle, grandparent) relative;
	  • An unexplained episode of documented pancreatitis occurring in a child that has required hospitalization, and where there is significant concern that hereditary pancreatitis should be excluded;
	  • Recurrent (two or more separate, documented episodes with hyper-amylasemia) attacks of acute pancreatitis for which there is no explanation (anatomical anomalies, ampullary or main pancreatic strictures, trauma, viral infection, gallstones, alcohol, drugs, hyperlipidemia, etc.); or
	  • Unexplained (idiopathic) chronic pancreatitis.		

CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81401	PRSS1 (protease, serine, 1 [trypsin 1]) (e.g., hereditary pancreatitis), common variants (e.g., N29I, A16V, R122H)

GENE:	**PTEN**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	PTEN gene testing is covered for the following indications: • For patients with ASDs and macrocephaly (Head circumference greater than 2 standard above the mean for age). • PTEN variant testing in individuals suspected of being affected with Cowden Syndrome (CS) or Bannayan-Riley-Ruvalcaba Syndrome (BRRS).		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81321	PTEN (phosphatase and tensin homolog) (e.g. Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis
		81322	known familial variant
		81326	duplication/deletion variant

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**RET**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	RET gene testing is covered for the following indications: • Multiple endocrine neoplasia type 2 (MEN2) gene testing in patients with the clinical manifestations of MEN2A, MEN2B, or familial medullary thyroid carcinoma (FMTC), including those with apparently sporadic Medullary Thyroid Carcinoma (MTC) or pheochromocytoma. • MEN2 gene testing to confirm a diagnosis in the at-risk relatives of genetically confirmed MEN2 patients.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81404 RET (ret proto-oncogene) (e.g., multiple endocrine neoplasia, type 2B and familial medullary thyroid carcinoma), common variants (e.g., M918T, 2647_2648delinsTT, A883F) 81405 RET (ret proto-oncogene) (e.g., multiple endocrine neoplasia, type 2A and familial medullary thyroid carcinoma), targeted sequence analysis (e.g., exons 10, 11, 13-16)

GENE:	**ROS1**	
Effective Date:	January 12, 2016	
Coverage Guidelines:	ROS1 gene testing is covered for the following indication:. • For patients who have wild type (negative) EGFR or ALK gene testing, reflex testing to ROS1 should be ordered for the treatment of non-small cell lung carcinoma.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	88274 Cytogenetics 25-99

GENE:	**RYR1**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	RYR1 gene testing is covered for the following indications: • To test clinically confirmed Malignant Hyperthermia Susceptibility (MHS) patients for variants in the RYR1 gene to facilitate diagnostic testing in at-risk relatives. • To diagnose MHS in at-risk relatives of patients with clinically confirmed MHS.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81408 RYR1 (ryanodine receptor 1, skeletal) (e.g., malignant hyperthermia), full gene sequence

GENE:	**SDHB**	
Effective Date:	June 16, 2014	
Coverage Guidelines:	SDHB gene testing is covered for the following indication: • To diagnose a hereditary paraganglioma (PGL) or pheochromocytoma (PCC) syndrome in patients with PGLs and/or PCCs.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81405 SDHB (succinate dehydrogenase complex, subunit B, iron sulfur) (e.g., hereditary paraganglioma), full gene sequence

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**SDHD**	
Effective Date:	June 16, 2014	
Coverage Guidelines:	SDHD gene testing is covered for the following indication: • To diagnose a hereditary PGL or PCC syndrome in patients with PGLs and/or PCCs.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81404 SDHD (succinate dehydrogenase complex, subunit D, integral membrane protein) (e.g., hereditary paraganglioma), full gene sequence

GENE:	**SERPINA1**	
Effective Date:	May 27, 2014	
Coverage Guidelines:	SERPINA1 gene testing is covered for the following indication: • For guidance in diagnosis of inconclusive cases of Alpha-1 Antitrypsin Deficiency (AATD) in individuals with Chronic Obstructive Pulmonary Disease (COPD), unexplained liver disease, family history of AATD, or environmental exposures leading to airflow obstruction after serum Alpha-1 Antitrypsin (AAT) protein levels and protein phenotyping has been completed.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81332 SERPINA1 gene

GENE:	**SMAD4**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	SMAD4 gene testing is covered for the following indications: • To clarify the diagnosis of individuals with JPS. • If a known SMAD4 mutation is in the family, genetic testing should be performed in the first six months of life due to hereditary hemorrhagic telangiectasia risk.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81405 SMAD4 (SMAD family member 4) (e.g., hemorrhagic telangiectasia syndrome, juvenile polyposis), duplication/ deletion analysis 81406 SMAD4 (SMAD family member 4) (e.g., hemorrhagic telangiectasia syndrome, juvenile polyposis), full gene sequence

GENE:	**SMN1/SMN2**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	SMN1/SMN2 gene testing is covered for the following indication: • Diagnosis of patients with hypotonia and muscle weakness who are suspected of having Spinal Muscular Atrophy (SMA).	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81400 SMN1 (survival of motor neuron 1, telomeric) (e.g., spinal muscular atrophy), exon 7 deletion 81401 SMN1/SMN2 (survival of motor neuron 1, telomeric/survival of motor neuron 2, centromeric) (e.g., spinal muscular atrophy), dosage analysis (e.g. carrier testing) 81403 SMN1 (survival of motor neuron 1, telomeric) (e.g., spinal muscular atrophy), known familial sequence variant(s) 81405 SMN1 (survival of motor neuron 1, telomeric) (e.g., spinal muscular atrophy), full gene sequence

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**SNRPN/UBE3A**		
Effective Date:	January 1, 2013		

Coverage Guidelines:	SNRPN/UBE3A gene testing is covered for the following indications:
	• When a clinical diagnosis of Prader-Willi Syndrome (PWS) is suspected, the following findings justify genetic testing:
	  • From birth to age two: Hypotonia with poor suck (neonatal period).
	  • From age two to age six: Hypotonia with history of poor suck, global developmental delay.
	  • From age six to age 12: Hypotonia with history of poor suck, global developmental delay, excessive eating with central obesity if uncontrolled.
	  • From age 13 years to adulthood: Cognitive impairment, usually mild intellectual disability; excessive eating with central obesity if uncontrolled, hypothalamic hypogonadism and/or typical behavior problems.
	• When a clinical diagnosis of Angelman Syndrome is suspected, the following findings justify genetic testing:
	  • As part of the evaluation of patients with developmental delay, regardless of age.
	  • As part of the evaluation of patients with a balance or movement disorder such as ataxia of gait. May not appear as frank ataxia but can be forward lurching, unsteadiness, clumsiness, or quick, jerky motions.
	  • As part of the evaluation of patients with uniqueness of behavior: any combination of frequent laughter/smiling; apparent happy demeanor; easily excitable personality, often with uplifted hand-flapping or waving movements; hypermotoric behavior.
	  • Speech impairment, none or minimal use of words; receptive and non-verbal communication skills higher than verbal ones.		

CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81331	SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (e.g., Prader-Willi syndrome and/or Angelman syndrome), methylation analysis

GENE:	**STK11**		
Effective Date:	January 1, 2013		
Coverage Guidelines:	STK11 gene testing is covered for the following indication: • To confirm a diagnosis of Peutz-Jeghers Syndrome (PJS) in proband patients with a presumptive or probable diagnosis of PJS.		
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81404	STK11 (serine/threonine kinase 11) (e.g., Peutz-Jeghers syndrome), duplication/deletion analysis
		81405	STK11 (serine/threonine kinase 11) (e.g., Peutz-Jeghers syndrome), full gene sequence

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**TBP**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	TBP gene testing is covered for the following indications: • Diagnosis of Spinocerebellar Ataxia Type 17 (SCA17) in ataxia patients exhibiting variable combinations of cognitive decline, psychiatric disturbance, and movement disorders. • Diagnosis of SCA17 in symptomatic family members of known SCA17 patients. • Diagnosis of SCA17 in patients suspected of having Huntington Disease (HD) who have tested negative for a pathogenic variant in the HD gene.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81401 TBP (TATA box binding protein) (e.g., spinocerebellar ataxia), evaluation to detect abnormal (e.g., expanded) alleles

GENE:	**TP53**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	TP53 gene testing is covered for the following indication: • Diagnosis of patients satisfying the criteria for classic Li-Fraumeni Syndrome (LFS) or Li-Fraumeni-Like Syndrome (LFLS), or the Chompret criteria for TP53 gene testing.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81404 TP53 (tumor protein 53) (e.g., tumor samples), targeted sequence analysis of 2-5 exons 81405 TP53 (tumor protein 53) (e.g., Li-Fraumeni syndrome, tumor samples), full gene sequence or targeted sequence analysis of >5 exons

GENE:	**TRG**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	TRG gene testing is covered for the following indication: • Diagnosis and treatment of T-cell neoplasms.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81342 TRG@ (T cell antigen receptor, gamma) (e.g., leukemia and lymphoma), gene rearrangement analysis, evaluation to detect abnormal clonal populations

GENE:	**UPD**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	UPD gene testing is covered for the following indication: • For neonates, infants, children or adults symptomatic for Beckwith-Wiedermann Syndrome (BWS) to diagnose Uniparental Disomy (UPD) for chromosome 11.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81402 Uniparental disomy (UPD) (e.g., Russell-Silver syndrome, Prader-Willi/Angelman syndrome), short tandem repeat (STR) analysis

FIGURE 18.3-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED (CONTINUED)

GENE:	**UGT1A1**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	UGT1A1 gene testing is covered for the following indications: • Prior to irinotecan administration in patients with CRC to lower the starting dose of irinotecan in patients with the UGT1A1*28/UGT1A1*28 genotype. • Prior to irinotecan administration in patients with CRC to increase the starting dose of irinotecan in patients with the UGT1A1*1/UGT1A1*1 or UGT1A1*1/UGT1A1*28 genotypes.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81350 UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (e.g., irinotecan metabolism), gene analysis, common variants (e.g., *28, *36, *37)

GENE:	**VHL**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	VHL gene testing is covered for the following indications: • Diagnosis of Von Hippel-Lindau (VHL) syndrome in patients presenting with pheochromocytoma, paraganglioma, or central nervous system hemangioblastoma. • Confirmation of diagnosis in individuals with symptoms consistent with VHL syndrome.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81403 VHL (von Hippel-Lindau tumor suppression) (e.g., von Hippel-Lindau familial cancer syndrome), deletion/duplication analysis 81404 VHL (Von Hippel-Lindau tumor suppression) (e.g., von Hippel-Lindau familial cancer syndrome), full gene sequence

GENE:	**VKORC1**	
Effective Date:	January 1, 2013	
Coverage Guidelines:	VKORC1 gene testing is covered for the following indication: • For the initiation and management of warfarin treatment.	
CPT Coding When Clinically Indicated By Coverage Guidelines:	CPT Code	81355 VKORC1 gene

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