TRICARE Operations Manual 6010.62-M, April 2021
Demonstrations, Pilot Projects, and Value-Based Initiatives

Chapter 18

Section 2

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

Revision: C-11, July 24, 2024

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 US 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 (MM) 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 had a 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 demonstration evaluates 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 demonstration project also extends 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. DHA will conduct an annual evaluation 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, DHA will decide whether or not 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 allows 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, will 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 are identified by the test's name or by the specific gene they test for as detailed in Figure 18.2-1.

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 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 This 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 MM of a rare disease, and otherwise meet TRICARE criteria for coverage and approve those that do for cost-sharing under this demonstration. The demonstration evaluates 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 this demonstration.

3.2 DHA will prioritize and review non-FDA approved LDTs for analytical validity, clinical validity, and clinical utility. DHA will base LDT reviews 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. 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, DHA will only consider those reports and articles containing scientifically valid data and published in the refereed medical and scientific literature 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 DHA may also review non-FDA approved LDTs under the new demonstration project for use in the diagnosis or MM 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 US. 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), DHA and/or the contractor reviews benefits for rare diseases on a case-by-case basis. In reviewing proposed benefits for rare diseases under the demonstration, consistent with TRICARE's rare disease policy, any or all of the following sources are 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 CF Carrier Screening

3.5.1 This demonstration project extends 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 cordocentesis, 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 is 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 contractor shall ensure the test is provided in accordance with the most current ACOG guidelines. For example, if a patient has been screened previously, the contractor shall ensure CF screening results are documented and not repeat the test.

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 18.2-1, will become available for cost-sharing for qualified TRICARE beneficiaries during the demonstration period when performed by CLIA certified labs. However, the contractor shall cost-share non-FDA approved LDTs covered under the LDT demonstration for qualified TRICARE Overseas Program (TOP) beneficiaries when performed by either CLIA certified laboratories or laboratories that are assessed by the TOP contractor to be in accordance with the host nation's credentialing/accreditation standards when those standards for credentialing/accreditation are comparable to CLIA standards

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 DHA will notify the contractor regarding publication of non-FDA approved LDT eligibility for cost-sharing. See Figure 18.2-1. The codes listed in Figure 18.2-1 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 18.2-1 may be covered only as part of the demonstration project as denoted with the Special Processing Code (SPC) **L2**.

3.9 The contractor 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 Director, DHA (or designee) approved the specific non-FDA approved LDT 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 18.2-1; 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 18.2-1; and

3.9.4 The contractor has, as noted in TRICARE Policy Manual (TPM), Chapter 1, Section 6.1, for dual eligible beneficiaries, applied all requirements when TRICARE is primary payer. As secondary payer under the TRICARE Dual Eligible Fiscal Intermediary Contract (TDEFIC), the contractor shall 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 The contractor shall ensure genetic counseling is provided by TRICARE-authorized providers ~~and precede the actual LDT,~~ in accordance with the TPM, Chapter 6, Section 3.1. The contractor shall not use the

LDT SPC for genetic counseling claims.

3.11 BRCA1 or BRCA2 Genetic Counseling and Testing

3.11.1 The contractor shall not charge a copayment or cost-share for genetic counseling rendered by a TRICARE-authorized provider that precedes BRCA1 or BRCA2 gene testing performed as a preventive service for women who are identified as high risk for breast cancer by their primary care clinician.

3.11.2 The contractor shall not charge a copayment or cost-share for BRCA1 or BRCA2 gene testing performed as a preventive service for women who meet the coverage guidelines outlined in Figure 18.2-1.

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

3.12 The demonstration expires on July 18, 2028. Requirements of this Chapter as related to this demonstration cease at midnight on July 18, 2028. Only TRICARE beneficiaries with current eligibility, as defined in paragraph 7.0, may participate in this demonstration project. The contractor shall not pay claims for individuals who are not eligible for TRICARE benefits. The contractor shall ensure all medical care, treatments, or testing, with the exception of the LDT which has approval during the demonstration period only, are 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 contractor shall meet the records management (RM) requirements described in Chapter 9.

4.0 APPLICABILITY

4.1 This demonstration applies to all TRICARE-eligible beneficiaries. Additionally, for purposes of Chapter 17, Section 3, LDTs are covered for Service members as specified in the demonstration and the contractor shall not require a Supplemental Health Care Program (SHCP) waiver.

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

4.3 The contractor shall not 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 shall 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 according to all indications detailed in Figure 18.2-1. The contractor shall document these facts according to and consistent with Chapter 1, Section 4. Following the contractor's identification of an appropriate request for an approved LDT, as identified within the terms of the demonstration, the contractor shall notify the TRICARE authorized provider requesting/ordering the LDT that they are authorized to use 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, the contractor shall perform a retrospective authorization review and approval prior to payment (e.g., promyelocytic leukemia (PML)/Retinoic acid Receptor alpha (RaRalpha) testing performed in an emergency room or inpatient hospital setting for acute PML patients where results are urgently needed and will immediately impact MM/treatment decisions).

6.0 DHA RESPONSIBILITIES

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

6.2 DHA will perform periodic reviews and evaluations of the demonstration claims adjudication process.

7.0 ADDITIONAL CONTRACTOR RESPONSIBILITIES

The contractor shall:

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- Verify the beneficiary's eligibility on the Defense Enrollment Eligibility Reporting System (DEERS).
- Correctly voucher the TRICARE Encounter Data (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 18.2-1. The contractor shall consider only the indications listed in the Coverage Guidelines 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 The contractor shall reimburse both laboratory and professional charges 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 ensure laboratories submit all charges on the basis of fully itemized bills. The contractor shall ensure the laboratories individually identify and submit each service and supply item on the appropriate claim form. If a claim associated with the demonstration has missing information, the contractor shall follow Chapter 8, Section 6 guidelines to either return or develop the claim.

8.3 The contractor shall ensure all claims for the demonstration approved LDT meet the requirements outlined in Figure 18.2-1. The contractor shall ensure all other covered care associated with treatment is provided in accordance with the respective provisions of the TPM or TRM. The contractor shall ensure care associated with the LDT is medically necessary and appropriate medical care and not otherwise excluded as a TRICARE benefit.

8.4 The contractor shall apply cost-shares and deductibles applicable to TRICARE under the demonstration.

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

8.6 The contractor shall pay claims for this demonstration from the applicable non-underwritten bank account (see Chapter 3), and submit claims 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 The contractor shall use SPC **L2** 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. The contractor shall process medical care, treatments, and associated testing based on medical necessity as a consequence of the demonstration approved LDT's results under the TRICARE Basic Program benefit.

8.8 The contractor shall submit claims for this demonstration 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 is 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 18.2-1.

9.2 Effective January 1, 2017, the contractor shall not apply a cost-share or copayment 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, the contractor shall not apply a cost-share or copayment for BRCA1 or BRCA2 gene testing for women who meet the coverage guidelines outlined in Figure 18.2-1.

9.4 Effective July 19, 2020, the TOP contractor shall cover non-FDA approved LDTs, for qualified TOP beneficiaries, from either CLIA certified laboratories or laboratories that are assessed by the TOP contractor to be in accordance with the host nation's credentialing/accreditation standards when those standards for credentialing/accreditation are comparable to CLIA standards.

FIGURE 18.2-1 APPROVED LABORATORY DEVELOPED TESTS (LDTs) BY TEST NAME OR BY GENE(S) TESTED

TEST NAME:	**Afirma Thyroid Fine-Needle Aspiration (FNA) Analysis**
Effective Date:	October 19, 2017
Coverage Guidelines:	The Afirma Thyroid FNA Analysis is covered for the following indication: • To aid in thyroid nodule diagnosis by reducing unnecessary surgeries in patients with indeterminate thyroid nodules.

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.

GENE:	**Adenomatous Polyposis Coli (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.

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.

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.

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.

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.

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.

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 Reverse Transcriptase-Polymerase Chain Reaction (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.

TEST NAME:	**Biotheranostics Breast Cancer Index**
Effective Date:	January 1, 2023
Coverage Guidelines:	The Biotheranostics Breast Cancer Index is covered for the following indications: • Women with diagnosed early-stage hormone-receptor positive (HR+), lymph node-negative (LN-) breast cancer being treated with adjuvant endocrine therapy. • Women with diagnosed early-stage hormone-receptor positive (HR+), lymph node positive (LN+) (1-3 nodes) breast cancer being treated with adjuvant endocrine therapy.

GENE:	**Bone Morphogenetic Protein Receptor Type 1A (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.

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.

GENE:	**BReast CAncer Gene 1 (BRCA1)/BReast CAncer Gene 2 (BRCA2)**
Effective Date:	January 1, 2013
Coverage Guidelines:	BRCA1/BRCA2 gene testing is covered in accordance with the most current National Comprehensive Care Network (NCCN) Guidelines for Breast Cancer.

GENE:	**Calcium Voltage-Gated Channel Subunit Alpha1 A (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.

GENE:	**CALM1, CASQ2, RYR2, and/or TRDN**

Effective Date:	January 1, 2013
Coverage Guidelines:	CALM1, CASQ2, RYR2, and/or 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.

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).

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).

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 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.

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.

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.

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.

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.

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.

GENE:	**CYP2C19**
Effective Date:	January 1, 2013
Coverage Guidelines:	CYP2C19 gene testing is covered for the following indication: • To manage dosing of clopidogrel.

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.

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.

TEST NAME:	**DermTech Pigmented Lesion Assay (PLSA)**
Effective Date:	January 1, 2023
Coverage Guidelines:	The DermTech Pigmented Lesion Assay is covered for the following indication: • Neoplasms of uncertain behavior of skin.

GENE:	**Duchenne Muscular Dystrophy (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 DMD or Becker Muscular Dystrophy

	(BMD).

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.

GENE:	**DSC2, DSG2, DSP, JUP, PKP2, RYR2, TGFB3, and/or TMEM43**
Effective Date:	January 1, 2013
Coverage Guidelines:	DSC2, DSG2, DSP, JUP, PKP2, RYR2, TGFB3, and/or 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.

GENE:	**DYT1/TOR1A**
Effective Date:	January 1, 2013
Coverage Guidelines:	DYT1/TOR1A gene testing is covered for the following indications: • For genetic testing for sequence variants of DYT1 for patients with primary dystonia with onset < 30 years of age. • For genetic testing for sequence variants of DYT1 for patients with primary dystonia with onset ≥ 30 years of age who have a relative who developed dystonia aged < 30 years.

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.

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.

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.

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.

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.

GENE:	**FLT3**
Effective Date:	October 7, 2013
Coverage Guidelines:	FLT3 gene testing is covered for the following indication: • For diagnosis and prognosis in AML.

GENE:	**FMR1**
Effective Date:	January 1, 2013
Coverage Guidelines:	FMR1 gene testing is covered for the following indication:

	• 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).

TEST NAME:	**FoundationOne® Heme**
Effective Date:	January 1, 2023
Coverage Guidelines:	The FoundationOne® Heme assay is covered for the following indications: • Assessment of gene alterations in hematologic malignancies. • Assessment of gene alterations in sarcomas.

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.

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.

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.

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.

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.

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.

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.

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.

GENE:	**HNF1B**
Effective Date:	May 1, 2016
Coverage Guidelines:	HNF1B gene testing is covered for the following indication: • Diagnosis of Maturity-Onset Diabetes of the Young Type 5 (MODY5) in patients with hyperglycemia or non-insulin-dependent diabetes who have a family history of abnormal glucose metabolism in at least two consecutive generations, with the patient or ≥ 1 family member(s) diagnosed before age 25, and who have structural or functional abnormalities of the kidneys.

GENE:	**HNF4A**

Effective Date:	May 1, 2016
Coverage Guidelines:	HNF4A gene testing is covered for the following indication: • Diagnosis of Maturity-Onset Diabetes of the Young Type 1 (MODY1) in patients with hyperglycemia or non-insulin-dependent diabetes who have a family history of abnormal glucose metabolism in at least two consecutive generations, with the patient or ≥ 1 family member(s) diagnosed before age 25.

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.

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.

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.

GENE:	**IL28B**
Effective Date:	February 28, 2013
Coverage Guidelines:	IL28B gene testing is covered for the following indication: • For IL28B single nucleotide polymorphism (SNP) testing in patients with chronic Hepatitis C Virus (HCV) genotype 1 being considered for treatment with PegIFN/RBV dual therapy.

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.

GENE:	**KCNQ1, KCNH2, SCN5A, KCNE1, and/or KCNE2**
Effective Date:	January 1, 2013
Coverage Guidelines:	KCNQ1, KCNH2, SCN5A, KCNE1, and/or KCNE2 gene testing is covered for the following indication: • For patients with suspected familial Long QT Syndrome for confirmation of diagnosis and treatment.

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.

GENE:	**KMT2D and/or KDM6A**
Effective Date:	January 1, 2013
Coverage Guidelines:	KMT2D and/or KDM6A gene testing is covered for the following indication: • To confirm a diagnosis of Kabuki Syndrome (KS) in patients with symptoms compatible with KS.

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.

TEST NAME:	**MDxHealth Confirm MDx**
Effective Date:	January 1, 2023
Coverage Guidelines:	The MDxHealth Confirm MDx is covered for the following indications: • Men with a previous diagnosis of prostate cancer that have undergone a previous prostate biopsy (within prior 24 months) and are being considered for a repeat prostate biopsy due to persistent cancer-risk factors. • Men with a previous diagnosis of prostate cancer that have undergone a previous prostate biopsy (within prior 24 months) and are being considered for a repeat prostate biopsy due to elevated cancer-risk factors.

TEST NAME:	**MDxHealth Select MDx**
Effective Date:	January 1, 2023
Coverage Guidelines:	The MDxHealth Select MDx is covered for the following indications: • Men with previous diagnosis of prostate cancer that are suspected of harboring prostate cancer.

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.

GENE:	**MEFV**
Effective Date:	June 16, 2014
Coverage Guidelines:	MEFV gene testing is covered for the following indications: • In patients exhibiting symptoms of Familial Mediterranean Fever (FMF), including periodic episodes of fever in combination with peritonitis, pleuritic, arthritis, and erysipelas-like erythema. • In patients from ethnic groups considered at high risk for FMF who present with nephrotic syndrome or amyloidosis, but do not meet the diagnostic criteria for FMF.

GENE:	**MLH1, MSH2, MSH6, MSI, PMS2, and/or EPCAM**
Effective Date:	January 1, 2013
Coverage Guidelines:	Genetic testing for Lynch Syndrome (LS) is covered in accordance with the most current NCCN Guidelines for Colon Cancer.

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.

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.

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.

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.

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.

TEST NAME:	**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.

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.

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.

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.

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.

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.

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.

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).

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.

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.

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.

GENE:	**SDHA, SDHB, SDHC, SDHD, SDHAF2, MAX, and/or TMEM127**
Effective Date:	June 16, 2014
Coverage Guidelines:	SDHA, SDHB, SDHC, SDHD, SDHAF2, MAX, and/or TMEM127 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.

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.

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.

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).

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.

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.

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.

GENE:	**TGFBR2**
Effective Date:	January 1, 2013
Coverage Guidelines:	TGFBR2 gene testing is covered for the following indication: • To facilitate the diagnosis of Marfan syndrome in patients testing negative for FBN1 gene variants.

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.

GENE:	**TPMT**
Effective Date:	January 1, 2013
Coverage Guidelines:	TPMT gene testing is covered for the following indication: • TPMT genotyping or phenotyping in patients with Inflammatory Bowel Disease (IBD) prior to administration of thiopurines (azathioprine, 6-MP, and 6-TG).

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.

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.

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.

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.

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.

TEST NAME:	**Y Chromosome Microdeletion Analysis**
Effective Date:	January 1, 2013
Coverage Guidelines:	Y Chromosome Microdeletion Analysis is covered for the following indication:

	• For detecting submicroscopic deletions involving the Y chromosome in men with azoospermia, oligozoospermia, or teratozoospermia.

- END -